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Case reports in coronary artery disease 2024

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Case reports in coronary artery disease: 2024

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Successful percutaneous coronary intervention of left main coronary artery dissection following mechanical aortic valve replacement surgery: a case report and literature review

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Background: Iatrogenic left main coronary artery (LMCA) dissection resulting from cardiac surgery is a rare complication. Its early detection is challenging and often poses a significant threat to the patient's life. However, evidence regarding the most effective management strategy for this condition remains limited at present.

Case presentation: We present a case of 65-year-old female patient who developed cardiogenic shock after mechanical aortic valve replacement surgery associated acute myocardial infraction. Despite concurrent coronary artery bypass graft (CABG) surgery, the patient's condition remained unimproved. Subsequent coronary angiography revealed extensive LMCA dissection involving the left circumflex (LCx) artery. Percutaneous coronary intervention (PCI) guided by intravascular ultrasound (IVUS) led to an immediate improvement in hemodynamic status. The patient was successfully discharged after 22 days of treatment.

Conclusions: Iatrogenic LMCA dissection is an uncommon complication following cardiac surgery. It can manifest in a variety of ways, including as incidental findings, cardiogenic shock or sudden cardiac arrest. The precise prevalence rates of causes linked to cardiac surgery remain largely unknown due to the scarcity of reported cases and the absence of research on this issue. Currently, a definitive management strategy for this condition has not been established. However, previous reported clinical cases provide insight that CABG could be considered if coronary artery dissection is detected during cardiac surgery. Upon postoperative identification, diagnostic coronary angiography and PCI may be feasible alternatives.

KEYWORDS

iatrogenic left main coronary artery dissection, mechanical aortic valve replacement surgery, coronary artery bypass surgery, percutaneous coronary intervention, intravascular ultrasound

Introduction

Iatrogenic LMCA dissection is a rare occurrence that arises from the manipulation of a guidewire or catheter during coronary angiography or interventional procedures. The incidence rate of this event is less than 0.1% (1). LMCA dissection resulting from cardiac surgery is extremely uncommon, with diverse clinical presentations ranging from incidental detection to life-threatening arrhythmias, hemodynamic instability, or progression to cardiogenic shock.

In the present case, a 65-year-old female underwent redo aortic valve surgery and subsequently developed cardiogenic shock secondary to acute myocardial infarction. Despite undergoing concurrent CABG surgery, the patient still experienced severe metabolic acidosis and life-threatening ventricular arrythmias. Subsequent coronary angiography revealed extensive LMCA dissection. A PCI was appropriately performed with the assistance of IVUS, leading to an improvement in the patient's hemodynamic condition. Additionally, a literature review was conducted on this condition. A search on PubMed using the keywords "dissection", "left main coronary artery", and "aortic valve replacement surgery" yielded 37 results, from which 5 case reports were included in the final review. Exclusion criteria included duplication, absence of specific dissection reports, and unavailability of full texts.

Case presentation

A 65-year-old female patient presented to the hospital with a one-month history of exertional dyspnea. Her medical history included permanent atrial fibrillation and mechanical mitral and aortic valve replacement, along with the placement of a bioprosthetic tricuspid valve ring 20 years prior, due to rheumatic heart disease. The patient has no prior history of genetic disorders or neuropsychiatric conditions. Furthermore, there is no documented family history of genetic disorders. She was on daily medication consisting of acenocoumarol 1 mg once daily and bisoprolol 2.5 mg once daily. Upon admission, physical examination revealed stable vital signs, with a grade 4/6 systolic murmur audible along the left sternal border. Laboratory tests indicated normal renal function, with a creatinine level of 0.55 mg/dl (normal range: 0.66–1.09 mg/dl), and a slightly elevated NT-proBNP concentration of 322 ng/L (normal range: <125 ng/L). (Figure 1) illustrates the patient's electrocardiogram (ECG) findings at the time of admission.

Echocardiography findings indicated normal left and right ventricular function as well as proper positioning and function of the bioprosthetic tricuspid and mechanical mitral valve. However, the mechanical aortic valve was severely stenosed, with a mean pressure gradient of 52 mmHg and a maximal velocity of 4.88 m/s across the valve. Additionally, a chest computed tomography (CT) scan revealed restricted aortic valve opening motion in the absence of a substantial thrombus. The assessment of the coronary artery system also revealed no significant stenosis.

The patient was diagnosed with symptomatic severe restenosis of mechanical aortic valve and underwent valve replacement surgery. The duration of the operation was ten hours and thirty minutes. Initially, extracorporeal circulation (with cardiopulmonary bypass) was established, and cardioplegia infusion was administered. The restricted movement of the leaflets of the mechanical aortic valve, when the ascending aorta was opened, was attributed to panus. The mechanical aortic valve was subsequently substituted with a size 21 On-X valve. Ventricular fibrillation occurred after the left ventricle was de-aired and the aortic clamp was released; therefore, initial biphasic defibrillation with 20J twice and 30J once was performed. Subsequent monitoring revealed atrial fibrillation with rapid ventricular response. Transesophageal echocardiography confirmed adequate left ventricular contractility, proper function of the mechanical aortic valve, and intact blood flow into the left anterior descending artery (LAD), LCx, LMCA while the patient was gradually weaned off bypass.

Nevertheless, recurrent ventricular fibrillation was observed during suturing, which persisted despite two ventricular defibrillation attempts. After re-establishing extracorporeal circulation and exposing the ascending aorta, it was observed that the RCA was patent, while the left coronary arteries was partially occluded by the mechanical aortic valve. As a result, a CABG was performed, utilizing a right great saphenous vein to provide two bypasses from the aorta to the LAD and RCA. Despite being administered four different vasopressors and inotropes (milrinone, dobutamine, adrenaline, and noradrenaline), the patient's mean arterial blood pressure remained inadequate, fluctuating between 55 and 60 mmHg. Afterwards, hemodynamic support with a counterpulsation balloon in the descending aorta was initiated.

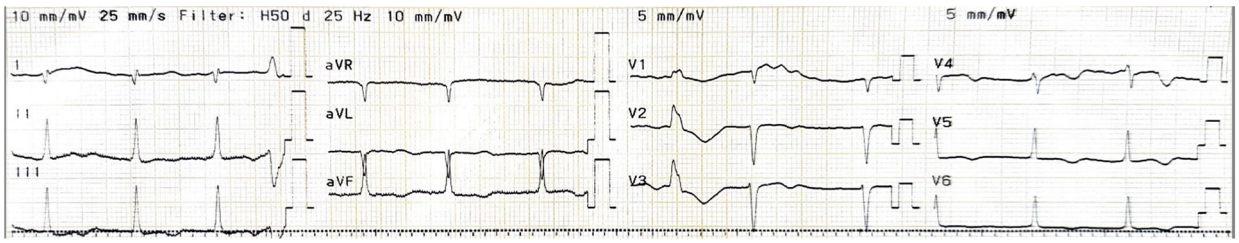

FIGURE 1
Pre-operative electrocardiogram. Atrial fibrillation with moderate ventricular response accompanied by T wave inversion in V2-6, poor R wave progression and premature ventricular complex.

The patient's hemodynamic status gradually deleriorated on the initial postoperative day despite the escalation in dosages of vasopressors and inotropes. Ventricular tachycardia was consistently observed on the monitor. Laboratory tests revealed profound metabolic acidosis with increasing blood lactate levels and a surge in troponin T levels from 4,168 to 5,803 ng/L, eventually exceeding 10,000 ng/L. Bedside echocardiography indicated a decrease in left ventricle ejection fraction (LVEF) from 53.8% to 36% and a reduction in mean aortic valve pressure gradient from 52 to 21 mmHg. NT-proBNP levels rose from 322 to 5,461 pg/ml. Additionally, there was modest renal impairment, evidenced by an increase in serum creatinine from 0.55 to 1.27 mg/dl, while hemoglobin levels remained relatively stable (130–133 g/L). The established diagnosis at this point was cardiogenic shock secondary to a very high-risk non-ST elevation myocardial infarction, following postoperative redo mechanical aortic valve and CABG.

Coronary angiography was subsequently performed on the patient via the femoral artery approach. The result demonstrated severe stenosis of the LMCA, with dissection extending into the ostium of the LCx. No significant stenosis was observed in the LAD, RCA, or bypass grafts. Using a sion wire, the lesion in the distal LCx was successfully crossed, after which a sion blue wire was advanced towards the distal LAD (Figure 2).

Afterwards, IVUS was used to assess the lesion. The findings indicated an absence of dissection in the LAD. However, examination of the LMCA to the LCx showed images suggesting complete separation of the intima-media from the adventitia, along with the presence of intramural hematoma. The initial dissection site extended approximately 16.8 mm from the ostium of the LMCA to the ostium of the LCx. The smallest true lumen area was measured at 5.84 mm^2, resulting in an 81% stenosis compared to the vessel lumen area of 30.45 mm^2. The dissection angle measured at this site was 230 degrees (Figure 3). The distal reference diameter of the landing zone was determined to be 4 mm (ranging from 3.85 to 4.14 mm), with a plaque burden of 22%.

A 4.0 × 24 mm drug-eluting stent (DES) was deployed in the LMCA-LCx, followed by post-dilation of the LMCA stent segment using a non-compliant (NC) balloon measuring at 5.0 × 15 mm. Subsequently, the sion blue wire was re-wired to the distal LAD, and the ostium of LAD was dilated with a 3.0 × 20 mm NC balloon. Following the initial post-dilation within the stent with a 4.0 × 20 mm NC balloon, second post-dilation was performed on the LMCA stent segment using a 5.0 × 15 mm NC balloon. Post-procedure coronary angiography confirmed TIMI 3 flow in the LMCA and LCx (Figure 4).

IVUS revealed no evidence of dissection at either the proximal or distal stent edges, as well as the absence of tissue prolapse following PCI. The minimal stent area (MSA) at the distal and proximal ends of the LMCA were measured at 16.16 mm^2 and 13.01 mm^2, respectively. Meanwhile, the MSA at the LCx ostium was 13.77 mm^2. The smallest MSA within the stent was 11.78 mm^2, accounting for 94% of the MSA at the distal reference, which was 12.59 mm^2. Additionally, IVUS verified

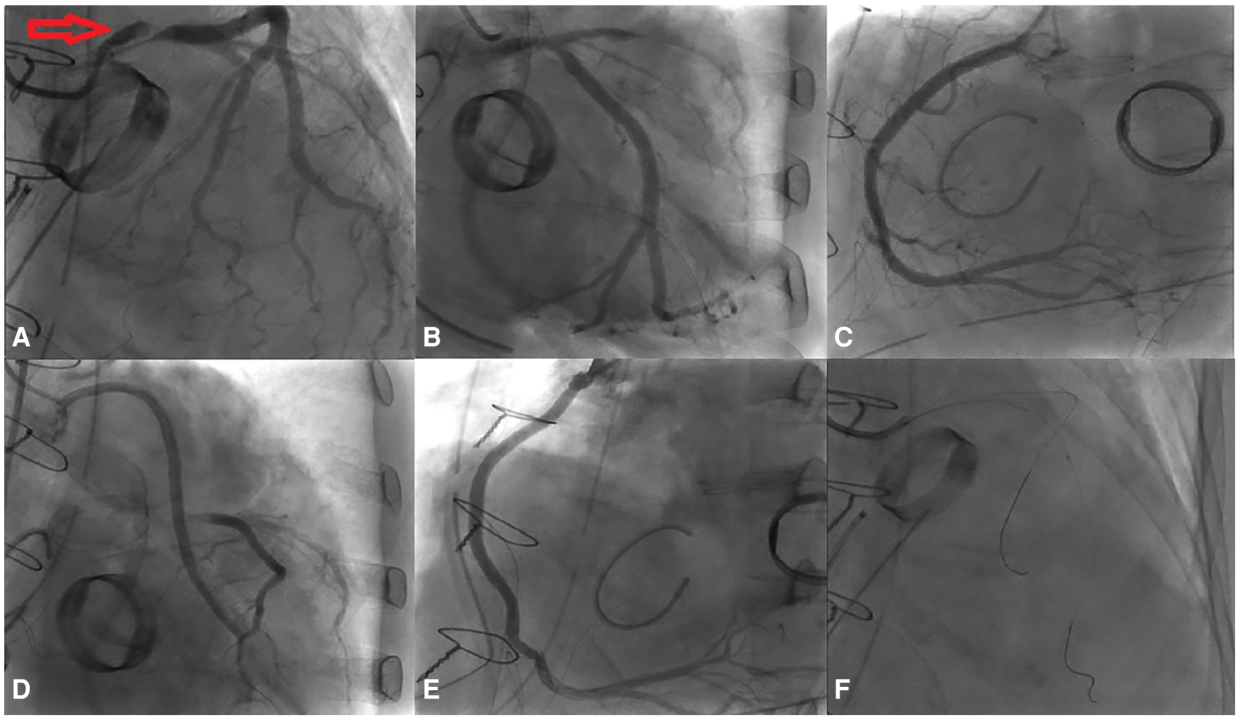

FIGURE 2
Results of the coronary angiography. **(A)** Dissection extending from the LM to the LCx (indicated by red arrow). **(B–E)** No significant stenosis observed in the LAD, RCA, Ao-vein-LAD, and Ao-vein-RCA. **(F)** Passage of the wire through both the LAD and the LCx, accompanied by an IVUS assessment.

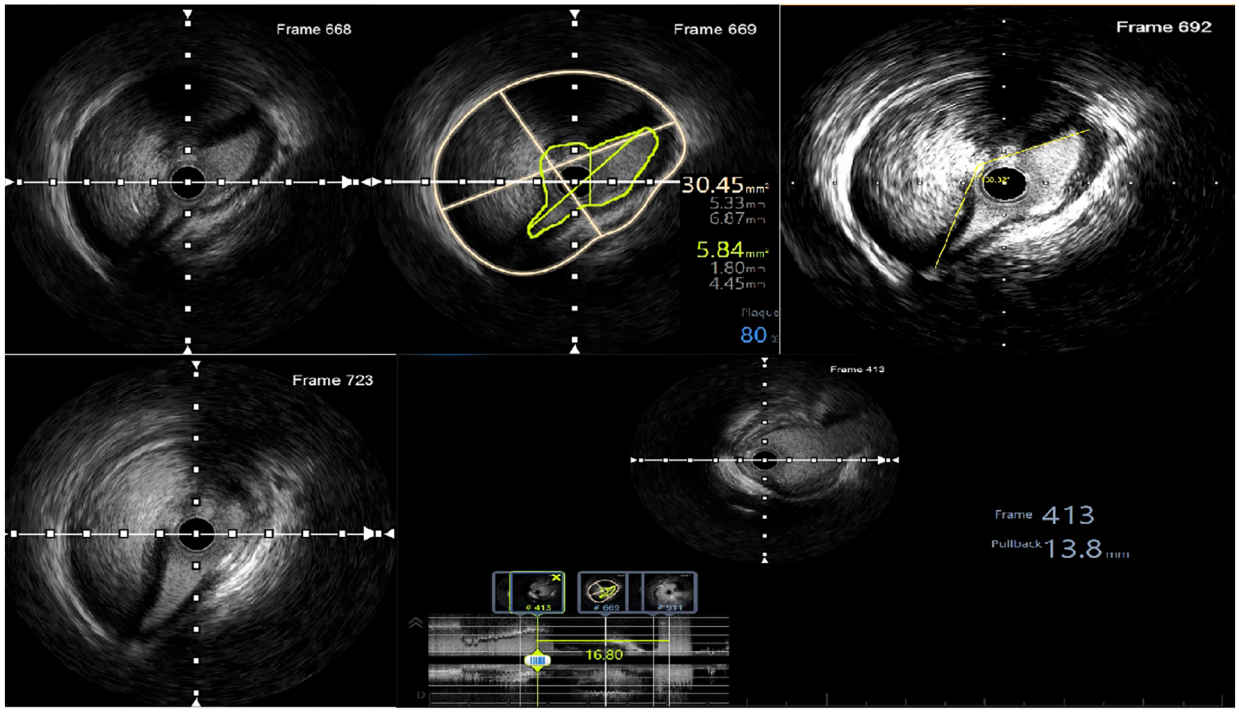

FIGURE 3
IVUS images of the LMCA dissection.

adequate stent apposition at both proximal and distal ends (Figure 5).

The patient's hemodynamics status and metabolic acidosis condition showed significant improvement post-procedure (Figure 6). Vasopressors and inotropes was gradually tapered and ceased entirely after 5 days following PCI. In addition, the patient was successfully weaned off mechanical ventilation and extubated. Laboratory tests revealed a decline in NT-proBNP levels, decreasing from 5,461 to 1,501 ng/L. A further echocardiography performed 14 days later revealed an enhancement in LVEF, rising from 36% to 51.7%. The patient was discharged after 22 days in a stable condition and was prescribed the following medications: warfarin, clopidogrel, spironolactone, dapagliflozin, atorvastatin, and valsartan/sacubitril. The patient continued to be monitored at the outpatient clinic and remained in a stable condition. An echocardiography performed two months after discharge indicated that the mechanical mitral and aortic valves were functioning well, with the mean pressure gradient across the aortic valve reduced from 52 mmHg to 8 mmHg and the maximum velocity decreased from 4.88 m/s to 2.61 m/s. However, the LVEF remained low at 38%. Laboratory tests revealed that the NT-proBNP level had decreased to 746 ng/L, and the INR fluctuated significantly between 1.7 and 2.75. Over the past four months, the patient attended four follow-up visits, with average heart rate and blood pressure readings of 80 beats per minute and 130/80 mmHg, respectively. The patient's treatment regimen remained relatively constant during these visits, including warfarin 3 mg, clopidogrel 75 mg, valsartan/sacubitril (total dose 100 mg), spironolactone 25 mg, furosemide 10 mg, and bisoprolol 1.25 mg.

Discussion

Iatrogenic coronary dissection following cardiac surgery has been occasionally reported. Although the incidence of this complication is not well-documented, early detection remains challenging and often results in extensive myocardial infarction. Management options include PCI, CABG or conservative therapy. However, there is limited evidence regarding the optimal approach for managing iatrogenic LMCA dissection complicating cardiac surgery (2).

Most complications arising from interventional procedures are typically identified promptly, either through ischemic symptoms or angiographic signs of dissection. However, in anesthetized patients undergoing cardiac surgery, symptoms and signs of ischemia may not be apparent if coronary flow remains unimpeded. Berroya et al. documented three cases of fatal LMCA dissection,in which all three patients unfortunately died and underwent postmortem evaluation (3). Conversely, Nakao et al. accidentally detected LMCA dissection using intraoperative transesophageal echocardiography, highlighting its potential diagnostic utility (4). Yukang et al. similarly reported a case

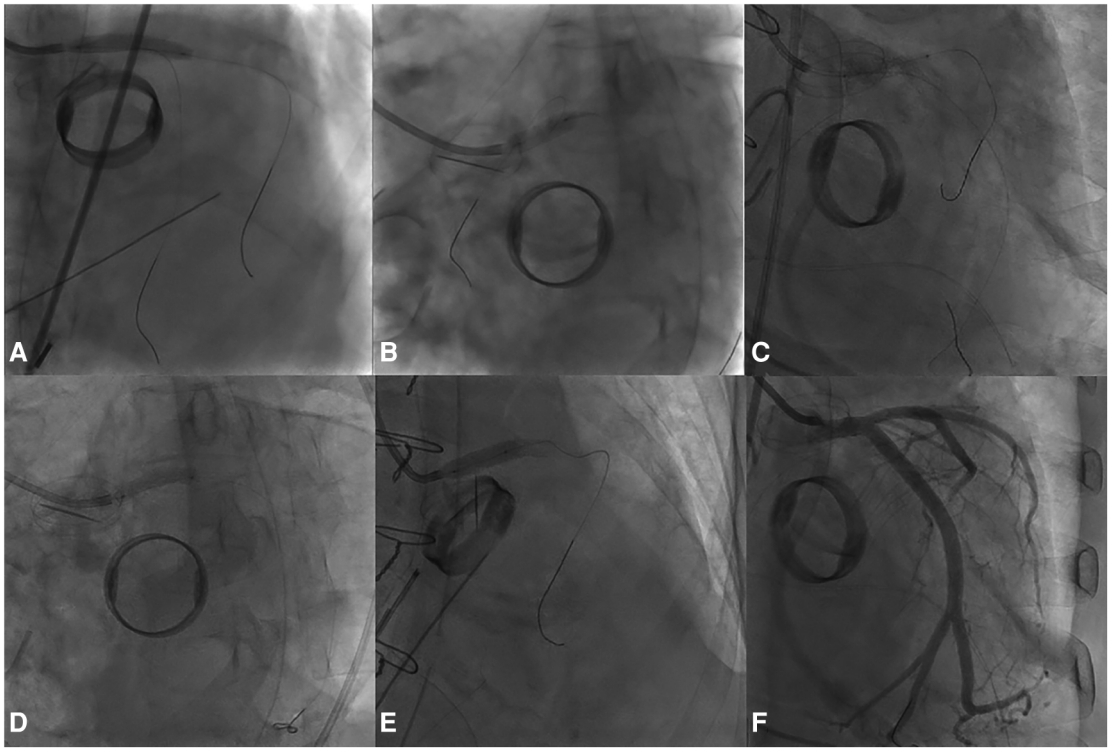

FIGURE 4
The PCI procedure for the LMCA and the LCx. **(A)** Deployment of a DES in the LMCA-LCx. **(B)** Initial Proximal Optimization Technique (POT) in the LM using a NC balloon. **(C)** Subsequent rewiring and dilation of the LAD ostium with a NC balloon. **(D)** In-stent post-dilation. **(E)** Second POT in the LMCA. **(F)** Final angiographic result.

with a clinical context resembling ours, where the complication was only recognized following myocardial infarction-induced hemodynamic instability. LMCA dissection exhibits diverse clinical manifestations, ranging from incidental detection to symptoms such as low cardiac output syndrome or cardiogenic shock, and even sudden death. Therefore, it is crucial to closely monitor vital signs, ECG, transthoracic echocardiography, and changes in cardiac injury markers postoperatively to facilitate early detection and develop appropriate treatment strategies. (Table 1) outlines the occurrences of coronary artery dissection subsequent to valve replacement surgery, as documented up to date.

The etiology of LMCA dissection following cardiac surgery involves several potential factors, such as the propagation of dissection from the aortic root, direct infusion of cardioplegia solution into the coronary artery, and intraoperative maneuvers, paticularly in cases with severe calcification of the aortic root. In the majority of documented clinical cases, the precise etiology remains uncertain (Table 1). In our case, the most plausible explanation is presumed mechanical injury to the left coronary ostium during the removal of mechanical aortic valve. This inference is supported by the challenges encountered during the extraction of the mechanical aortic valve and the subsequent development of hemodynamic instability coupled with ventricular arrhythmias immediately post-removal of the aortic clamp, indicative of exacerbation of pre-existing coronary artery dissection.

Current data do not offer a clear consensus or guideline for the treatment of LMCA dissections. In our case, the patient experienced hemodynamic instability and immediate onset of ventricular arrhythmias following aortic valve replacement surgery. While grafts were successfully established to revascularize the LAD and RCA, concerns regarding potential injury and heightened risk of myocardial rupture during the rotational manipulation required to establish a graft to the LCx in a patient with a pre-existing mechanical mitral valve led the surgical team to opt against further intervention. Following surgery, the patient continued to exhibit persistent indications of low cardiac output syndrome and ventricular arrhythmias, which remained unresponsive to treatment, prompting the consideration for coronary angiography.

In coronary artery interventions, particularly those involving LMCA, the utilization of intravascular imaging has garnered recommendations from various cardiology societies. The European Society of Cardiology advised considering the use of IVUS to optimize the outcomes of PCI for unprotected LMCA disease with class IIA level of evidence (7). Meanwhile, the role of IVUS in complex coronary interventions such as bifurcation lesions, calcified lesions, or bifurcation lesions in Asian countries is recommended with a higher level of evidence with class I (8).

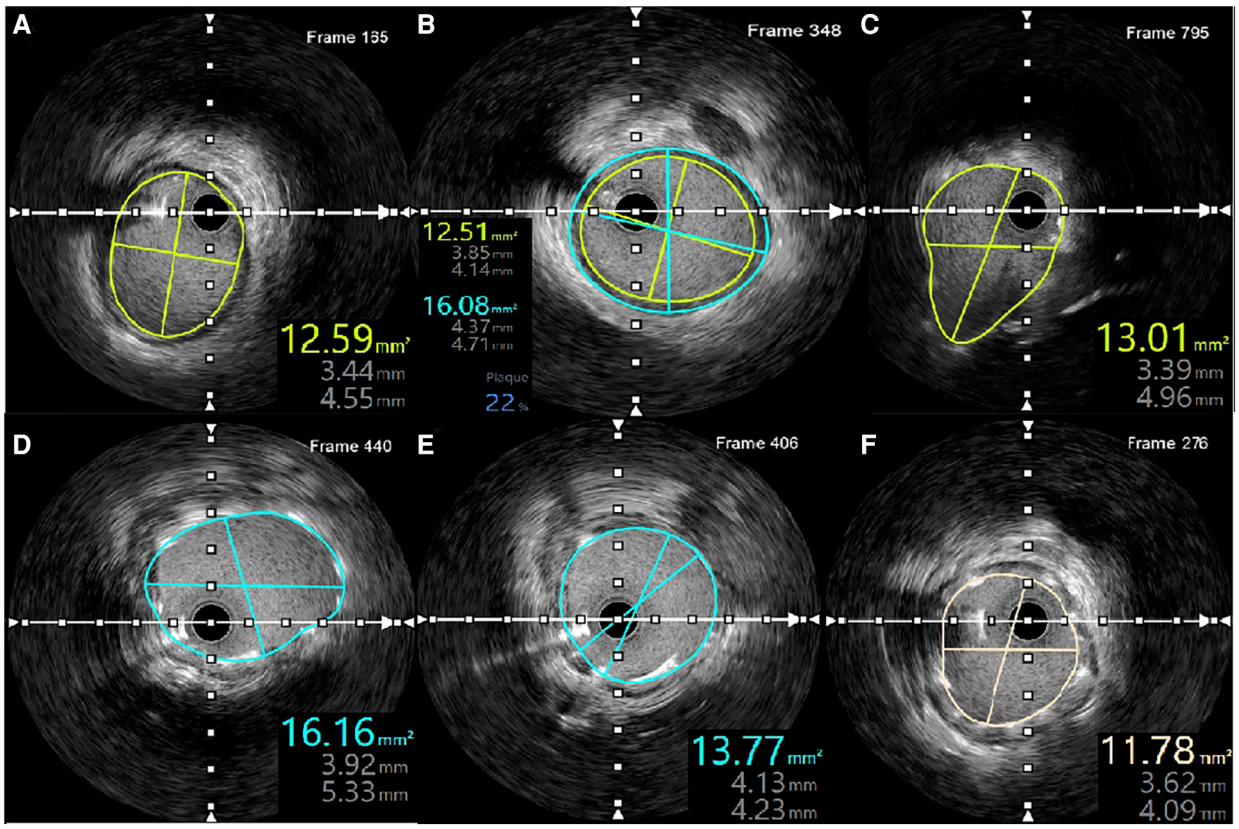

FIGURE 5
IVUS measurements following LMCA-LCx PCI. **(A)** MSA of the distal reference. **(B)** Plaque burden and distal reference diameter. **(C)** MSA at the proximal LMCA. **(D)** MSA at the distal LMCA. **(E)** MSA at the ostium of the LCx. **(F)** Smallest MSA within the stent.

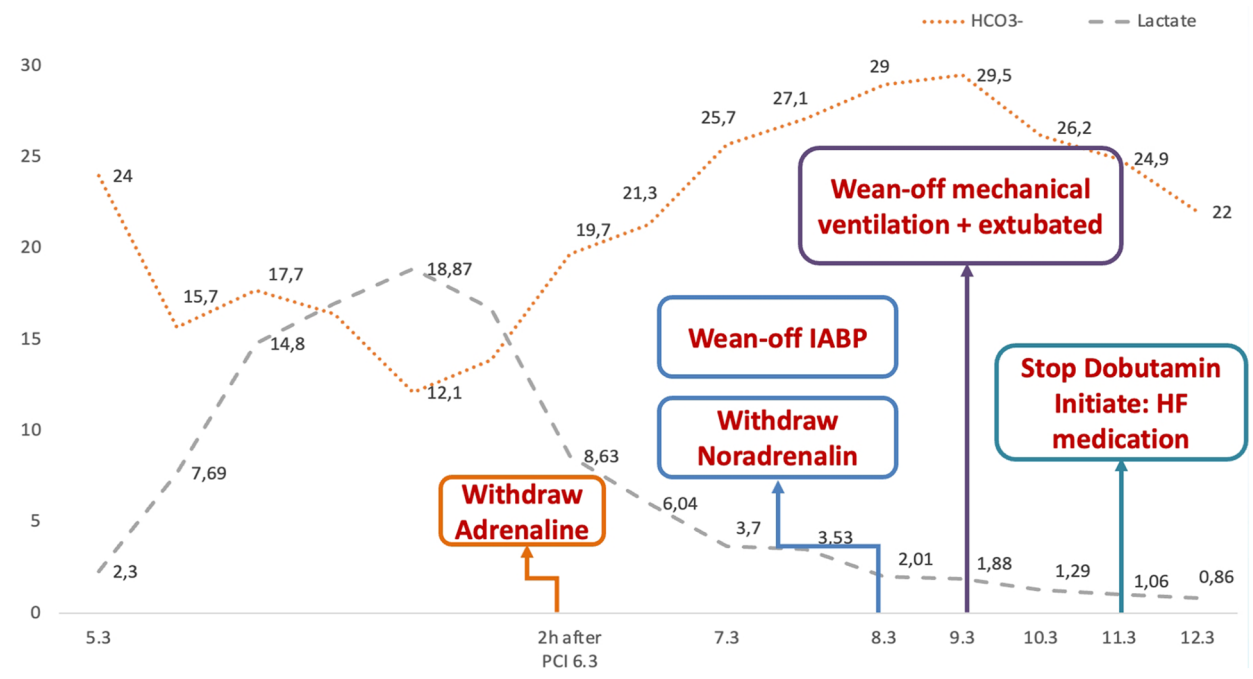

FIGURE 6
Dynamics of blood lactate and bicarbonate (HCO3-) levels during hospitalization.

TABLE 1 Summary of clinical cases reporting coronary artery dissection following cardiac surgery.

Author	Year of publication	Age	Gender	Type of surgery	Diagnosis method	Type of intervention	Clinical prensentation	Outcomes
Berroya et al. (3)	1970	Unknown	Unknown	Aortic valve replacement	Postmotem evaluation	None	Sudden cardiac arrest	Death
Nakao et al. (4)	2017	73	Male	Aortic valve replacement	Accidentally via transesophageal echocardiography identified intimal flap within LMCA lumen	OCT guidance PCI	Accidentally	Survival
Molek et al. (5)	2019	Case series: 3 patients with average age: 73 (minimum: 56–maximum: 85)	2 female 1 male	Aortic valve replacement	Coronary angiography identified LMCA dissection	PCI	Acute MI following the surgery	2 survival 1 death
Yu Kang et al. (2)	2020	43	Female	Aortic and mitral valve replacement	Coronary angiography identified a dissection from LMCA to LAD and LCx	None	Acute MI induced low-cardiac output syndrome	Survival
Haval Sadraddin et al. (6)	2021	73	Female	Aortic valve replacement	Coronary angiography identified diffuse coronary dissection from the ostium of the LAD to the left coronary system	CABG	Acute MI following the surgery	Death
Our case	2024	65	Female	Aortic valve replacement	Coronary angiography identified a dissection from the ostium of the LMCA to the ostium of the LCx	IVUS guidance PCI	Cardiogenic shock secondary to acute MI	Survival

However, the utility of IVUS or optical conherence tomography in managing LMCA dissections following valve replacement surgery in unstable patients remains underexplored due to limited available data. This case represents the third instance of intravascular imaging implementation in such scenarios, with OCT having been employed once before, and IVUS now being documented for the second time amidst hemodynamic instability. With IVUS support, we successfully precisely evaluate the underlying mechanism and characteristics of injury, confirm the positioning of the guidewire, and enhance the efficacy of PCI.

Regarding the patient's condition post-discharge, the LVEF has not significantly improved compared to the time of hospitalization, although blood pressure and heart rate have allowed for the escalation of foundational heart failure medications. The dosages of the patient's heart failure medications have remained nearly constant over the past four months, and SGLT-2 inhibitors have not yet been initiated. This needs to be addressed promptly to improve cardiac function and reduce future cardiovascular events for the patient. Additionally, adjusting anticoagulation therapy to achieve the target INR through patient education on diet, adherence to treatment, and regular monitoring is crucial in managing patients with mechanical valves.

Conclusion

This case signified the importance of closely monitoring patients postoperative to promtly identify and diagnose this fatal complication following cardiac valve replacement surgery. Currently, there is no established definitive management approach for this complication. The treatment should be based on the timing of diagnosis, patient's condition, physician's expertise. In our case, where dissection is identified after surgery, PCI with the help of IVUS image was safe, effective and help to reduce the necessity for further surgery. Given the current scarcity of evidence, a multidisciplinary approach should be adopted in the management of LMCA dissection, which involve both cardiac surgeons and interventional cardiologists.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

VV: Conceptualization, Methodology, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

HT: Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. HT: Validation, Visualization, Writing – original draft, Writing – review & editing. KC: Validation, Visualization, Writing – original draft, Writing – review & editing. BD: Validation, Visualization, Writing – original draft, Writing – review & editing. TT: Validation, Visualization, Writing – original draft, Writing – review & editing. BT: Validation, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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A case report of Cogan's syndrome with recurrent coronary stenosis

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Cogan's syndrome (CS) is recognized as a form of variable vasculitis. This report presents the case of a middle-aged woman experiencing recurrent coronary artery stenosis, accompanied by a history of non-syphilis keratitis, vestibular auditory symptoms, and venous thrombosis. Positron emission tomography/computed tomography revealed an elevated uptake of (18)F-fluorodeoxyglucose in the subclavian artery, common carotid artery, aortic arch, and thoracic aorta. A diagnosis of Cogan's syndrome was made. The aim of this study was to increase clinicians' awareness of the vascular manifestations in CS and to emphasize the importance of thorough history taking. CS should be included in the differential diagnosis when patients present with recurrent coronary artery stenosis.

KEYWORDS

Cogan's syndrome, variable vasculitis, recurrent coronary stenosis, case report, coronary angiography

Introduction

Cogan's syndrome (CS) is a rare autoimmune disease, often categorized as a variable vasculitis, and is most commonly diagnosed during the third or fourth decade of life, with a similar prevalence in women and men. The presence of non-syphilitic keratitis and vestibuloauditory symptoms within 2 years is indicative of typical CS (1). Aortitis may affect approximately 10% of CS patients (2). This case report highlights a rare case of coronary artery stenosis in the context of CS, underscoring the need for vigilance in clinical practice.

Case description

A 49-year-old female patient was admitted in 2021 with a complaint of chest tightness and a shortness of breath, symptoms that had been present for a year and were exacerbated by satiety and physical activity. She was diagnosed with non-ST segment elevation myocardial infarction with stenosis of the left main trunk (LM) and right coronary artery (RCA) (Figure 1) and had undergone percutaneous trans-luminal coronary angioplasty and intervention, followed by secondary prevention and treatment for coronary heart disease. Recently, the aforementioned symptoms have re-emerged. The patient reported no fever, rash, oral or genital ulcers, erythema nodosum, or intermittent claudication.

Abbreviations
CS, Cogan's syndrome; CAG, coronary angiography; LM, left main trunk; PET/CT, positron emission tomography/computed tomography; 18F-FDG, (18)F-fluorodeoxyglucose.

A comprehensive medical history (Figure 2) revealed a history of sudden hearing loss, vertigo, and nausea, with recurrent episodes from 9 years ago. She had experienced episodes of redness and blurred vision in both eyes 8 years ago, which improved with antibiotic and corticosteroid treatment. Over the years, she had also suffered from symptoms of vertigo and blurred vision, accompanied by photophobia, which were alleviated with glucocorticoid use, although her hearing progressively declined. In addition, she had a history of limb venous thrombosis, which responded to anticoagulant treatment. There were no special family and psychosocial histories and genetic disorders.

Physical examination findings included a nebula on the lateral edge of the cornea in both eyes, decreased hearing in both ears, and reduced pulsation in the radial, brachial, and dorsal pedal arteries, particularly on the right side. Vascular murmurs were detected in the auscultation areas of the bilateral carotid, subclavian, renal, and iliac arteries and abdominal aorta.

In laboratory tests, the erythrocyte sedimentation rate was 97 mm/1 h, C-reactive protein was above 20 mg/L, complement C3 was 1.72 g/L, complement C4 was normal, immunoglobulin and serum immunoglobulin G4 were normal, and IL-6 was 49.67 pg/ml. Antinuclear antibody profile, neutrophil cytoplasmic antibody, antiphospholipid antibody, interferon-gamma release assay for mycobacterium tuberculosis, syphilis antibody, and tumor marker tests were all negative, and n-terminal prohormone B-type natriuretic peptide was 185.00 pg/ml.

Upon review, coronary angiography (CAG) showed in-stent restenosis (Figure 1). Echocardiography revealed thinning of the left ventricular inferior wall basal segment, mild aortic regurgitation, and decreased left ventricular diastolic function. Positron emission tomography/computed tomography (PET/CT) demonstrated an increased uptake of (18)F-fluorodeoxyglucose (18F-FDG) in the aorta and its primary branches, as well as in the coronary arteries (Figure 3).

Given the patient's ocular, auditory, vestibular, and vascular symptoms, a diagnosis of CS was confirmed. We conducted a differential diagnosis to rule out the following conditions: (1) Takayasu's arteritis: the patient presented with multiple arterial stenoses, necessitating the consideration of Takayasu's arteritis. However, the occurrence of stromal keratitis and sensorineural hearing loss did not align with the typical manifestations of this condition. (2) Antiphospholipid syndrome: the patient's history

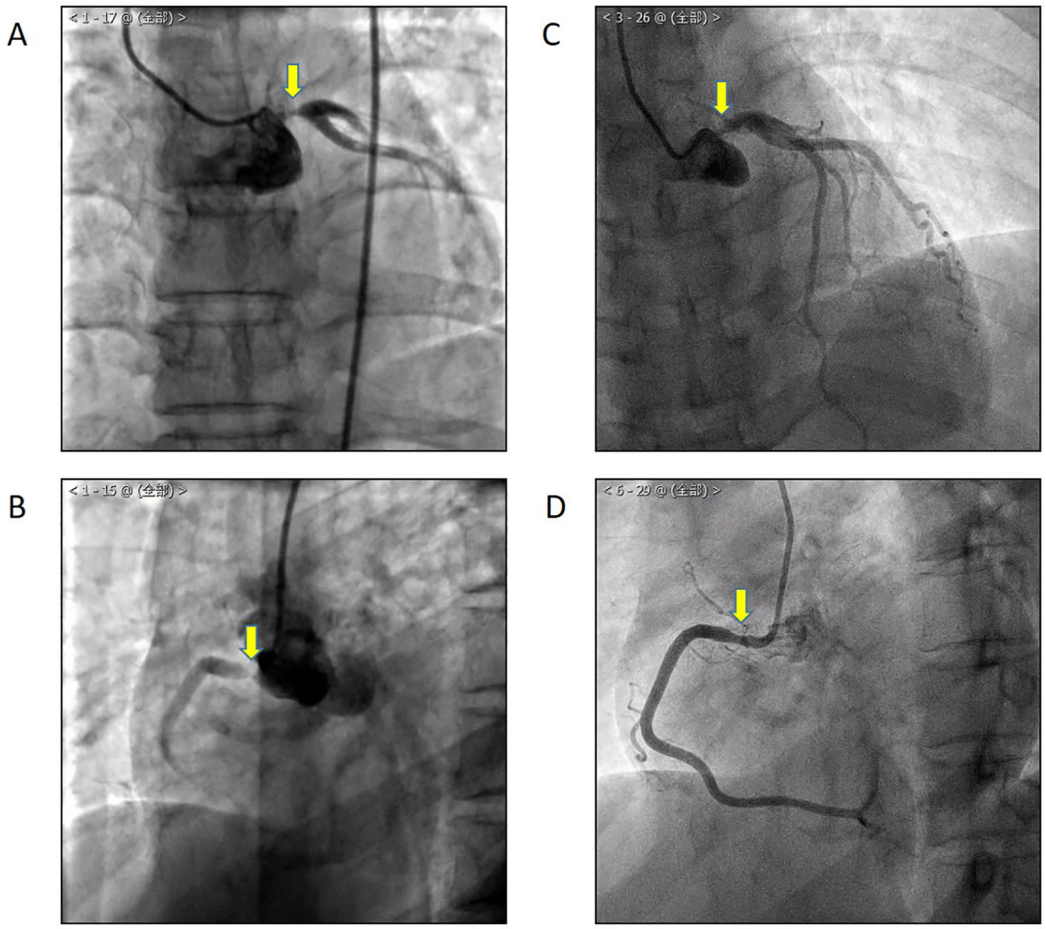

FIGURE 1
In 2020, CAG showed LM (A) and RCA (B) stenosis. One year after percutaneous coronary intervention, the patient suffered from chest tightness and a shortness of breath again, and CAG showed LM (C) and RCA (D) in-stent restenosis.

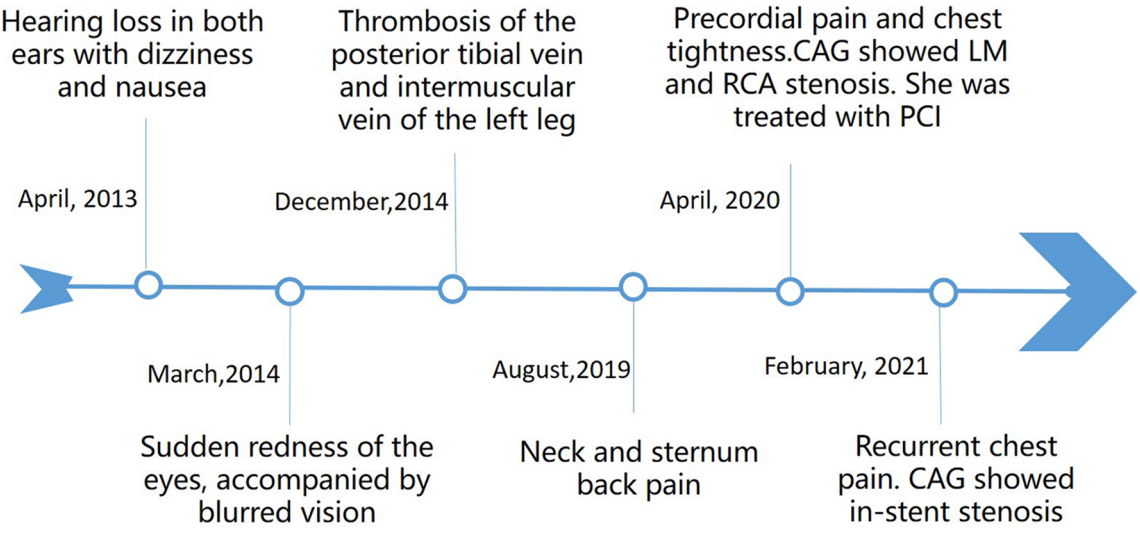

FIGURE 2
A timeline with the relevant data from the episode of care.

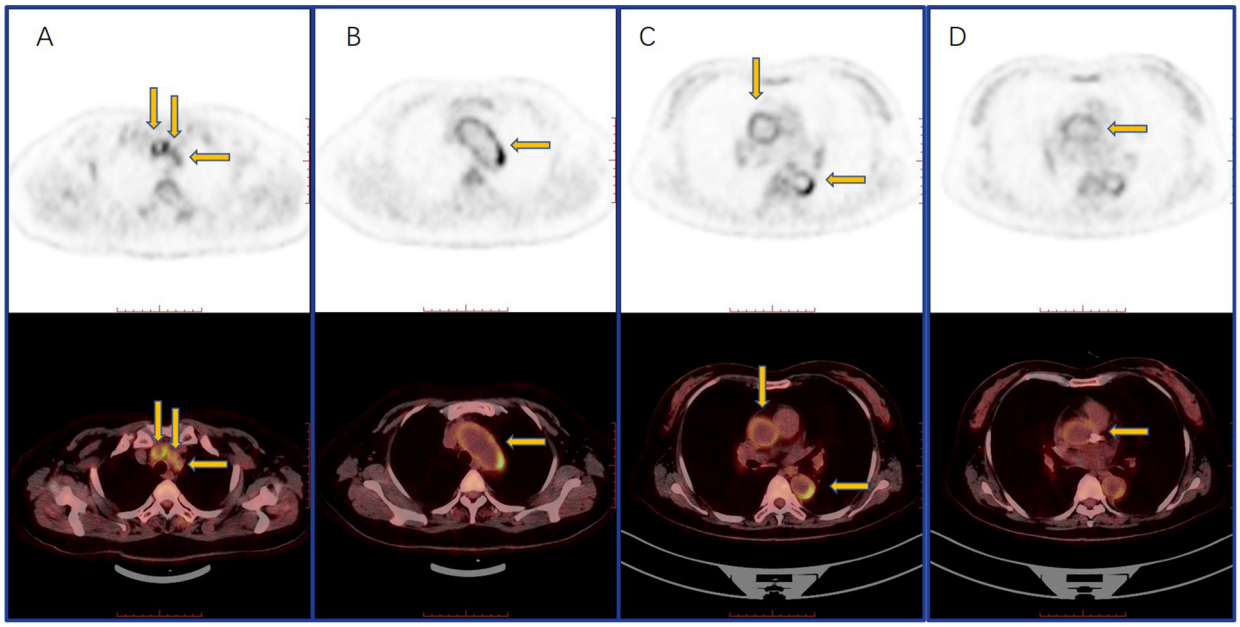

FIGURE 3
PET-CT showed an increased circular and linear 18F-FDG uptake in the subclavian and common carotid arteries (**A**), aortic arch (**B**), thoracic aorta (**C**), and coronary (**D**).

of recurrent thrombosis and multiple arterial stenoses raised the possibility of antiphospholipid syndrome. However, the absence of phospholipid antibodies in all tests negated this diagnosis. (3) Behçet's syndrome: despite the need to consider Behçet's syndrome given the patient's symptoms, the lack of oral and genital ulcers, erythema nodosum, and other characteristic skin changes, as well as the absence of ocular involvement, did not fulfill the criteria for this diagnosis.

The patient was managed conservatively without undergoing repeat percutaneous coronary intervention (rePCI) or bypass surgery involving the internal mammary artery (IMA) to the left anterior descending artery (LAD). The patient was managed conservatively with aspirin, clopidogrel, and isosorbide mononitrate. In tandem with this approach, we initiated a therapeutic regimen that included a combination of corticosteroids and cyclophosphamide to address vasculitis at the same time. The

treatment began with prednisone at a dosage of 50 mg once daily, complemented by intravenous cyclophosphamide at 0.4 g administered biweekly. Subsequently, we implemented a gradual reduction in prednisone and transitioned to methotrexate at 15 mg weekly to alleviate the potential long-term adverse effects associated with cyclophosphamide.

The patient maintained remission over the subsequent 3 years, with no recurrence of chest pain, stable vision and hearing, and no further episodes of venous thrombosis. Laboratory tests and coronary angiography remained stable. The patient had good adherence and tolerability to the intervention, and no adverse or unanticipated events occurred.

Discussion

This case highlights the importance of considering Cogan's syndrome in the differential diagnosis for patients presenting with recurrent coronary artery stenosis. The patient's history of ocular abnormalities, hearing loss with vertigo, and subsequent development of multiple artery stenoses and venous thrombosis, along with PET/CT (a valuable tool in the diagnostic and therapeutic management of vasculitis due to its comprehensive and detailed imaging capabilities) findings of a high 18F-FDG uptake in the aorta and its branches, supports this diagnosis. We conducted a differential diagnosis to rule out other conditions. The limitation was that the patient was not assessed using intravascular ultrasound (IVUS) or fractional flow reserve (FFR) during the coronary angiography. A previous study (3) has suggested that the histological presence of inflammatory cells in the vessel walls of CS patients may be indicative of the disease's vasculitic nature, which can be managed with immunosuppressive therapy (4). When faced with such cases, clinicians are encouraged to conduct thorough history taking and consider CS as part of the differential diagnosis.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material; further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Medical Ethics Committee of Anzhen Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

GN: Data curation, Funding acquisition, Writing – original draft. ZN: Data curation, Resources, Writing – review & editing. MJ: Data curation, Writing – review & editing. PL: Supervision, Writing – review & editing.

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Case Report: Anomalous origin of the right coronary artery leading to cardiac arrest induced by sexual activity: a previously unreported pathogenetic condition

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Background: The Anomalous Origin of the Right Coronary Artery from the Left Coronary Sinus (ARCA-LCS) is a rare congenital cardiac condition where the right coronary artery emerges from the left sinus instead of the right coronary sinus of Valsalva. The clinical significance of ARCA-LCS lies in its potential to cause myocardial ischemia or sudden cardiac death, particularly under physical exertion. In this case, a patient experienced sudden cardiac arrest during sexual activity, which has not previously been reported.
Case presentation: Six years ago, a 37-year-old man was admitted with sudden cardiac arrest during sexual intercourse. No previous history of hypertension or diabetes. There was no abnormality in physical examination. Transthoracic echocardiogram, bilateral carotid Doppler ultrasound, and electrocardiogram were normal. Cranial magnetic resonance imaging and magnetic resonance angiography showed no abnormalities. A treadmill exercise test revealed ischemic changes. Coronary computed tomography angiography showed ARCA-LCS, and passage through the vessel wall between the aorta and pulmonary artery.
Conclusion: This case illustrates a patient with asymptomatic ARCA-LCS for 37 years who did not receive appropriate treatment during a previous visit, but who subsequently experienced a serious cardiovascular event that demonstrated the potential harm of the disease. Therefore, timely intervention in patients with ARCA-LCS, especially in high-risk groups, is critical to prevent potentially catastrophic cardiovascular events. However, in the present case report, the patient did not experience a similar event during the 6-year follow-up by avoiding overexertion and changing his lifestyle at the time of previous onset of the disease. Further studies are needed to optimize diagnostic and therapeutic strategies for ARCA-LCS.

KEYWORDS

coronary artery anomalies, cardiac arrest, ARCA-LCS, coronary angiography, multislice computed tomography, cardiac magnetic resonance imaging

Introduction

Anomalous Origin of the Right Coronary Artery from the Left Coronary Sinus (ARCA-LCS) is a rare cardiac anatomical variant that belongs to a subspecies of coronary artery developmental anomalies. As reported in the literature, the two largest and most comprehensive angiography series to date, conducted by Yamanaka and Hobbs (1) over a 28-year period, enrolled a total of 126,595 patients and reported a prevalence of anomalous coronary arteries of 1.3%. Of these patients, 1,689 (1.3%) had coronary anomalies noted, and an additional 136 (0.107%) had a right coronary artery (RCA) arising from the left coronary artery sinus. Krasuski et al. (2) noted that during a retrospective analysis of 210,700 cardiac catheterizations performed over a 35-year period at a single institution, 301 adults were identified as having an anomalous coronary artery arising from the contralateral sinus of Valsalva. Interestingly, 79% of these individuals demonstrated an RCA originating from the left cusp of the aortic valve (0.11%). The results of these two large data sets suggest that there is little difference in the incidence of ARCA-LCS. Due to the heterogeneity of coronary arteries between individuals, a variety of coronary arteries abnormalities have been caused. Therefore, many classification systems are proposed for different classification criteria, including classification systems based on different dimensions, such as anatomical structure, function, or clinical significance (3, 4). As a type of coronary artery origin anomaly (or ACAOS), the prevalence of ARCA disease is estimated to be 0.92% based on angiographic data (5). To date, its incidental detection is commonly observed during coronary angiography (CAG) or other cardiac imaging procedures. Of course, the evolution of non-invasive imaging technologies, specifically the utilization of multislice computed tomography (MSCT) and cardiac magnetic resonance imaging (MRI), has assumed a pivotal role in facilitating a definitive diagnosis.

After the diagnosis of the disease, the choice of treatment requires careful consideration. This anomalous course can cause external compression, sharp angulation, or twisting (torsion) of the artery, particularly during physical exertion when oxygen demand is increased, leading to compromised myocardial perfusion. If not surgically corrected, these factors can result in myocardial ischemia, which may progress to myocardial infarction, life-threatening arrhythmias, or sudden cardiac deaths (6). Therefore, timely diagnosis and treatment are crucial for these patients. However, the question of whether surgical treatment should be undertaken when a patient is diagnosed with ARCA-LCS disease requires careful consideration. The clinical outcome for ARCA is most often benign (7). Therefore, is surgery needed for every patient and does a more optimal treatment strategy exist for cases where the disease prevalence is low and the majority of patients are asymptomatic?

Case report

Six years ago, a 37-year-old man with a history of vertigo spanning over a decade experienced sudden cardiac arrest during sexual activity. He had no previous history of hypertension or diabetes. According to his wife, he lost consciousness immediately, which lasted for approximately 10–20 s before resolving spontaneously. He was then urgently taken to the hospital by his family. The patient was a habitual smoker and had a known allergy to alcohol. After hospitalization, the patient's physical examination (PE) revealed no obvious clinical signs and no heart murmur was heard. No abnormalities were identified in the patient's medical examination. Electrocardiogram (ECG) confirmed a sinus rhythm. Bilateral carotid ultrasound showed no significant stenosis or plaque formation. Transthoracic echocardiogram revealed an ejection fraction of 60% with normal ventricular wall motion and no evidence of hypertrophic cardiomyopathy. Laboratory tests such as blood routine, liver and kidney function, electrolytes, blood glucose and lipid, myocardial enzyme profile, troponin, and coagulation function did not reveal any significant results. To determine the underlying cause of a condition or disease, the necessary tests must be performed to clearly identify the etiological factors. We conducted a series of examinations on the patient, including MRI and magnetic resonance angiography (MRA) of the brain, to assess neurological status. The results indicated that there were no significant abnormalities in the intracranial soft tissue or vasculature. During the treadmill exercise test (TET), the patient's ST-segment depression was recorded in leads II, III, and aVF (approximately 0.2–0.3 mV), suggesting possible myocardial ischemia (Figure 1), but no chest pain or syncope was observed in the patient during the TET. Due to insufficient physical endurance, the test was ultimately terminated. The TET reached a level classified as stage II (submaximal exercise), indicating that the patient's exercise tolerance was within normal limits; however, further evaluation of cardiovascular health is warranted. During CAG, the patient's RCA may have an abnormal origin due to the inability to selectively engage the vessel during selective right coronary angiography (Figure 2A). With the patient's consent, we proceeded with coronary computed tomography angiography (CCTA) to further assess his condition. The CCTA results revealed an anomalous origin of RCA, which courses between the aorta and pulmonary artery (Figure 2B). In addition, the ARCA forms an acute angle with the left main artery, with mild proximal narrowing (Figures 2C,D). Given the patient's symptoms after exertion and this anatomical variation, surgical intervention was recommended; however, the patient opted for conservative management. We advised him to prioritize rest, avoid strenuous activities, and adjust his sexual lifestyle if necessary. The patient did not experience anything resembling cardiac arrest during a recent follow-up.

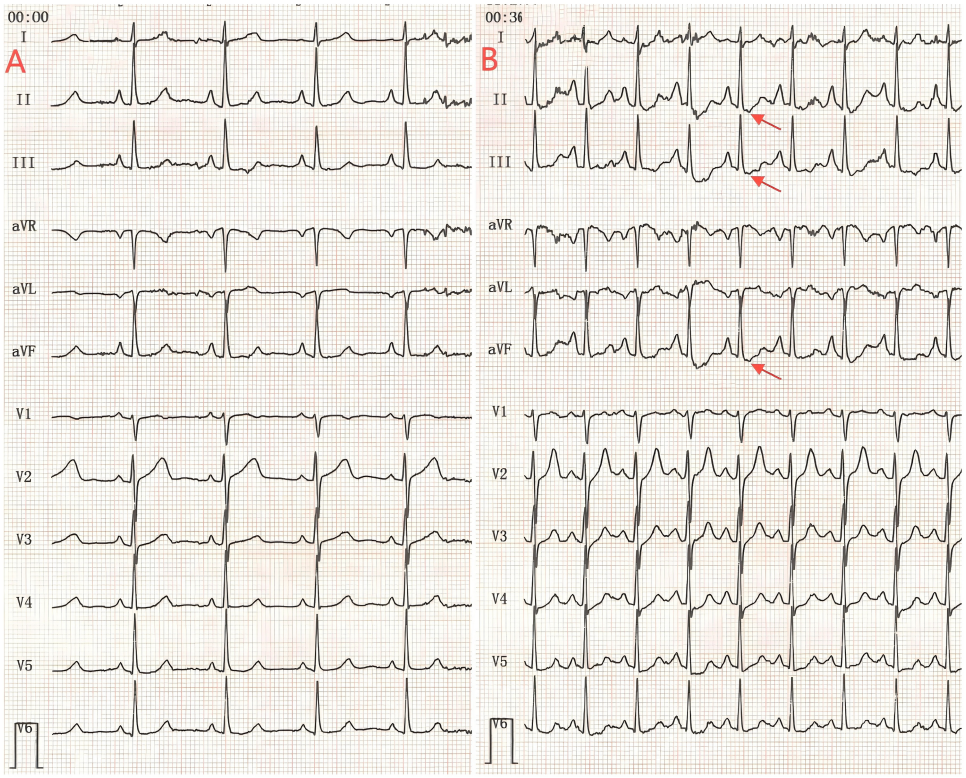

FIGURE 1
(A) The ECG recorded at rest, showing baseline readings. (B) Captured during the recovery phase after exercise, leads II, III, and aVF exhibit a noticeable ST-segment depression (red arrow). This finding suggests ischemic changes in these inferior leads, likely provoked by physical exertion.

Discussion

The most common congenital heart lesions associated with sudden death during exercise include hypertrophic cardiomyopathy, coronary artery anomalies, Marfan's syndrome, and aortic valve disease (8–10). Most coronary artery abnormalities do not produce any symptoms, but some patients may experience adverse events, such as arrhythmia, angina, syncope, myocardial infarction, and even sudden death, with an incidence of up to 33% (11, 12). Even though ARCA-LCS is a rare coronary artery anomaly, the diagnosis of this disease is essential to prevent possible cardiovascular complications. In 2000, Basso et al. summarized the left and right coronary arteries originating from the wrong aortic sinus based on the clinical characteristics of the patients and identification of clinical markers (13). Today, CAG and MSCT play a key role in the diagnostic process of targeting ARCA-LCS. In these patients, MSCT was able to provide more accurate three-dimensional vascular images than conventional angiographic techniques, thereby facilitating the identification of high-risk alignments of the coronary arteries between the pulmonary arteries and the aorta (14). With the increasing sophistication of imaging equipment, there is a need to think about and understand this issue in depth and to recognize that MSCT can more accurately diagnose patients with ARCA-LCS. In addition, recent studies have identified myocardial scarring in regions supplied by coronary arteries with anomalous origins in sudden cardiac death cases involving individuals with prior R-ACAOS, as observed in autopsies. This underscores the importance of using cardiac MRI (CMRI) with late gadolinium enhancement (LGE) to assess both the prevalence and clinical implications of these scars in living patients (15).

Nowadays, pathophysiological studies have revealed that the onset of symptoms of such diseases stems from ischemia triggered by insufficient oxygen supply to the myocardium (16). This may be attributable to numerous surgically correctable anatomic factors (17, 18), including the interarterial path of the anomalous coronary artery, the morphology of the anomalous coronary artery lumen (i.e., round, slit), the angle of origin, the intramural course, and the length of the wall. In addition, in the case of R-ACAOS, which travels between arteries, it leads to a significantly higher incidence of atherosclerosis-related symptoms and events (19). After analyzing the imaging findings of this patient, the following features were identified, including the presence of coronary arteries of abnormal origin traveling between the aorta and the pulmonary artery, emanating from the aorta at an acute angle, with a slit-like pattern of openings, and the presence of intramural segments of coronary arteries, as well as their length. For this reason, the main goal of surgery in this disease is to reduce the risk of ischemia and to graft the abnormal coronary arteries to a suitable location. If feasible, coronary unroofing is typically favored in patients with an

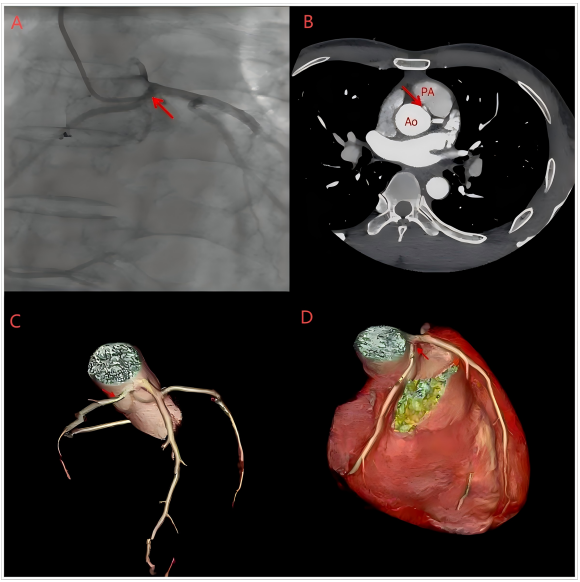

FIGURE 2
(A) CAG revealed a common ostium (red arrow) that produced the right coronary artery and the left coronary artery. (B) CCTA shows the proximal region of the right coronary artery located between the aorta and the pulmonary artery. (C,D) Three-dimensional reconstruction of the coronary artery showing the abnormal origin of the RCA, with its branches crossing the left main trunk at an acute angle. In addition, the RCA runs between the aorta and the pulmonary artery, and its proximal part of the diameter is slightly reduced.

early intramural course. Alternatively, coronary reimplantation, fenestration, neo-ostia formation, or a combination of these techniques may be employed to provide additional treatment options (20). For patients with this type of disease who fail to undergo surgical treatment, some restrictive activity measures may be required. The American Heart Association/American College of Cardiology guidelines have clarified the limitations of exercise for anomalous coronary artery origins. These are described under the heading "Anomalous Coronary Arteries from the Contralateral Coronary Sinus" (21). Recently, Sajjadieh Khajouei et al. showed that interarterial traveled R-ACAOS resulted in significantly higher rates of atherosclerosis-related symptoms and events compared to other types of RCA abnormalities, and coronary intervention significantly improved cardiac function class irrespective of R-ACAOS category (19).

A great deal of research has been carried out on the causes of symptoms in ARCA-LCS; however, to date, there has not been an absolute key factor, and Taylor et al. suggest that the slit pattern of the coronary artery openings and the stenosis of the distal intramural arteries may be the most important factors (22). In the future, by deepening our understanding of the pathophysiology and etiology of this rare coronary artery anomaly and by improving diagnostic and therapeutic strategies, we expect to provide better clinical management and improved prognosis for patients affected by it. In the meantime, a large-scale, multicenter prospective study is necessary to obtain more epidemiological data on this rare coronary artery anomaly and its therapeutic effects.

Conclusion

RCA originating in the left coronary sinus is a rare anomaly that can lead to serious cardiovascular complications in some patients due to the possibility of arterial compression or abnormal alignment during exertion. However, in cases such as ours, conservative treatment focusing on changing sexual lifestyles and reducing exertion is effective in preventing symptom recurrence and adverse events. This highlights the value of an individualized approach to treatment, as in the past it was thought that asymptomatic or low-risk patients could benefit from non-surgical interventions, whereas patients with symptoms or evidence of ischemia could be treated with interventional strategies. In any case, in patients with R-ACAOS, a comprehensive analysis is necessary to further define management and treatment strategies for this disease.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Clinical Trial Ethics Committee, Xinyu People's Hospital, Xinyu, China. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

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Supplementary material

The supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2024.1414821/full#supplementary-material

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Uncommon presentation of left main congenital coronary aneurysm: a rare case report

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Coronary aneurysm, a dilated segment of the coronary artery, is a rare condition with a prevalence ranging from 0.02% to 0.2%. According to the current literature, reports of large aneurysms in the left main artery are extremely rare. We present a case of a 43-year-old male patient presenting with cough, wheezing, and dyspnea after a cold. Initial examinations suggested viral myocarditis, but further evaluation revealed a giant aneurysm in the left main coronary artery. Due to the high surgical risk, conservative treatment was chosen. Follow-up assessments showed no significant changes in the coronary aneurysm, with slight improvement in dyspnea. This rare case of a left main congenital coronary aneurysm suggests that treatment should consider the patient's overall condition, thrombosis presence, suitability for anticoagulant therapy, and aneurysm location and size.

KEYWORDS

coronary aneurysm, conservative treatment, coronary angiography, myocarditis, interventional therapy

1 Background

Coronary angioma is characterized as a dilated segment of the coronary artery that exceeds 1.5 times the diameter of adjacent normal segments (1). Based on current literature, the prevalence of large coronary aneurysms ranges from 0.02% to 0.2% (2). However, the prevalence of large coronary aneurysms measuring 5 cm or more in diameter is even lower, less than 0.02% (1–3). The right coronary artery is the most commonly affected, accounting for 40%–70% of cases, followed by the circumferential artery (23%) and the anterior descending branch (32%) (1, 2, 4). Involvement of all three vessels or the left coronary trunk is rare.

2 Case presentation

This case report presents the clinical details of a 43-year-old male patient who developed a cough and sneezing following a recent cold. Although the cold symptoms improved with self-administered medication, the patient experienced wheezing and paroxysmal dyspnea after physical activity. An electrocardiography(ECG) at a local hospital revealed rapid ventricular rate atrial fibrillation with variable conduction.

The cardiac ultrasound indicated that the LVEF was 38% and the left atrium and ventricle were enlargement with weakened ventricular septal motion. Moderate mitral and mild aortic and pulmonary regurgitation were also noted. The patient also displayed a troponin sensitivity of 0.023 ug/L. Based on these findings, the local hospital suspected viral myocarditis. The patient was referred to our cardiovascular department

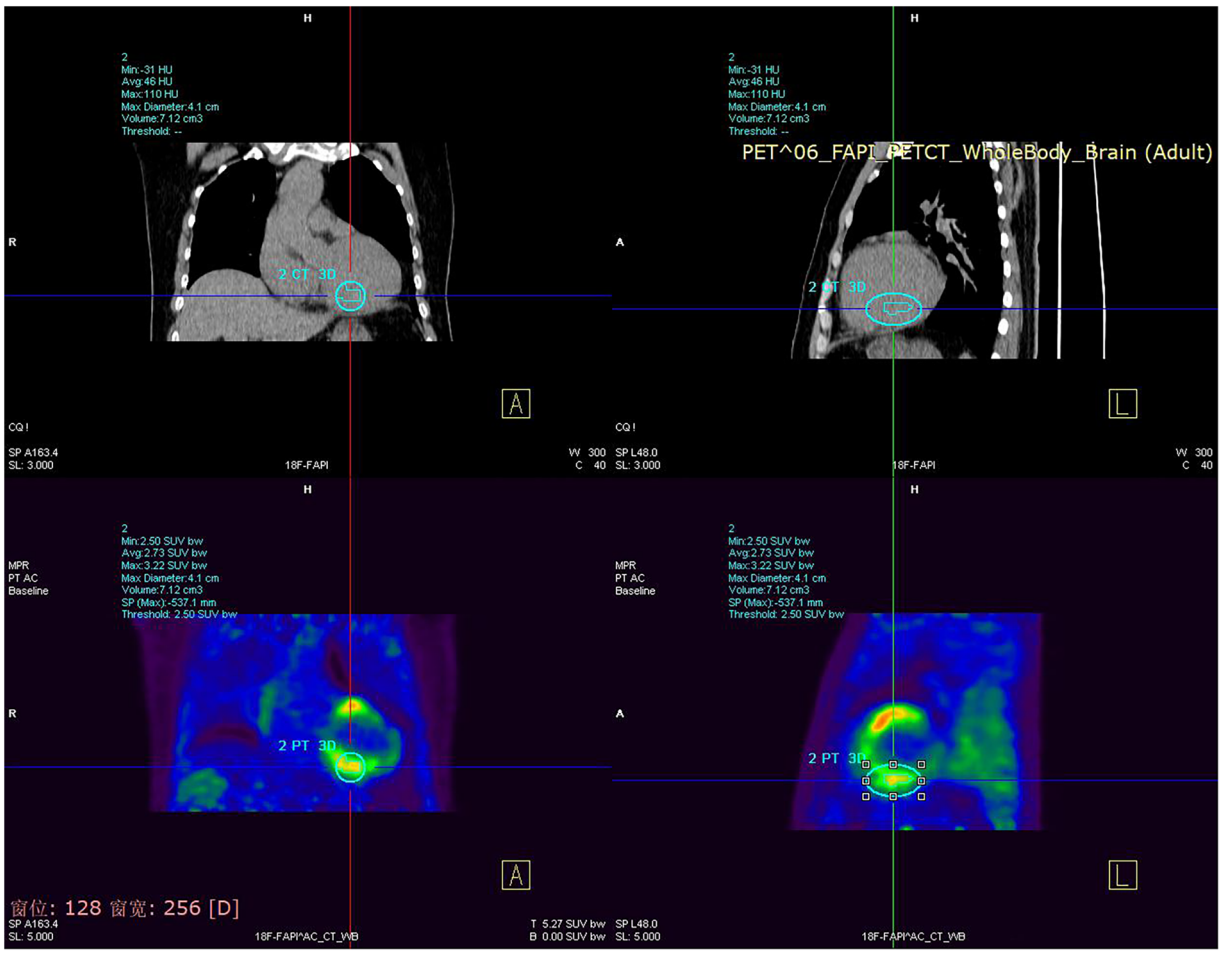

FIGURE 1
Myocardial nuclide imaging (PET) revealed increased FAPI uptake throughout the left ventricle and right atrium.

for further assessment. The patient's NT pro-BNP level was measured at 1,169 pg/ml, and myocardial nuclide imaging (PET) revealed increased fibroblast activation protein inhibitors(FAPI) uptake throughout the left ventricle and right atrium (Figure 1), supporting a diagnosis of myocarditis. The patient received symptomatic treatment, including hormone anti-inflammatory therapy, nutritional support for myocarditis, and gamma globulin therapy. However, these interventions provided limited relief from wheezing. Coronary angiography showed a left coronary dominant type, with no obvious stenosis in the left main trunk but a 2.7×2.3 cm aneurysm in the distal part of the left main trunk. No stenosis was observed in the anterior descending branch, circumflex branch, or right coronary artery (Figure 2). Autoimmune workup, including ANA, anti-dsDNA, ENA antibody profile, and ANCA, returned negative results, ruling out autoimmune causes of the aneurysm. Given the giant aneurysm in the left main trunk, myocarditis, and heart failure with intermediate ejection fraction, open-heart surgery with cardiopulmonary bypass, partial tumor resection, and coronary artery bypass grafting was recommended. However, due to the high risk, the patient and family opted for conservative treatment. As intravascular ultrasound (IVUS) was not performed during coronary angiography, antithrombotic or anticoagulant therapy was not initiated. Instead, the patient was prescribed atorvastatin 20 mg nightly and metoprolol succinate sustained-release 47.5 mg daily.

The patient was closely monitored at 3, 6, 9, and 12 months post-discharge. During follow-up, the coronary aneurysm showed no significant changes, and the patient reported slight improvement in dyspnea, though other symptoms and physical signs remained stable.

3 Discussion

The exact cause of coronary aneurysm formation remains unclear. However, studies have shown that matrix metalloproteinases play a role in the pathogenesis of CAA formation by increasing the breakdown of proteins in the extracellular matrix (5, 6). These enzymes have the ability to degrade various components of the arterial wall matrix and are found in higher concentrations in aneurysms. There is no

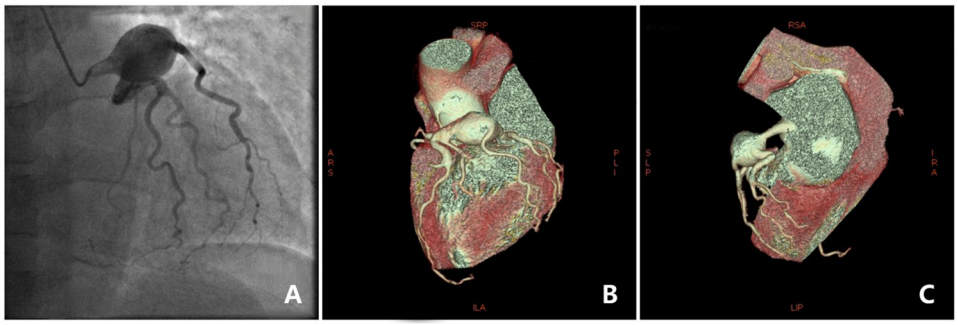

FIGURE 2
Coronary angiography image and 3D reconstruction. **(A)** Coronary angiography showed a large aneurysm. **(B,C)** 3D reconstruction of an aneurysm in a coronary artery.

consensus on the definition of a giant coronary aneurysm. In most literature, it is considered a giant coronary aneurysm if the dilation of the coronary artery is more than 1.5 times the diameter of adjacent normal reference vessels or if the vessel diameter is directly greater than 20 mm (7–9).

Coronary aneurysms can have several etiologies, including atherosclerosis, autoimmune diseases, and Kawasaki disease (9, 10). In this case, the patient's autoimmune screening and coronary angiography findings were negative, suggesting a high likelihood of congenital origin. Coronary aneurysms can present with a range of clinical manifestations, such as asymptomatic chest pain, chest tightness, and pericardial tamponade (11). Initially, the patient did not experience any symptoms but was admitted to the hospital this time due to wheezing and dyspnea after catching a cold. Myocardial nuclide imaging was performed to consider myocarditis, but the symptoms did not improve significantly with treatment. Subsequent coronary angiography revealed the presence of a large coronary aneurysm.

Thrombus formation occurs in coronary aneurysms due to slow blood flow and platelet activation. To better assess aneurysm condition, intravascular ultrasound (IVUS) is recommended when a coronary aneurysm is detected via angiography. In the case with thrombosis, coagulation function, thromboelastography (TEG), and platelet function tests are advised. With timely anticoagulation or antithrombotic therapyare necessary. According to a 2021 study by Tuncay Taskesen, patients without symptoms, coronary occlusion, or thrombosis may not require specialized treatment (12). Additionally, Cihan Ozturk reported a case of an asymptomatic patient with a right coronary aneurysm who remained symptom-free for many years (13). However, for patients with obstructive coronary artery disease symptoms or myocardial ischemia due to embolization, surgical intervention is appropriate. Surgical options include interventional therapy, aneurysm excision, ligation, or coronary artery bypass surgery (2). In a notable 2024 case report by Najdat Bazarbashi, a patient with a large coronary aneurysm was successfully treated with a combination of stent placement and coil embolization (14). For cases involving multiple vessel disease, left main coronary artery aneurysm, or complications like fistula, compression, or rupture, surgical treatment is typically indicated. However, our patient opted for conservative management, which led to symptom alleviation over follow-up. If symptoms worsen, surgical or interventional treatments may become necessary, though surgical costs are high, and clinical evidence on specific prognostic outcomes is limited.

4 Conclusion

Left main congenital coronary aneurysms are exceedingly rare. Proper diagnosis and treatment require assessment of thrombus presence within the aneurysm, along with evaluation of coagulation and platelet function to guide anticoagulation or antiplatelet therapy. For surgical decision-making, factors such as aneurysm location, size, arterial wall condition, and overall patient health should be carefully considered to select an appropriate treatment approach.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

PX: Conceptualization, Writing – original draft, Writing – review & editing. SZ: Data curation, Visualization, Writing –

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Case Report: Recurrent cardiogenic shock caused by inter-arterial left coronary artery originating from the right coronary sinus, successfully rescued by mechanical circulatory support

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A young female patient suffered cardiogenic shock after undergoing surgery for an ectopic pregnancy. Coronary artery computed tomography angiography (CTA) revealed a left main artery (LM) originating from the right coronary sinus and traveling between the aorta and pulmonary artery. We successfully resuscitated the patient with mechanical circulatory support using veno-arterial extracorporeal membrane oxygenation (VA-ECMO) and an intra-aortic balloon pump (IABP). The patient subsequently underwent surgery thereafter. When sudden cardiogenic shock occurs in a young patient, it is important to be vigilant for anomalous aortic origin of a coronary artery (AAOCA).

KEYWORDS

VA-ECMO, IABP, cardiogenic shock, AAOCA, case report

1 Introduction

Anomalous aortic origin of a coronary artery (AAOCA) is the second-leading cause of sudden cardiac death (SCD) in healthy people (1). Although AAOCA has a low prevalence in the population, the left coronary artery originating from the right sinus (L-AAOCA) is even rarer, with a prevalence of only 0.02%–0.05% (2, 3). Inter-arterial left coronary artery originating from the right coronary sinus is a high-risk anatomical typing of L-AAOCA (4). Herein, we report the case of a patient with an inter-arterial left main artery (LM) originating from the right coronary sinus. In this patient, cardiogenic shock was induced by blood loss and recurred over a relatively short period of time. We successfully resuscitated the patient with veno-arterial extracorporeal membrane oxygenation (VA-ECMO) and intra-aortic balloon counter-pulsation (IABP), after which the patient underwent surgery successfully. During treatment, we observed that IABP relieved the compression of the LM that traveled inter-arterially, which has not been noted in previous studies. This case provides valuable insights into the resuscitation of AACOA-related cardiogenic shock.

2 Case report

The patient was a 33-year-old healthy woman who was 165 cm tall and weighed 55 kg, and she delivered a baby boy spontaneously eight years earlier. Neither she nor her family had a history of cardiac disease, and there were no signs of upper respiratory tract infection or enterovirus infection when she was admitted to the hospital. This patient was admitted to the hospital for vaginal bleeding that recurred for two months after an abortion. She was diagnosed with incomplete abortion and underwent surgery. Her hemoglobin level decreased from 11 g/L to 7 g/L due to heavy bleeding during surgery.

The patient was transfused with blood cells and balanced crystalloids after surgery. Six hours later, the patient demonstrated weakness and chest tightness, with a blood pressure of 78/34 mmHg. We considered this a manifestation of hypovolemic shock; however, continuous blood transfusion and fluid resuscitation could not raise the blood pressure. Subsequently, the patient manifested respiratory and circulatory failure, and the electrocardiogram (ECG) demonstrated ventricular fibrillation (Figure 1). We immediately initiated cardiopulmonary resuscitation (CPR) and subsequently performed electrical defibrillation. After two minutes of CPR, sinus rhythm was restored and her blood pressure increased to 81/40 mmHg. After 12 min, the patient's heart rate dropped to 46/min, her blood pressure was undetectable, and her aortic pulsation disappeared; thus, we performed extracorporeal cardiopulmonary resuscitation on her. VA-ECMO (left femoral vein-right femoral artery) was implanted and the initial ECMO centrifugal pump speed was 3,490 rpm and the support flow rate was 3.36 L/min. The patient was anticoagulated with heparin, maintaining the activated partial thromboplastin time between 60 s and 80 s. A distal perfusion catheter was placed to direct a proportion of the returned oxygenated blood flow from the ECMO circuit to the distal right femoral artery. The patient's blood temperature was maintained below 36°C for cerebral resuscitation. Continuous renal replacement therapy was initiated via the ECMO circuit due to the patient's volume overload, anuria, severe metabolic acidosis, and acute kidney injury. At this time, the patient's ECG revealed myocardial ischemia (Figure 1), and the cardiac ultrasound revealed diminished myocardial contractile motion in the left ventricle with a left ventricular ejection fraction (LVEF) of 30% and a pulmonary artery pressure of 61 mmHg. The patient regained consciousness on day 2. We began administering digoxin on the fourth day of the ECMO treatment.

We attempted to make a definitive diagnosis of the patient's condition and what we could ascertain was that she did not have hypoxia, acidosis, electrolyte disturbances, and hypothermia before shock. Chest x-ray and post-CPR cardiac ultrasound did not show tension pneumothorax or pericardial effusion, and the patient did not show any signs of intoxication. Pulmonary embolism was ruled out by pulmonary artery computed tomography angiography (CTA). This patient had annual health checkups, and her electrocardiogram and cardiac ultrasound revealed no abnormalities. Epidemiologically, this patient is not at high risk of coronary heart disease. We initially considered the patient to suffer from hypovolemic shock. Shock and CPR caused the patient's myocardial injury.

With the help of ECMO, the patient's condition gradually improved and the dose of vasoactive drugs was gradually decreased. After seven days of ECMO, the patient's cardiac ultrasound still revealed a generalized decrease in myocardial contractile motion in the left ventricle; however, the LVEF had returned to 36% at an ECMO flow rate of 2 L/min. At this time, the patient's blood pressure was 112/55 mmHg, the dose of norepinephrine was 0.15 μg/kg/min, and all her organ functions were normal except for the renal function, which had not been recovered. Therefore, we decreased the flow rate of ECMO to 1 L/min. After approximately an hour, there was no considerable change in the patient's vasoactive drugs and the ECMO was discontinued. The patient was successfully weaned from the ventilator on the third day after the ECMO was discontinued. To further investigate the etiology, we improved the coronary CTA, and the image suggested that the LM originated from the right coronary sinus and traveled between the aorta and the pulmonary artery. Coronary angiography suggested that the left coronary artery originated from the upper part of the right coronary sinus, with eccentric stenosis of 80%–90% from the opening of the LM to the proximal vessel lumen, and no notable stenosis was found in the rest of the vessels (Figure 2). Therefore, we changed the diagnosis to cardiogenic shock associated with AAOCA. The patient should have undergone surgery; however, she had poor cardiac function and was in a state of malnutrition at this time (the patient's body mass index was 15.2 kg/m^2). We continued to provide medication, nutritional therapy, and rehabilitation. After these treatments, the patient's cardiac function and nutritional status improved. However, early in the morning of the 10th day after the first withdrawal of VA-ECMO, the patient suffered from cardiogenic shock again and developed an intermittent third-degree atrioventricular block. The patient remained conscious and her blood pressure reached a minimum of 69/43 mmHg, requiring a high dose of vasoactive amines. Her left atrium was enlarged (LA: 41 mm) and her LVEF dropped to 28%. Since the patient's cardiogenic shock was difficult to correct, she was treated with VA-ECMO again (The initial ECMO centrifugal pump speed was 3,050 rpm which supported a flow rate of 2.63 L/min).

Seven days after the second VA-ECMO treatment, the patient's condition improved (her LVEF increased to 38%, her blood pressure rose to 105/65 mmHg, and the norepinephrine dose was 0.1 ug/Kg/min) and the ECMO was discontinued again. To avoid the recurrence of cardiogenic shock, we placed an IABP to support her circulation (Mode: Automatic, Trigger signal: ECG, Auxiliary frequency: 1:2, Rebound pressure: 88 mmHg). We performed echocardiography on this patient daily, and the findings suggested a decrease in the LM's lumen, a faster blood flow rate within the LM, and an increase in the pressure differential. This demonstrated that the LM was in a state of continual compression, a situation that was relieved during the period of the IABP. Also, the patient's cardiac function improved, the brain natriuretic peptide (BNP) level decreased, and the LVEF increased after IABP therapy (Figure 3). Ten days

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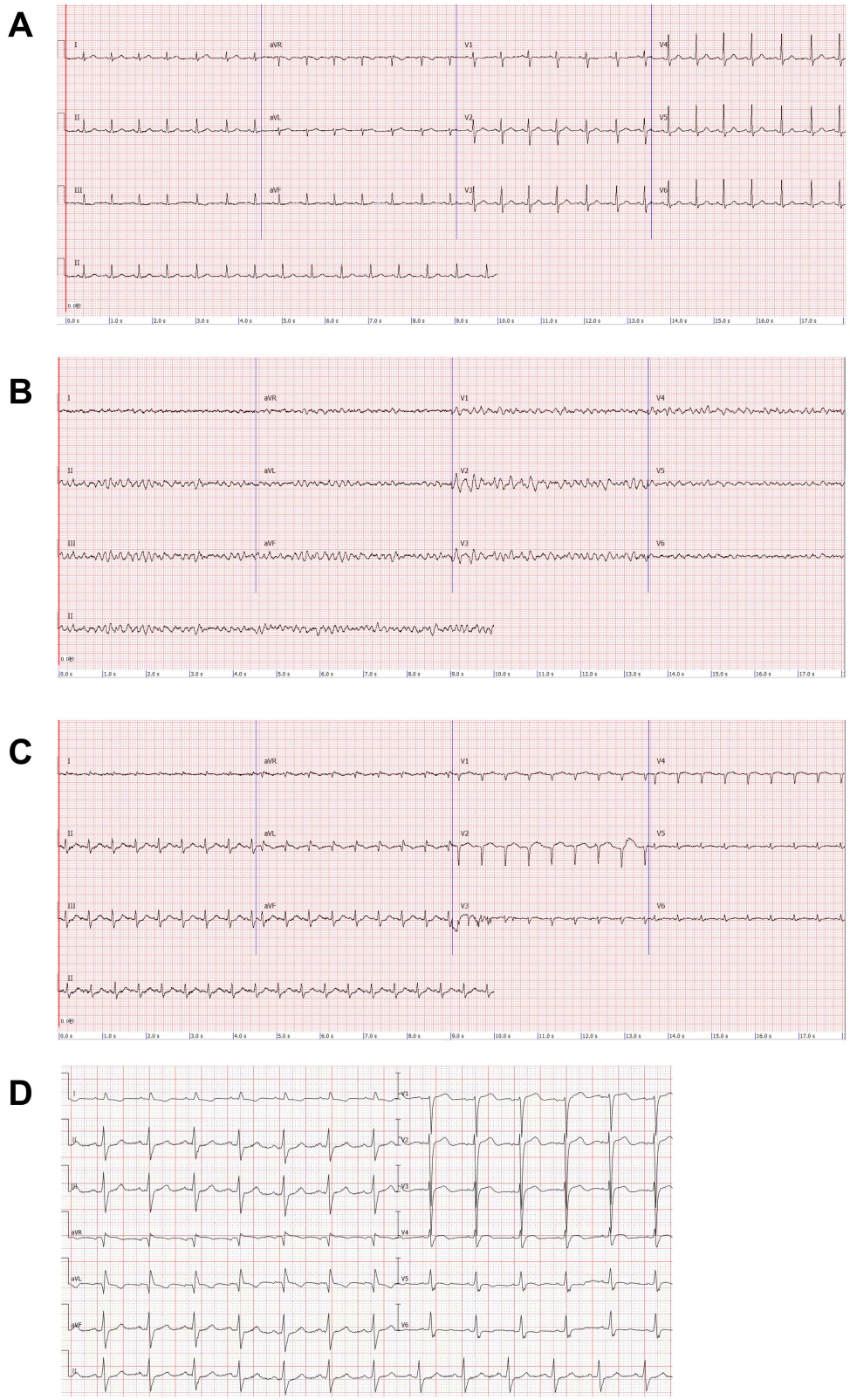

FIGURE 1
Electrocardiogram (ECG). **(A)** Patient's pre-surgical ECG. **(B)** Patient develops ventricular fibrillation after shock. **(C)** ECG after ECMO implantation: poor R-wave progression in the anterior wall leads, abnormal Q-waves in the high lateral wall leads, T-wave alterations, and a decrease in the voltage of the QRS wave in the left thoracic lead. **(D)** ECG of the patient one month after receiving unroofing.

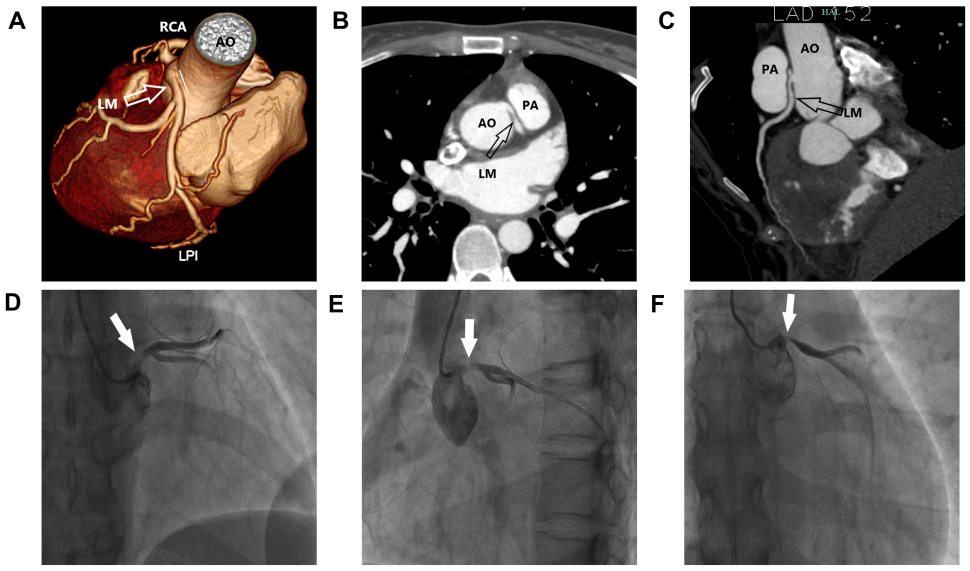

FIGURE 2
Clinical images. **(A–C)** Multiplanar reformat image showing an acute takeoff angle (<45°) of the inter-arterial left main coronary artery (LM) originating from the right coronary sinus. **(D–F)** Multi-angle coronary angiography showing LM originating from the upper part of the right coronary sinus, with an eccentric stenosis of 80%–90%.

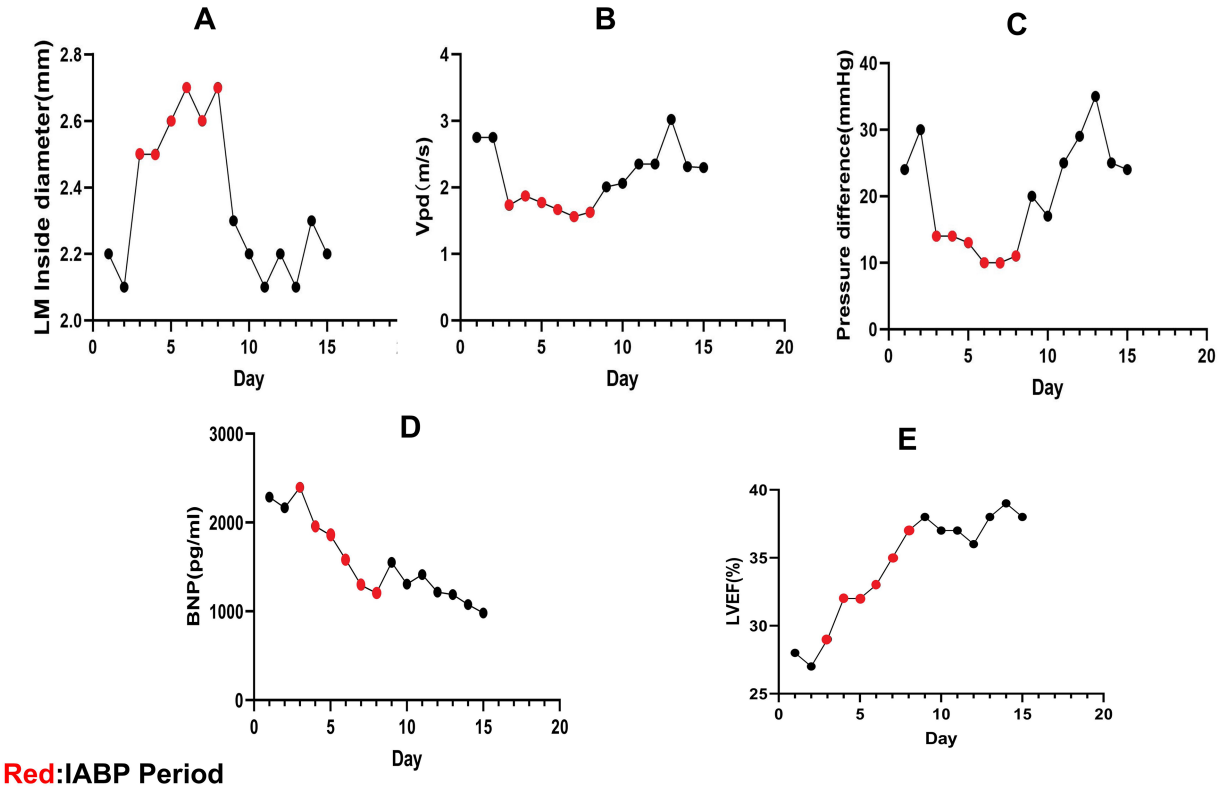

FIGURE 3
Echocardiographic data. **(A–C)** LM compression is relieved during intra-aortic balloon counter-pulsation (IABP), the LM internal diameter increases, the peak diastolic coronary flow (Vpd) velocity drops, and the LM pressure difference decreases. The LM is compressed again after stopping IABP. **(D,E)** After starting IABP therapy, this patient's brain natriuretic peptide (BNP) levels decreased and her left ventricular ejection fraction (LVEF) increased.

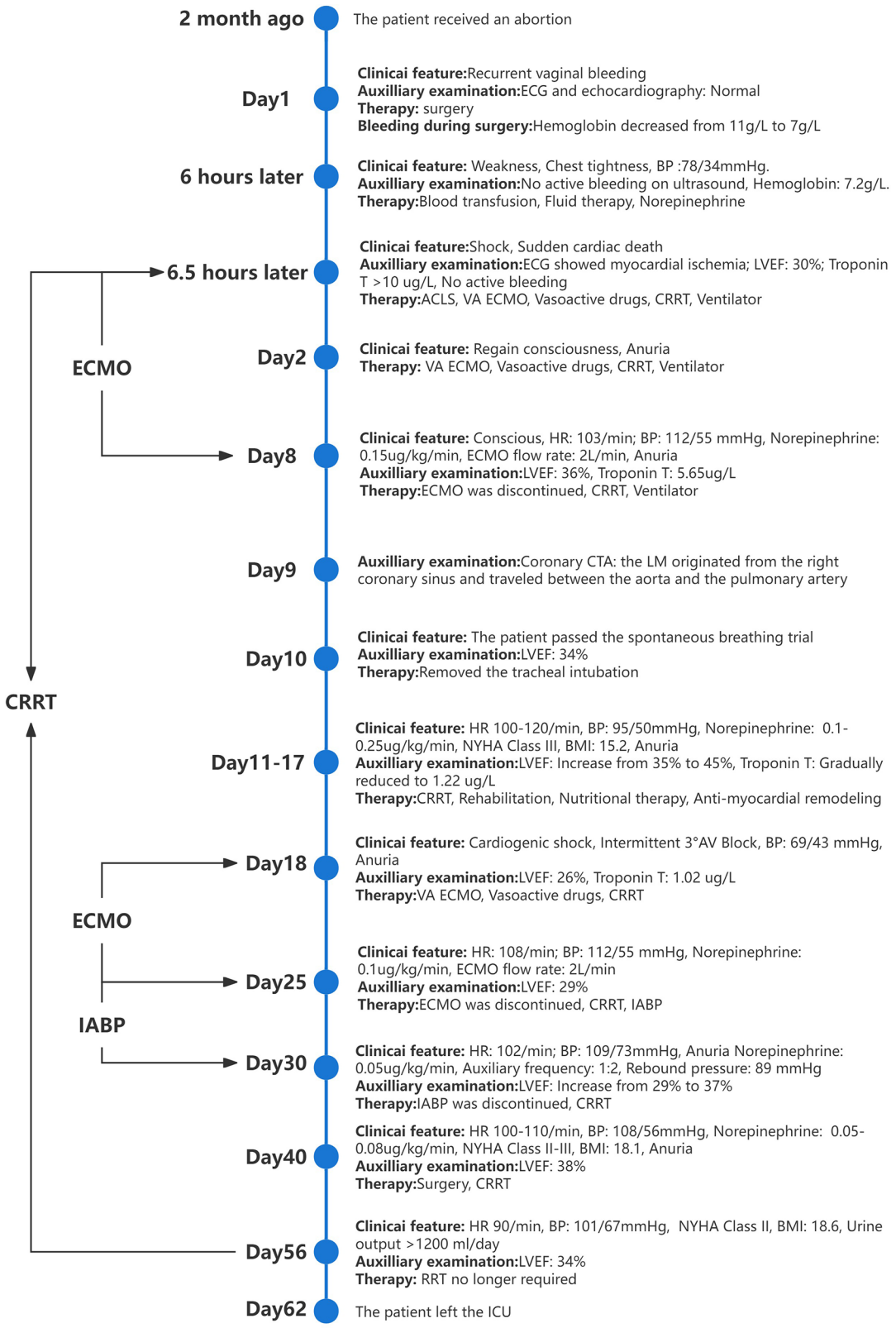

FIGURE 4
The timeline of the patient's case.

after discontinuing the IABP, we performed surgery on this patient, during which we saw the inter-arterial LM originating from the right coronary sinus and the LM within the aortic wall. She underwent unroofing of the intramural portion to relocate the LM in the appropriate sinus. In the end, the patient was in good physical and psychological condition. She was asymptomatic at rest, with minor limitations in physical activity (NYHA Class II cardiac function). Her renal function was restored on day 56, before which she had been on renal replacement therapy. Her glomerular filtration rate is currently 120 ml/min and her urine output is >1,200 ml/day. One month after receiving unroofing, the patient's ECG results suggested significant improvement in myocardial ischemia. Figure 4 summarised the patient's treatment history by way of a timeline.

3 Discussion

Due to the high risk of SCD with an inter-arterial left coronary artery originating from the right coronary sinus, the American College of Cardiology and American Heart Association guidelines recommend surgery even in asymptomatic patients (*Class I, Level of evidence B*) (5). The presence of a coronary artery within the aortic wall, the length of the inter-arterial coronary artery, slit-like coronary ostium, and stenosis proximal to the LM ostium are all anatomical risk factors for SCD (6, 7).

Traditionally, the inter-arterial pathway between the aorta and the pulmonary artery has been considered the primary mechanism of ischemia caused by compression between the two vessels (8). It is currently widely accepted that intramural travel in the aorta is the primary mechanism of myocardial ischemia in these patients. This is because the pressure in the coronary arteries and aorta is significantly higher than that in the pulmonary arteries (9). When the heart is in systole, the coronary arteries within the aortic wall are significantly compressed (10). During sympathetic excitation, the aortic stress increases and the coronary arteries within the aortic wall are further compressed to narrow the vessel lumen further. Also, because the left coronary artery originates from the right coronary sinus, the length of the former is increased. According to the Hagen-Poiseuille law, the smaller vessel lumen and the increased pipe length can cause a significant reduction in the coronary artery's volume flow. In this case, the patient has an inter-arterial LM originating from the right coronary sinus, and LM traveling within the aortic wall. This patient's sympathetic excitability increased significantly after massive blood loss, resulting in LM lumen compression and a decrease in blood flow through the left coronary artery. During the unroofing procedure, we found that the LM was at an acute takeoff angle to the aortic wall, and the ostium of the LM was slit-like. When these two conditions coexist, valvular coronary artery obstruction may occur (11, 12). At the same time, the oxygen-carrying capacity of the patient's blood is markedly reduced due to decreased hemoglobin levels. All these factors may have contributed to the pathogenesis of this patient's first episode of cardiogenic shock.

In a related study, a patient with a left inter-coronary artery originating from the right coronary sinus underwent an exercise test. During the test, the electrocardiogram showed myocardial ischemia; however, the patient was asymptomatic and the electrocardiogram returned to normal afterward. This patient also had no clinical symptoms in daily life, indicating that the myocardial ischemia occurred intermittently (13). It remains unclear whether such patients experience coronary artery compression when they are asymptomatic. In this case, we found through echocardiography that this patient's LM was persistently compressed despite the absence of clinical symptoms. This persistent compression may explain the recurrent cardiogenic shock observed during this patient's treatment, as LM flow was already markedly reduced, and any situation that increases cardiac workload could further aggravate myocardial ischemia.

VA-ECMO has been widely used in the treatment of cardiogenic shock (14). In this case, the patient had two episodes of cardiogenic shock within a short period, both of which resolved with VA-ECMO support. IABP is a common treatment applied to percutaneous mechanical circulatory support in acute myocardial infarction combined with cardiogenic shock (AMICS). In recent years, the IABP-SHOCK II study has suggested that IABP does not improve the thirty-day, one-year, and six-year mortality rates in patients with AMICS (15, 16). As of 2018, the European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery Guidelines for myocardial revascularization no longer recommend the routine use of IABP in patients with AMICS (*class III*) (17). Currently, studies focusing on the use of IABP in patients with L-AAOCA-related cardiogenic shock are rare. A case report of L-AAOCA revealed that bridging IABP could help restore cardiac function in patients who still had cardiac insufficiency after ECMO removal (18). However, the pathophysiologic mechanisms regarding the improvement of cardiac function by IABP in this type of patients are not described in the study. In our case, we bridged the IABP after the second withdrawal of VA-ECMO to help improve the patient's cardiac function and facilitate surgical treatment. During this procedure, we found (by echocardiography) that the IABP relieved the compression of the LM that traveled inter-arterially. This finding may provide experience in the resuscitation of L-AACOA-related cardiogenic shock. We still need large-sample studies to demonstrate the positive effect of IABP in inter-arterial left coronary artery originating from the right coronary sinus-related cardiogenic shock.

4 Conclusion

In our clinical practice, we must remain vigilant for the rare disease of AAOCA when encountering unexplained circulatory failure. Patients with inter-arterial left coronary arteries originating from the right coronary sinus are at risk of experiencing recurrent cardiogenic shock over a short period. VA-ECMO and IABP can effectively resuscitate patients with this condition, helping them regain cardiac function and creating opportunities for surgical treatment.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Ethics Committee of Taizhou Central Hospital (Taizhou University Hospital). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

TJ: Writing – original draft, Writing – review & editing, Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration. RW: Writing – original draft, Writing – review & editing, Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration. LD: Supervision, Writing – review & editing, Resources, Software, Validation. YL: Supervision, Writing – review & editing.

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Conflict of interest

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2024.1466524/full#supplementary-material

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Case Report: Delayed diagnosis: a case of left main coronary artery spasm

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Left main coronary artery (LMCA) spasm is an exceedingly rare but potentially fatal condition. We present a case of severe stenosis of LMCA found by coronary angiography (CAG) due to recurrent chest pain, and subsequently received coronary artery bypass grafting (CABG). Nine years later, the patient was readmitted to the hospital because of precordial discomfort. During hospitalization, CAG was performed once again and showed no significant stenosis in the LMCA, leading to the diagnosis of LMCA spasm. This case emphasizes to interventional cardiologists the critical need to consider the possibility of LMCA spasm when diagnosing LMCA lesions. It highlights the importance of thorough and proactive pretreatment and comprehensive clinical judgment to minimize the risk of misdiagnosis.

KEYWORDS

left main coronary artery (LMCA) spasm, angina, coronary angiography (CAG), coronary artery bypass grafting (CABG), coronary artery spasm (CAS)

Introduction

Coronary artery spasm (CAS) is an abnormal contraction of the epicardial coronary arteries caused by various factors, which can occur in both normal vessels and areas of plaque stenosis, resulting in partial or complete vessel occlusion and can trigger a spectrum of severe cardiac events such as angina, myocardial infarction, heart failure, and malignant arrhythmias, and may even result in sudden death (1). Coronary artery spasm is not uncommon, especially right CAS (2), and it has attracted considerable attention from interventional cardiologists. However, left main coronary artery (LMCA) spasm is relatively rare, often underestimated, and potentially misdiagnosed. The LMCA originates from the left aortic sinus and typically bifurcates into the left anterior descending artery (LAD) and the left circumflex artery (LCX). The LAD supplies the anterior wall of the left ventricle and the interventricular septum, while the LCX supplies the lateral and posterior walls of the left ventricle (3). Understanding the anatomy of the LMCA and its branches is crucial for diagnosing and managing LMCA spasm, as it helps differentiate between spasm-induced stenosis and atherosclerotic disease. Therefore, timely and definitive diagnosis, along with the establishment of appropriate treatment plans for patients, remains a significant challenge. Here, we present a case of a patient who inadvertently underwent coronary artery bypass grafting surgery due to LMCA spasm. We hope that this case report will raise further awareness among interventional cardiologists about this rare but critical condition.

Case report

A 54-year-old man presented to the hospital 11 years prior due to recurrent chest pain. Coronary angiography (CAG) revealed stenosis of left main coronary artery (LMCA) and triple vessel disease (Figure 1). Considering the risk factors of coronary heart disease (type 2 diabetes and hyperlipidemia) and multi-vessel disease, the patient was referred to the Cardiac Surgery Department and underwent left internal mammary artery (LIMA) to left anterior descending artery (LAD) and aorta (AO) to diagonal branch (Diag) and posterior left ventricular branch (PLV). After discharge, the patient regularly underwent treatments for coronary dilation, reduction of myocardial oxygen consumption, lipid-lowering, and plaque stabilization.

Two years ago, the patient experienced recurrent precordial discomfort without any apparent cause. Coronary computed tomography angiography (CTA) revealed the following: (1) Changes after coronary artery bypass grafting: (a) Graft 1 originated from the left subclavian artery, with faint opacification in the proximal segment and no clear opacification in the mid to distal segments; (b) Graft 2 was mostly not opacified; (2) Coronary artery sclerosis; Atherosclerosis of the aorta. To further clarify the coronary artery lesions and the condition of the bypass grafts, the patient underwent CAG the next day, which revealed that the LMCA did not have significant stenosis, and at the same time, the bypass grafts had become occluded (Figures 2A,B). Therefore, we concluded that the stenosis of the left coronary artery found during the patient's first coronary angiography eleven years ago was due to spasm rather than plaque-induced narrowing. Upon this new diagnosis, the management strategy was revised to focus on medical therapy for potential LMCA spasm. The patient was prescribed a regimen of calcium channel blockers and nitrates to manage symptoms and prevent future spasmodic episodes. Additionally, lifestyle modifications were recommended, including smoking cessation and stress management, to address known risk factors for coronary artery spasm (CAS). Follow-up visits and periodic non-invasive cardiac imaging were scheduled to monitor the patient's condition and the effectiveness of the treatment. Over the subsequent six months, the patient reported a significant reduction in chest pain episodes, and follow-up assessments showed stable cardiac function without evidence of new coronary artery lesions. The patient's quality of life improved, and he remained free from severe cardiac events at the last follow-up, one year after the implementation of the new management plan.

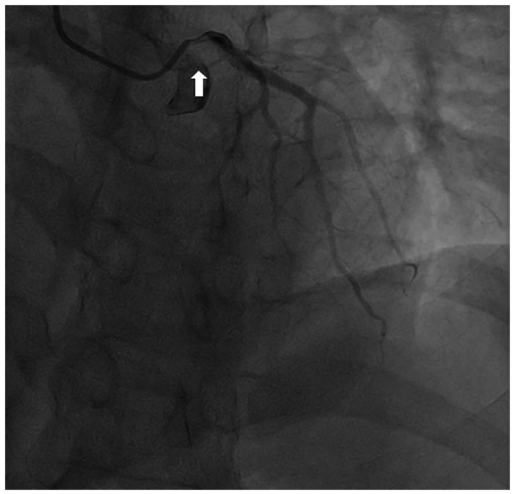

FIGURE 1
Coronary angiography was performed at the patient's first visit 11 years ago. A significant stenosis in the LMCA (arrow) was identified, suggesting the possibility of coronary artery spasm or atherosclerotic stenosis.

Discussion

Left main coronary artery (LMCA) spasm is a relatively rare but severe form of coronary artery spasm (CAS), which is infrequently reported in the literature (4). LMCA spasm manifests as symptoms of coronary heart disease and appears as localized stenosis of the LMCA in coronary angiography (CAG), which can easily lead to misdiagnosis as severe left main coronary atherosclerosis and result in inappropriate referral for surgical intervention, as seen in this case (5, 6). When LMCA spasm is suspected, initial treatment should focus on medical therapy rather than immediate surgical intervention. Medical treatment for CAS mainly includes calcium channel blockers and nitrates, which have been proven effective in relieving vasospasm and reducing ischemic symptoms (7, 8). In addition, lifestyle modifications such as smoking cessation and stress management are also important measures, as smoking is a significant risk factor for CAS and stress can trigger spasmodic episodes (7). This case underscores the critical importance of differentiating LMCA spasm from atherosclerotic disease to prevent unnecessary CABG and to implement appropriate medical therapy. It also highlights the potential long-term benefits of an accurate diagnosis and tailored management plan for LMCA spasm.

LMCA spasm can be either spontaneous or catheter-induced, and sometimes it is challenging to differentiate between the two. Hung et al. reported a case of a patient who developed LMCA stenosis during a treadmill exercise test, and the stenosis was alleviated upon the administration of an adequate dose of nitroglycerin during CAG, suggesting spontaneous LMCA spasm (9). Catheter-induced LMCA spasm, though rare, is a recognized complication of CAG (10, 11). Therefore, if left main stenosis is observed during this procedure, we must consider the possibility of catheter-induced vasospasm, which typically occurs within 1 mm of the catheter tip (12), and may result from mechanical irritation of the coronary artery wall by the catheter (13). Edris et al. (10) reported two cases of catheter-induced LMCA spasm. The first patient underwent CABG, and repeat CAG after 6 years showed a normal LMCA, while the second patient had a repeat angiogram just two days later showing a normal LMCA. In a large retrospective study of 7,295 coronary angiographies, Chang et al. (14) identified 30 cases of catheter-induced LMCA spasm (incidence rate of 0.41%). The use of various

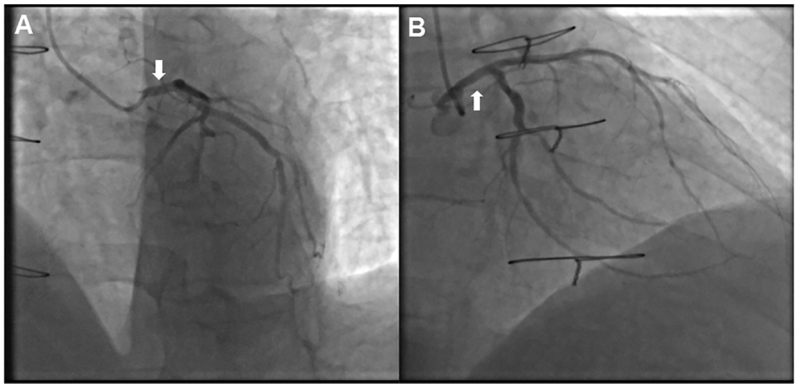

FIGURE 2
Coronary angiography was performed two years ago, showing the vascular conditions under different views. **(A)** No significant stenosis in the LMCA (arrow), compared to the previously stenosed area identified 11 years prior. **(B)** No significant stenosis in the LMCA (arrow), confirming the absence of organic narrowing and supporting the diagnosis of LMCA spasm.

vasoconstrictive drugs is also a triggering factor for CAS. Hau et al. reported a case of a 42-year-old woman who suffered from severe CAS leading to acute myocardial infarction after taking a high dose of misoprostol for labor induction (15). Additionally, several literature reports have described the phenomenon of LMCA spasm induced by fluctuations in thyroid hormone levels (16–18). However, no abnormalities in thyroid function were found in our patient upon admission.

Previous cases have demonstrated that diagnosing LMCA spasm remains a challenge for interventional cardiologists. This process first necessitates a comprehensive assessment of clinical risk factors in patients, such as the presence of a smoking history, as smoking is the most significant risk factor for CAS. Additionally, it is recommended that thyroid function tests be included as a routine examination. When there is a high suspicion of vasospasm during CAG, such as isolated LMCA stenosis, which has an extremely low incidence (19), the intracoronary use of nitroglycerin is suggested as a standard practice, and provocation tests should be encouraged. Provocation tests with pharmacological agents (such as acetylcholine or ergonovine) during coronary angiography are considered the most reliable methods for diagnosing CAS (8, 20). The specific procedure involves the intracoronary injection of either acetylcholine or ergonovine, during which observations are made for any symptoms experienced by the patient, changes in electrocardiogram (ECG), and angiographic images that indicate CAS. A positive result is defined as transient, complete, or subtotal focal occlusion (>90% stenosis) of a coronary artery, accompanied by signs/symptoms of myocardial ischemia (angina and ischemic ECG changes), or induction of >90% diffuse vasoconstriction in two or more contiguous segments of a coronary artery (21). Furthermore, intravascular ultrasound (IVUS) and fractional flow reserve (FFR) can play crucial roles in differentiating coronary artery spasm from atherosclerotic disease (22–24). IVUS provides detailed images of the coronary artery lumen and wall, allowing for the identification of non-atherosclerotic causes of stenosis, such as vasospasm. FFR, on the other hand, measures the physiological significance of a coronary stenosis by assessing the ratio of distal coronary pressure to aortic pressure during maximal hyperemia. This functional assessment can help determine whether a stenosis is causing significant ischemia, thereby guiding appropriate therapeutic decisions (24).

Conclusion

Inability to differentiate coronary artery spasm from left main coronary artery (LMCA) obstructive disease can lead to inappropriate referrals for coronary artery bypass grafting (CABG) surgery. The true incidence of unnecessary CABG in patients with LMCA spasm remains unknown. Therefore, it is imperative to enhance our capacity to identify LMCA spasm in order to prevent unnecessary revascularization procedures. In summary, a comprehensive approach that includes clinical assessment, advanced diagnostic tools (such as IVUS and FFR), and tailored medical therapy is essential for managing patients with suspected LMCA spasm.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by The Ethics Committee of The Second Hospital of Hebei Medical University. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

YZ: Conceptualization, Investigation, Writing – original draft, Writing – review & editing. WS: Writing – review & editing, Investigation. ZZ: Writing – review & editing. DL: Conceptualization, Funding acquisition, Resources, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Acute branch retinal arteriolar occlusion after intravascular ultrasound: a case report

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Intravascular ultrasound is mainly used for the diagnosis and interventional treatment of coronary heart disease. Retinal artery occlusion caused by intravascular ultrasound is very rare. We report a case of acute branch retinal arteriolar occlusion after intravascular ultrasound examination of the coronary artery in a patient with coronary heart disease. A 79-year-old male patient diagnosed with coronary heart disease suddenly complained of a black shadow blocking his left eye approximately 3 min after the intravascular ultrasound examination was completed. The patient was diagnosed with branch retinal arteriolar occlusion in the left eye after completing ophthalmic examination. To the best of our knowledge, this is the first report of acute branch retinal arteriolar occlusion after a coronary artery intravascular ultrasound examination.

KEYWORDS

branch retinal arteriolar occlusion, intravascular ultrasound, case report, coronary heart disease, acute

Introduction

The central retinal artery and its branch arterioles are considered terminal branches providing blood to the central retina. Disruption of blood flow leads to ischemia of the inner retinal cell layers and ganglion cell death, characterized by sudden and painless visual impairment. Retinal artery occlusion may affect the main central retinal artery or its arteriolar branches with varying degree of visual impairment dependent upon the extent of ischemic damage to the central retinal. Many different causes of retinal artery occlusion have been identified with proximal embolism being considered one of the most important pathophysiologic mechanisms.

Coronary heart disease is a common heart disease that leads to myocardial ischemia, hypoxia, and even necrosis via various mechanisms, and it has high morbidity and mortality rates worldwide (1, 2). We report a case of branch retinal arteriolar occlusion after intravascular ultrasound examination of the coronary artery in a patient with coronary heart disease.

Case report

A 79-year-old male with known coronary heart disease and past coronary artery stenting of the left anterior descending artery presented to our hospital with new chest tightness and discomfort, which developed during the last month. Coronary CT angiography performed in our outpatient department showed that the left anterior descending coronary stent was unobstructed, and the right coronary artery

had moderate stenosis in the proximal segment and severe stenosis in the middle segment. We planned to review the coronary angiography and admit the patient for coronary heart disease. The patient has a history of hypertension of 3 months duration, with a maximum blood pressure of 160/70 mmHg, and is currently not being administered antihypertensive medication. In addition, the patient had high fasting blood sugar levels for 3 months but denied any history of eye or other diseases. Upon admission, no significant abnormalities were found in the heart and lungs during physical examination. The three myocardial markers and N-terminal B-type natriuretic peptide precursor tests showed no significant abnormalities. The electrocardiogram showed no significant abnormalities, but the chest CT scan showed small nodules in both lungs and calcified plaques in the coronary and aortic arteries. Cardiac ultrasound revealed left atrial enlargement, aortic valve calcification, and mild reflux. The diagnoses upon admission were (1) acute coronary syndrome, (2) coronary atherosclerotic heart disease after intracoronary stent implantation, (3) grade 2 hypertension (extremely high risk), and (4) impaired glucose tolerance.

Before the operation, the patient was given aspirin and clopidogrel bisulfate for antiplatelet therapy and low-molecular-weight heparin calcium for anticoagulation. On the second day of admission, a coronary angiography was performed in the cardiac catheterization room. Heparin anticoagulation therapy was administered to the patient during the operation. The angiographic report showed that the anterior descending branch had a stent shadow in the proximal segment, no restenosis in the stent, and approximately 30%–40% stenosis in the middle segment; the circumflex branch had approximately 30%–40% proximal stenosis; and the right coronary artery had approximately 50%–60% stenosis in the proximal segment and approximately 70% localized stenosis in the middle segment (Figure 1).

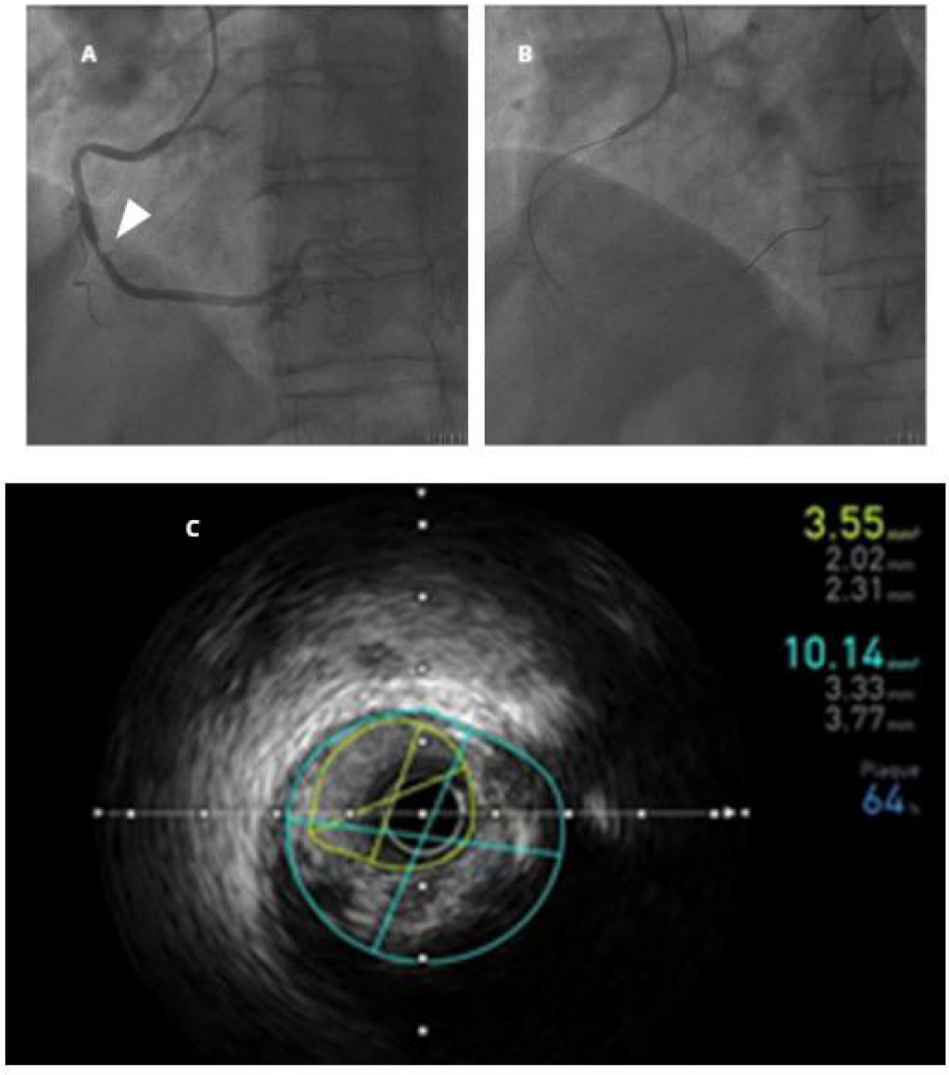

FIGURE 1
(A) Right coronary angiography, with white arrows indicating the location of vascular lesions; (B,C) intravascular ultrasound examination.

After coronary angiography, the patient did not report any discomfort in the eyes or other parts of the body. After the patient and their family consented, intravascular ultrasound examination was performed on the right coronary artery (Figure 1). After the SAL.75 guide tube was in place, the Sion guidewire was placed in the distal segment of the right coronary artery. The intravascular ultrasound examination showed that the minimum cross-sectional area of the right coronary artery was approximately 3.55 mm^2, with a plaque burden of 64%. Therefore, coronary intervention therapy was proposed. At this point, approximately 3 min after the intravascular ultrasound examination the patient complained of a black shadow blocking his left eye. Considering the possibility of left fundus hemorrhage in the patient, the coronary intervention treatment was temporarily suspended, and the surgery was terminated after consultation with the patient's family. We immediately consulted with an ophthalmologist. The ophthalmologist diagnosed branch retinal arteriolar occlusion in the left eye after bedside direct fundoscopy. The necessity and risks of intravenous thrombolysis for retinal artery occlusion were explained to the patient and their family. After careful consideration, the patient and their family refused intravenous thrombolysis treatment. Anterior chamber puncture, eyeball massage to reduce intraocular pressure, sublingual administration of nitroglycerin, retrobulbar injection of atropine to dilate blood vessels, and systemic vasodilator administration were performed. Because of the nighttime emergency, no objective fundus examination could be performed. A detailed ophthalmologic examination was performed in the special examination room of the ophthalmology clinic the morning after the onset of the disease. Ophthalmological examination of the left eye revealed that the visual acuity (Log MAR) was 0.3, the intraocular pressure was 15 mmHg, the conjunctiva was free of congestion, the cornea was transparent, the pupil was round, the direct light reflection was dull, the lens was turbid, and the retinal artery of the superior temporal branch became thinner, with gray edema of the superior temporal retina. Fundus photos and optical coherence tomography are shown in Figure 2. Therefore, the patient was diagnosed with left eye branch retinal arteriolar occlusion and left eye senile cataract.

The cranial MRI did not show any new cerebral infarction. Carotid artery ultrasound revealed a thickening of the intima-media and multiple plaques in both carotid arteries. After 1 week of treatment, the patient reported no significant improvement in the occlusion of the left eye by the black shadow. The patient and their family requested to be discharged. At discharge the diagnoses were: (1) coronary atherosclerotic heart disease with unstable angina pectoris after coronary stent implantation, (2) grade 2 hypertension (extremely high risk), (3) impaired glucose tolerance, (4) left eye branch retinal arteriolar occlusion, and (5) left eye senile cataract.

Discussion

Retinal artery occlusion is considered an ophthalmological emergency, the onset of which can lead to a sudden decline or even loss of vision. The causes of retinal artery occlusion are complex and mainly involve arterial spasm, embolism, endarteritis or atherosclerosis, and other causes of retinal artery blood flow interruption, resulting in retinal tissue hypoxia, degeneration, and necrosis. Common emboli include cholesterol emboli, platelet fibrin emboli, and calcification emboli. Cholesterol emboli are the most common, and they are relatively small and reflect yellow light. Platelet fibrin emboli are common in cases of atherosclerotic plaques, and they are large and gray-white in color. Calcified emboli are relatively rare, mostly single, white in color, dull, and oval in shape.

Retinal artery occlusion caused by coronary angiography and coronary intervention is very rare. Some scholars have reported retinal artery occlusion after a percutaneous coronary intervention (3–5). Previous studies have reported several cases of retinal artery occlusion related to coronary angiography (6–8). Branch retinal arteriolar occlusion occurred approximately 30 min after the completion of coronary angiography in this patient and only approximately 3 min after the completion of intravascular ultrasound examination. In addition, the patient had not undergone the interventional treatment when the retinal artery occlusion occurred. There was a close relationship between the intravascular ultrasound examination and the branch retinal arteriolar occlusion. To our knowledge, there are currently no reports of retinal artery occlusion after a coronary artery intravascular ultrasound examination.

The patient in this case developed branch retinal arteriolar occlusion shortly after intravascular ultrasound examination, which is likely due to the shedding or tearing of the intima or the detachment of small coronary artery plaques caused by the entry and exit of the intravascular ultrasound catheter used during the ultrasound examination. Small plaques may also exist in blood vessels in other parts of the body, but there may be no obvious symptoms in other body parts because of compensatory blood flow via collateral circulation. However, the retinal artery is a terminal artery, and once it is blocked, patients may experience significant visual impairment or visual field defects. The patient developed branch retinal arteriolar occlusion 3 min after the procedure, possibly due to tiny emboli dislodged by the ultrasound catheter that circulated to the retinal branch artery after passing through several blood channels in the body. The diameter of the branch retinal artery is very small, making it more likely to be occluded. In addition, we observed that the ultrasound catheter probably touched the plaque during the ultrasound examination. Moreover, the brightness and morphology of the thrombus during the fundus examination were highly homologous to the echo intensity of the plaque in contact with the catheter during the intravascular ultrasound examination. Therefore, we concluded that the thrombus in the retinal branch artery of the patient was closely related to the intravascular ultrasound examination. To the best of our knowledge, this is the first report of acute branch retinal arteriolar occlusion after a coronary artery intravascular ultrasound examination.

It is important to note, that conservative treatment approaches in retinal artery occlusion, such as ocular massage or anterior chamber paracentesis have not been shown to be effective in

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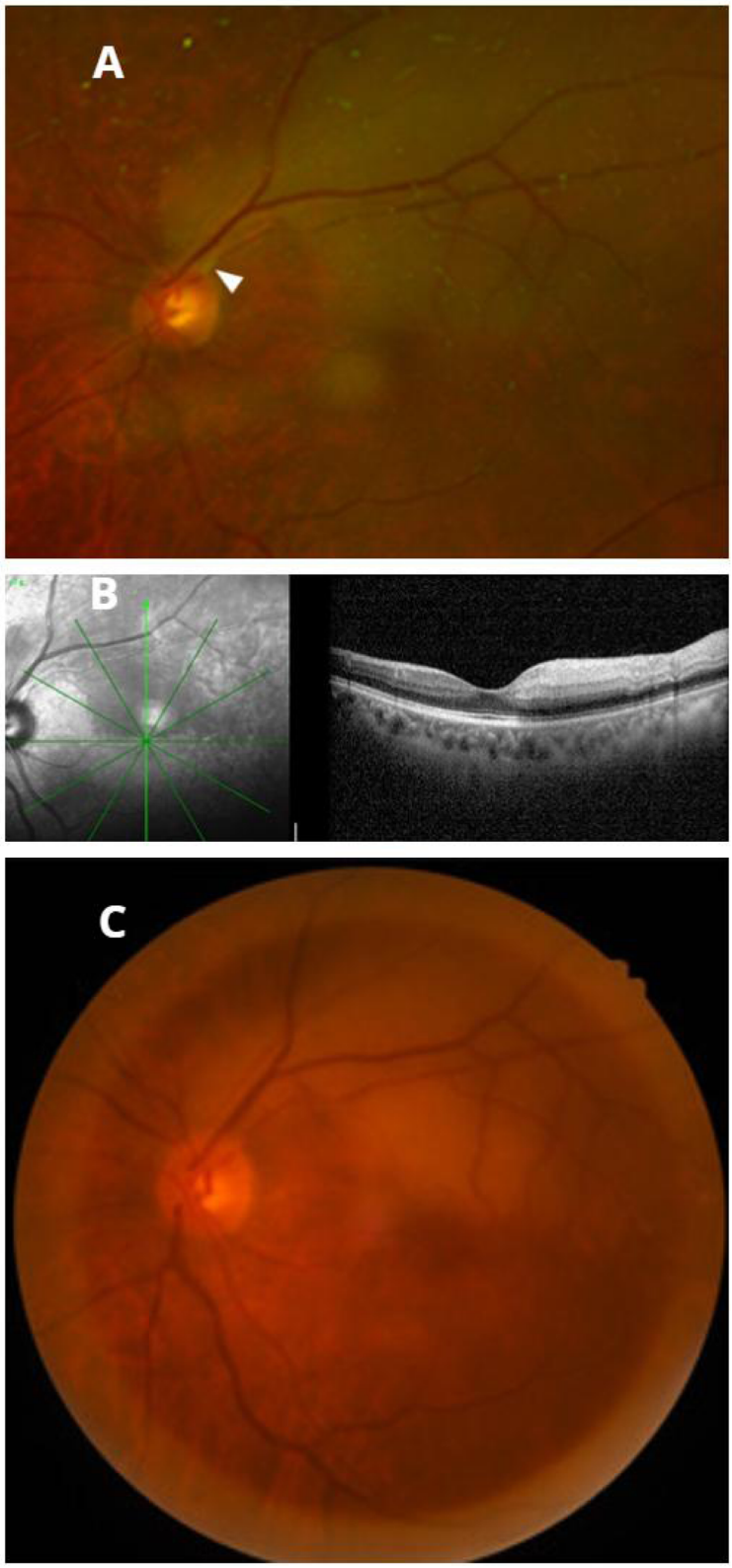

FIGURE 2
(A) Optos ultra-widefield imaging system: the white pointed tip indicates the location of the gray-white thrombus in the left temporal branch of the retinal artery. **(B)** Optical coherence tomography shows edema, thickening, and enhanced reflex in the inner layer of the temporal retina of the left eye. **(C)** Photograph of the posterior pole of the fundus: the retinal artery of the superior temporal branch became thinner with gray edema of the superior temporal retina.

randomized controlled trials. We applied the aforementioned measures because intravenous thrombolysis treatment was refused by the patient and their family. Recent studies report a favorable visual outcome in patients with retinal artery occlusion receiving early intravenous thrombolysis—however randomized controlled trials are still ongoing (e.g., the REVISION trial) (9).

Retinal artery occlusion is an ophthalmic emergency that can cause sudden loss of vision or even loss of light perception in patients, and it requires early diagnosis and treatment. With the increase in the incidence rate of coronary heart disease and the increasing number of invasive cardiac examinations and operations, cardiologists should improve their understanding of ocular complications of intravascular ultrasound. During intravascular ultrasound examination and related procedures, attention should be paid to changes in the patient's visual quality to alert cardiologists to possible retinal artery occlusion caused by intravascular ultrasound examination and other procedures. Preventing the occurrence of this complication is particularly important; therefore, the ultrasound catheter should be gently inserted and removed from the coronary artery during intravascular ultrasound examination to prevent embolism caused by intimal or plaque detachment.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Ethics Committee of Zibo Central Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

GZ: Writing – original draft, Writing – review & editing. CS: Writing – review & editing. HT: Writing – review & editing. YS: Writing – original draft, Writing – review & editing.

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Conflict of interest

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Publisher's note

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Case Report: Dual-lumen microcatheter-facilitated wiring technique to correctly access a protruded aorto-ostial stent: a case series

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Background: Percutaneous coronary intervention (PCI) through the aorto-ostial coronary stent that is protruding into the aorta remains a technical challenge because of the poor coaxial alignment of the guiding catheter and the inability to advance the guidewire into the distal vessel through the stent's central lumen. In this article, we introduce a dual-lumen microcatheter–facilitated wiring technique performed on two patients to overcome this difficulty.
Case summary: The first case was a 75-year-old man who presented with chest pain. He was diagnosed with an unstable angina, and coronary angiography showed near-total in-stent occlusion of the previously placed stent protruding into the aorta. Despite several attempts, the guidewire passed through the side strut of the stent instead of the central stent lumen. Thus, we placed the tip of the microcatheter proximally to the side strut, outside the stent. Then, a second wire was passed through the central lumen successfully. After confirming the wire's position via intravascular ultrasound, we inflated a drug-eluting balloon, subsequently obtaining a successful angiographic result. The second case was a 78-year-old woman diagnosed with non-ST segment elevation myocardial infarction. Coronary angiography revealed tight stenosis at the ostial left anterior descending artery with a previous stent deployed from the left main to the circumflex artery. Owing to the excessive overhanging stent into the aorta, the wire could not be advanced into the stent's central lumen. However, with the facilitation of a dual-lumen microcatheter, a second wire successfully passed through the stent's central lumen. Finally, the patient received a successful PCI with a stent.
Conclusion: A dual-lumen microcatheter–facilitated wiring technique may be useful in overcoming wiring difficulty caused by the excessive protrusion of an aorto-ostial stent into the aorta.

KEYWORDS

coronary artery stent, in-stent restenosis, percutaneous coronary intervention, myocardial infarction, acute coronary syndrome

Introduction

Performing percutaneous coronary intervention (PCI) in patients with protruding aorto-ostial stent may be technically challenging because of a poor coaxial alignment of the guiding catheter and the inability to insert a wire through the central stent lumen (1). Several techniques, including a double-wire technique, balloon-assisted technique, snare technique, side-strut sequential ballooning technique, and guide extension catheter-facilitated side-strut stenting, have been proposed to treat this challenge. However, these methods have some limitations, such as frequent failure and procedure-related complications (2). Herein, we describe two cases of chest pain that necessitated technically challenging PCI for complex lesions with excessive stent protrusion into the aorta. The two cases were intervened by a novel dual-lumen microcatheter (DLC)-facilitated wiring technique with a successful angiographic result.

Case presentation

Case report 1: the right coronary artery

A 75-year-old man presented with chest pain diagnosed as unstable angina and previously underwent multiple PCIs with stents. Coronary angiography revealed tight in-stent restenosis of the ostial right coronary artery (RCA). Fluoroscopy revealed that the previous ostial RCA stent was excessively protruding into the aorta. The RCA was engaged using a Judkins Right 3.5 guiding catheter. Passing the wire through the central column was extremely difficult because the guiding catheter was unstable. After several attempts, the SION blue (Asahi Intecc, Aichi, Japan) wire could only cross through a side strut of the previous stent and advance deeply into the distal RCA. Furthermore, the double-wire technique using a second guidewire failed to pass through the stent's central lumen. After we loaded Sasuke DLC (Asahi Intecc, Aichi, Japan) onto the wire and placed the DLC tip in the proximity of the side strut, the guiding catheter was slightly withdrawn away from the aortic wall. Ultimately, we achieved stable coaxial alignment of the guiding catheter a few millimeters away from the previous stent. A second SION (Asahi Intecc, Aichi, Japan) wire successfully accessed the central stent lumen through the over-the-wire port of the DLC, as confirmed by intravascular ultrasound (IVUS). It took 22 min from the introduction of DLC to the confirmation of the proper position of the second wire by IVUS. A 3.5×15 mm drug-eluting balloon was inflated at high pressure after proper balloon angioplasty preparation. The final angiography revealed excellent results without procedure-related complications (Figure 1).

Case report 2: the left main coronary artery

A 78-year-old woman presented with chest pain and elevated cardiac biomarkers. She experienced myocardial infarction with PCI from the left main to the circumflex coronary artery and RCA at another hospital five years ago. Coronary angiography demonstrated severe stenosis of the ostial left anterior descending artery crossed by the previous stent. The left main portion of the stent was protruding deeply into the aorta. We then selected a Judkins Left 3.5 guiding catheter. However, the initial SION blue wire failed to pass through the stent's central lumen but entered the left circumflex artery through the side strut of the stent. Using a Sasuke DLC loaded onto the SION blue wire, we successfully advanced a second SION wire into the stent's central lumen through the DLC's over-the-wire port, and its position was confirmed by IVUS. It took 6 min from employing the DLC to the confirmation of central stent lumen position of the wire by IVUS. Subsequently, PCI with stent was performed successfully (Figure 2).

Discussion

The aorto-ostial stent often protrudes into the aorta and more so after proximal optimization or aortic flaring, which is shown to elongate the stents (3). Repeat PCI on previously stented aorto-ostial lesions is extremely challenging and is associated with a higher risk for procedure-related complications. The DLC-facilitated wiring technique is a new approach to successfully pass through the stent's central lumen in patients with a protruding prior stent in the aorto-ostial location. DLC has been used to facilitate PCI for bifurcation lesion and chronic total occlusion (CTO). In bifurcation lesion, DLC is helpful for side-branch wiring because of the angulated side branches when conventional wiring has failed. DLC may also be useful for patients requiring a parallel wire technique during antegrade CTO PCI. The main concept of DLC is that the first wire acts as a guide through the rapid-exchange port and supports the second wire through the over-the-wire port that can be manipulated to find the target lumen (4). In DLC-facilitated wiring technique, we insert the first wire to the cell formed by the stent's strut and advance it deeply into the distal vessel; meanwhile, the DLC is positioned close to the stent, providing ample support. Subsequently, we manipulate the guiding catheter to create a slight distance from the stent ostium and align it coaxially. The DLC tip need not be anchored directly to the side strut; its proximity to the stent is usually sufficient. Then, we pass a second wire into the stent's central lumen through the over-the-wire port of the DLC. Once the second wire successfully traverses the central stent lumen, we remove the DLC and the first wire. Confirming the position of the second wire using intracoronary imaging is crucial, and if unsuccessful, we repeat the process (Figure 3).

Several aorto-ostial wiring techniques, including a double-wire technique (1), balloon-assisted access technique (2), double-guide snare technique (5), side-strut sequential ballooning technique (6), and guide-extension–facilitated side-strut stenting (7), have been proposed to address this challenge. However, we need to be aware of the caveats of each method. In the double-wire technique (1), a single wire must provide all the support for the catheter while being manipulated for alignment; consequently, system instability and prolonged PCI time often occur. The balloon-assisted access technique (2) offers enhanced support

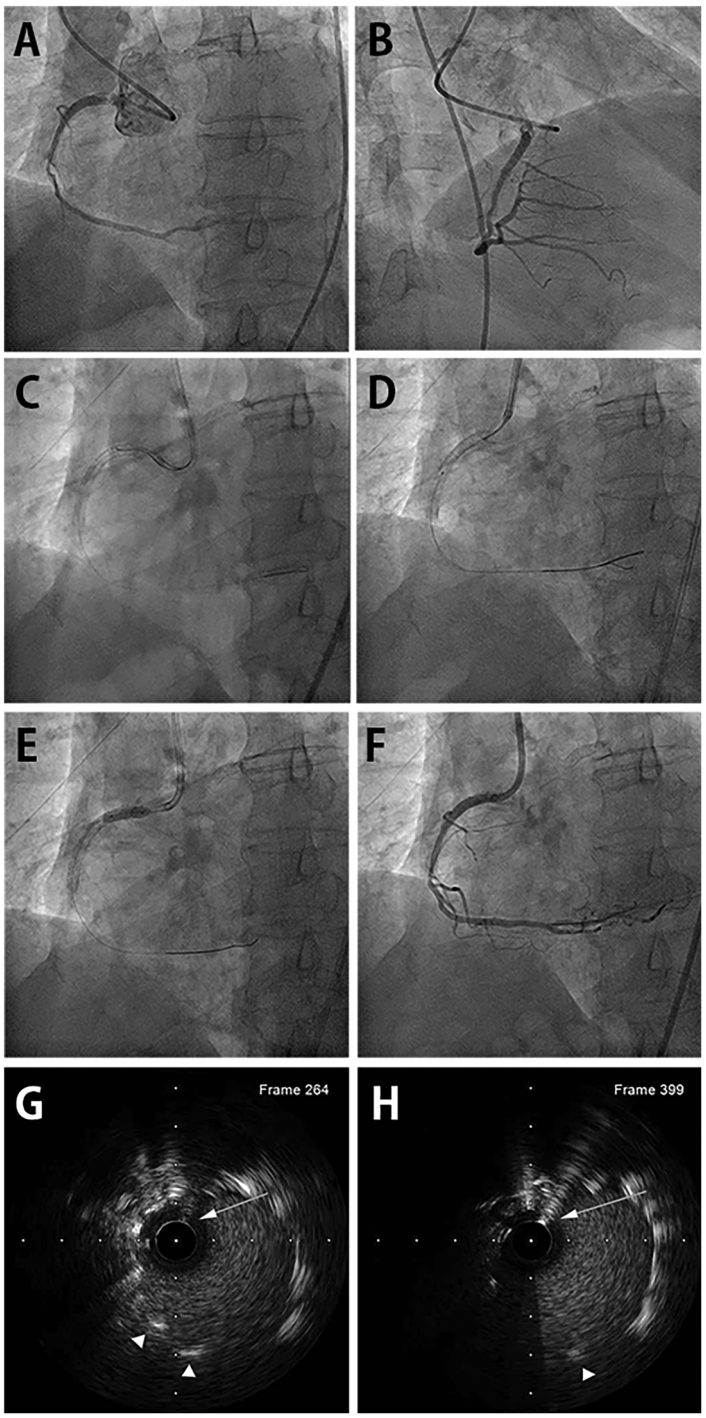

FIGURE 1
DLC-facilitated aorto-ostial wiring technique in the RCA. **(A)** Coronary angiography from the left anterior oblique view shows in-stent restenosis of the previously placed aorto-ostial RCA stent. **(B)** Non-selective angiography from the right anterior oblique view also reveals the in-stent restenosis, alluding challenging cannulation. **(C)** The first wire is inserted in the RCA through the stent-side strut. The second wire successfully enters the central stent lumen facilitated by DLC. **(D)** The wire's central position is confirmed using an intravascular ultrasound catheter. **(E)** The drug-eluting balloon is inflated after proper lesion preparation. **(F)** Final coronary angiography shows a good angiographic result with coaxially engaged guiding catheter. **(G)** IVUS image revealing luminal position of the second wire in the mid portion of the protruding stent outside the coronary artery. First wire was retracted before IVUS imaging. **(H)** IVUS image showing luminal position at the very proximal end of the protruding stent. DLC, dual-lumen microcatheter; RCA, right coronary artery; IVUS, intravascular ultrasound. (Arrows indicate second wire. Arrowheads indicate stent strut.)

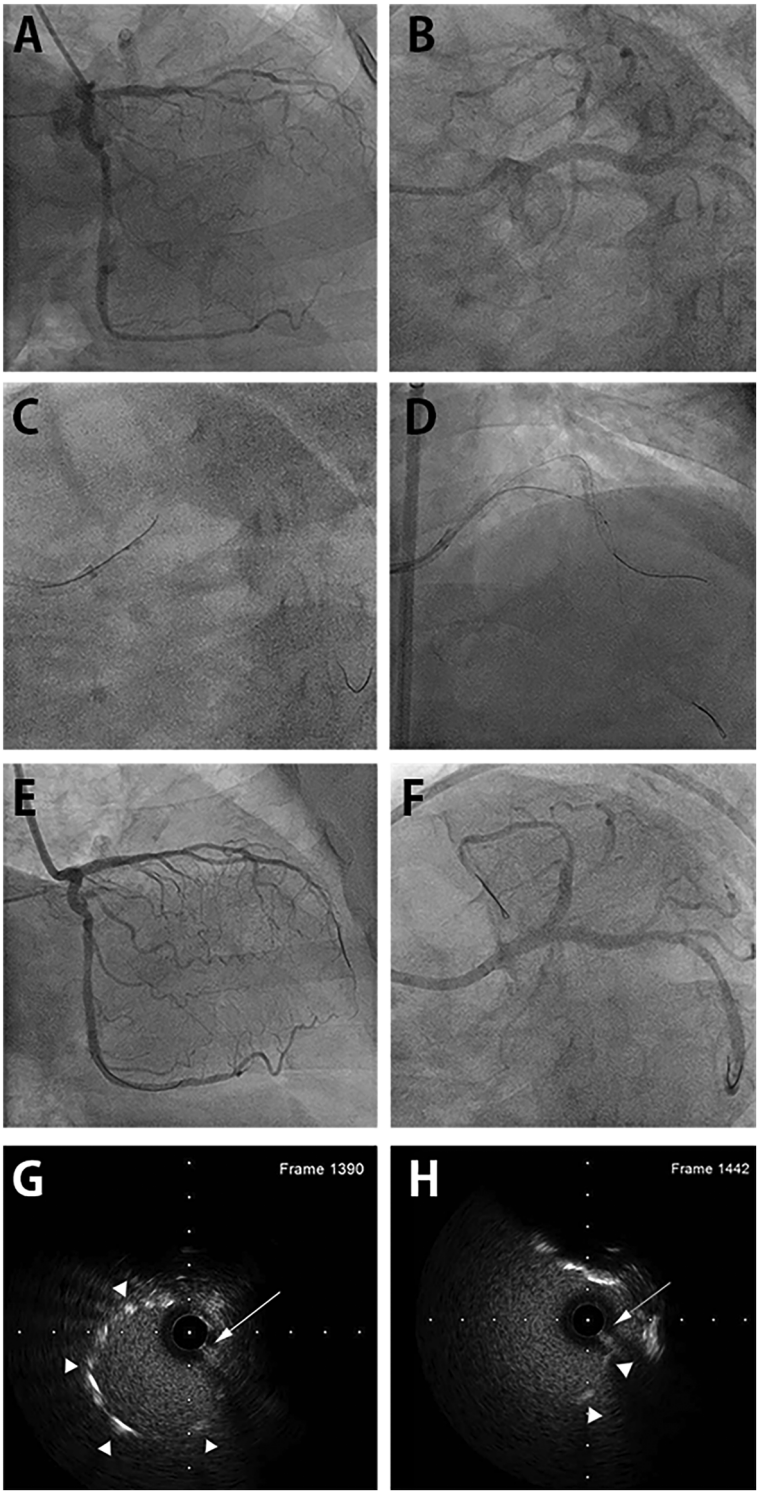

FIGURE 2
DLC-facilitated aorto-ostial wiring technique in the left main coronary artery. **(A)** Coronary angiography with a misaligned catheter from the right anterior oblique caudal view demonstrates a tight ostial stent in the left anterior descending artery and a patent stent spanning from the left main to the left circumflex artery. **(B)** The left anterior oblique caudal view exhibits the same finding, with the catheter tip placed next to the protruding aorto-ostial stent. **(C)** DLC is loaded onto the first wire and anchored at the protruding stent strut. The second wire enters the central stent lumen. **(D)** The wire's central position is confirmed by IVUS. **(E)** The final angiography from the right anterior oblique caudal view after stenting shows acceptable angiographic results with proper coaxial engagement of the guiding catheter. **(F)** Angiography from the left anterior oblique caudal view demonstrates a well-expanded stent with the coaxial position of the guiding catheter. **(G)** IVUS image revealing luminal position of second wire in the mid portion of the protruding stent outside the coronary artery. First wire was retracted before IVUS imaging. **(H)** IVUS image showing luminal position at the very proximal end of protruding stent. DLC, dual-lumen microcatheter; IVUS, intravascular ultrasound. (Arrows indicate second wire. Arrowheads indicate stent strut.)

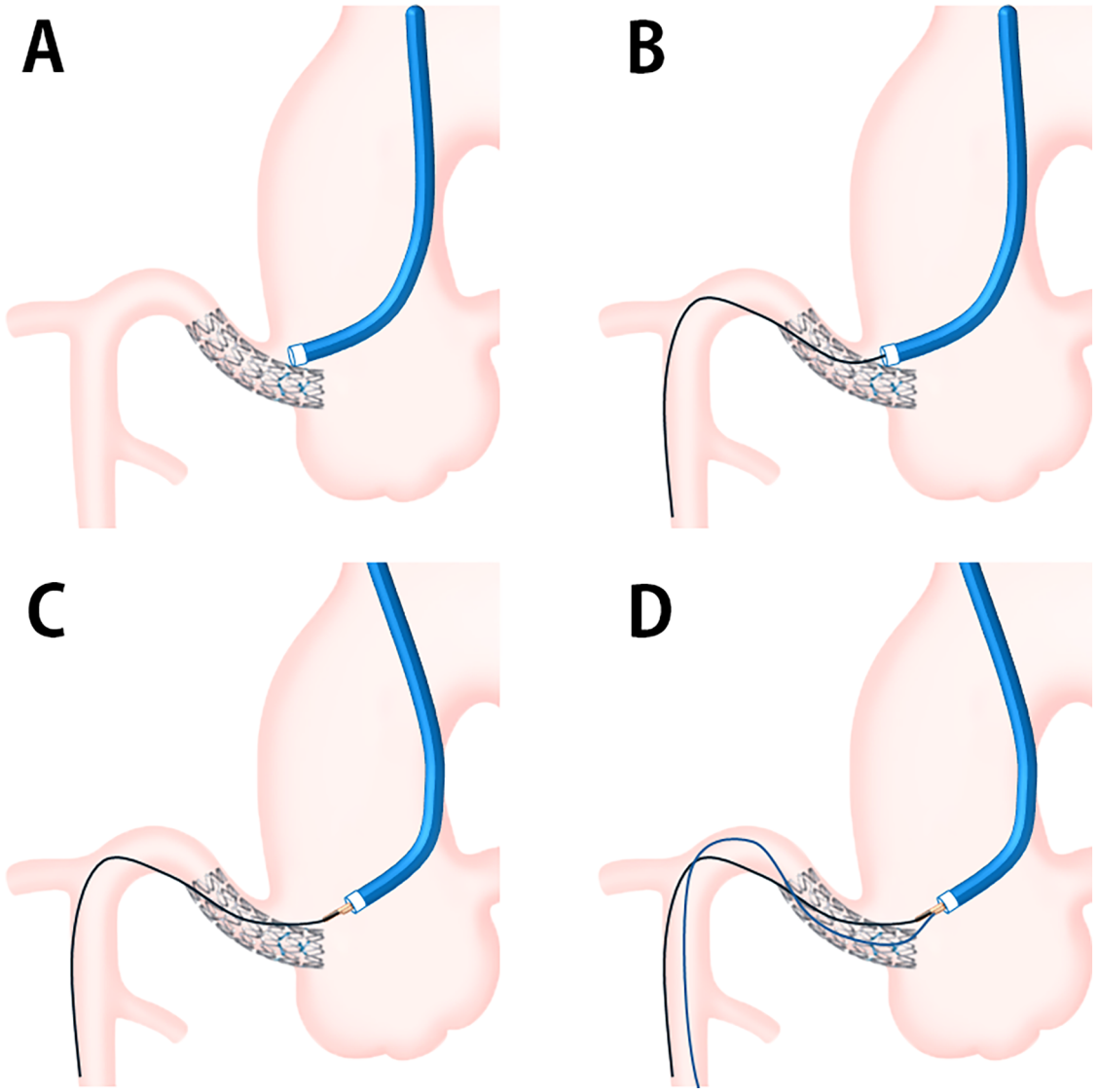

FIGURE 3
Schematic presentation of DLC-facilitated wiring technique. **(A)** Coaxial cannulation to the protruding aorto-ostial stent segment is challenging. **(B)** The first wire is advanced across the stent strut and deeply into the coronary artery. **(C)** DLC is loaded onto the first guidewire and placed on or near the protruding stent segment, providing sufficient support for guiding catheter manipulation to achieve coaxial access. **(D)** The second guidewire enters the central stent lumen through the over-the-wire port. DLC, dual-lumen microcatheter.

with minimal risk of stent deformation, avulsion, or extraction. However, continual torquing of the wire for central lumen wiring may cause entanglement and intertwining with the first wire and balloon catheter, thereby compromising the procedure. Moreover, the double-guide snare technique (5) requires double arterial access. Given that the side-strut sequential ballooning technique (6) and guide-extension–facilitated side-strut stenting technique (7) are performed through the side strut, the risk of stent deformation increases; hence, they are used only for extremely protruding stents as the last resort. Other potential complications, such as wiring failure, stent avulsion, deformation, and extraction, should also be considered (7, 8). The DLC-facilitated aorto-ostial wiring technique provides sufficient support for creating a gap between the catheter and the stent while avoiding device intertwining in the shaft of the guiding catheter as well as stent deformation and avulsion, even during prolonged procedures. It applies to both aorto-ostial RCA and left main coronary artery with protruding stents, as shown in this report. Furthermore, our experience demonstrates that this technique substantially reduces the time required to wire the stent's central lumen. After passing the second wire, intracoronary imaging confirmation of its proper location is mandatory. While we utilized the Sasuke DLC, other DLCs designed for the same purpose from different companies may also offer similar performance benefits. The difference between the recently reported DLC and the floating-wire technique by Wong et al. (9) is that DLC is anchored at or near the protruding stent segment, providing augmented support and coaxiality at the same time until central lumen wiring is achieved;

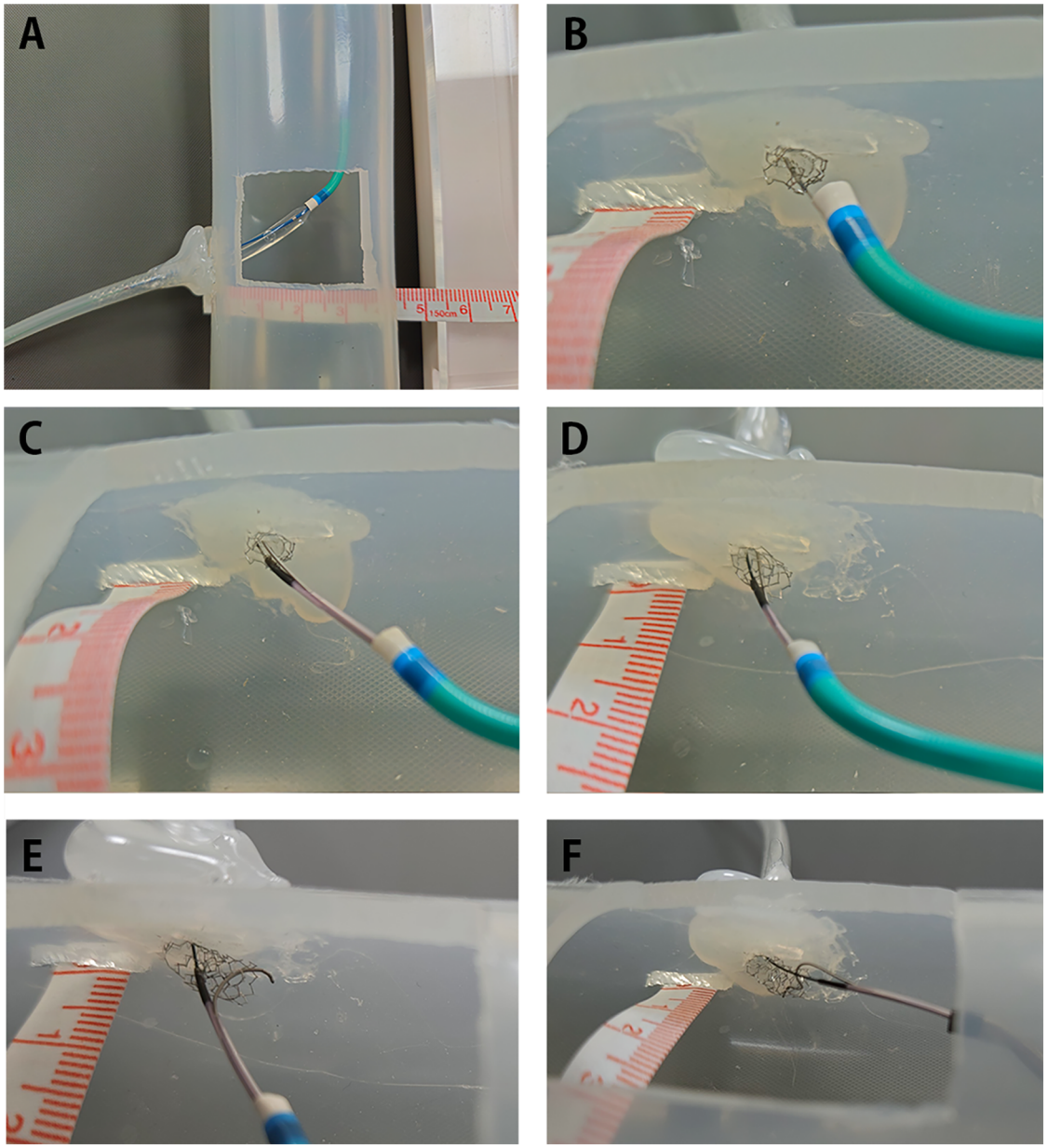

FIGURE 4
Bench test of wiring a protruding aorto-ostial stent. Bench test showing DLC-facilitated wiring for 2, 4, and 6 mm stent protrusion. Note that the first wire in each test crossed the stent cell from below. The procedural times in this bench test do not include the time spent on location confirmation using intracoronary imaging. The guide catheter used in **(A–E)** was a 6 Fr Judkins Right. Video files for **(C–F)** are available. **(A)** A silicone tube with a diameter of 4.0 mm, representing the right coronary artery, was attached to a silicone tube with a diameter of 40 mm, simulating the aorta. A rectangular window was cut to allow clear visualization of the wiring process. A 4-mm Synergy (Boston Scientific, Natick, MA, USA) or Orsiro (Biotronik AG, Bülach, Switzerland) drug-eluting stent was deployed to achieve the intended length of protrusion with sequential flaring in each test. **(B)** Aggressive pushing of the guide catheter against the stent easily crushed the stent, complicating subsequent procedures. **(C)** Successful wiring into the central stent lumen when the stent protruded 2 mm into the aorta. It took approximately 3 min to correctly direct the wire, guided by visual observation. **(D)** Successful wiring into the central stent lumen when the stent protruded 4 mm into the aorta. It took approximately 10 min to correctly direct the wire, guided by visual observation. **(E)** Even with meticulous manipulation guided by visual observation, the stent column tended to tilt upward, losing coaxial alignment with the second wire when the stent protruded 6 mm into the aorta. Repeated attempts failed to pass the wire correctly after 30 min. **(F)** Exchanging the guide catheter for a 6 Fr Amplatz Left improved alignment but also failed to pass the second wire when the stent protruded 6 mm into the aorta. Although the second wire successfully entered the central lumen a few times, it frequently lost its correct position, escaping through the side cell. Attempts to use stiff or polymer-coated soft wires also failed. DLC, dual-lumen microcatheter.

therefore, it does not serve solely as a tool to fine-tune the coaxiality over the dummy wire.

There are several limitations to our technique. First, aggressively pushing the system, such as the DLC and guide catheter, may crush the stent and should be avoided. Second, although we successfully managed to place the wire properly in the two cases mentioned, it may not always be possible to pass the wire into the central stent lumen within a limited time

frame. Running intracoronary imaging with each attempt and restarting the technique if the second wire crosses the side cell will prolong the procedure and may be inappropriate in certain clinical situations. Third, exaggerated stent protrusion (more than a few millimeters) may hinder the DLC from keeping the guide catheter aligned with the axial stent opening. We performed a bench test to explore this issue (Figure 4; Supplementary Video S1). Initially, we hypothesized that utilizing the Sasuke DLC would enable us to correctly wire the central lumen up to 6-mm protrusion, as the distance between the rapid exchange port and the over-the-wire port is 6.5 mm, which should direct the second wire from the proximal stent lumen. We were able to successfully position the wire for up to 4 mm of protrusion within an acceptable time frame. However, when the protrusion exceeded 4 mm, the stent lumen lost coaxial alignment, and it was no longer possible to wire through it from the proximal beginning. Therefore, the cut-off length for successfully wiring from the proximal stent lumen appears to depend on the protrusion length itself rather than the properties of the DLC. For excessive protrusions greater than 4 mm, creating a new central lumen through the side cell may be the only practical option. Since it is difficult to accurately recognize the protruding stent length without prior PCI records or information, determining when to stop attempting to wire the central lumen can help reduce unnecessary fluoroscopy exposure and procedure time—an issue that our study could not address. Finally, our report is based on only two cases, and comparisons regarding whether DLC-facilitated wiring is superior to other techniques in terms of safety and procedural time cannot be made. Further studies with a larger sample size are needed to explore the appropriate strategy for specific scenarios. However, the purpose of our study is to report the utility of easily applying familiar instruments to challenging PCI situations.

Conclusions

In conclusion, the DLC-facilitated wiring technique is useful in overcoming the difficulty of wiring the aorto-ostial stent that protrudes excessively into the aorta while minimizing the risk of wire intertwining, stent strut deformation, and procedural failure.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material; further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Institutional Review Board of the Pusan National University Yangsan Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

SK: Data Curation, Investigation, Methodology, Project Administration, Resources, Validation, Visualization, Writing – original draft. KC: Conceptualization, Formal Analysis, Funding Acquisition, Project Administration, Software, Supervision, Visualization, Writing – review & editing, Writing – original draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2025.1467926/full#supplementary-material

SUPPLEMENTARY VIDEO S1
Bench test of wiring a protruding aorto-ostial stent.
Clip 1 2-mm protrusion.
Clip 2 4-mm protrusion.
Clip 3 6-mm protrusion (JR, failed).
Clip 4 6-mm protrusion (AL, failed).

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Case Report: Complete AV block in two patients with a congenital absence of the right coronary artery: an unusual correlation

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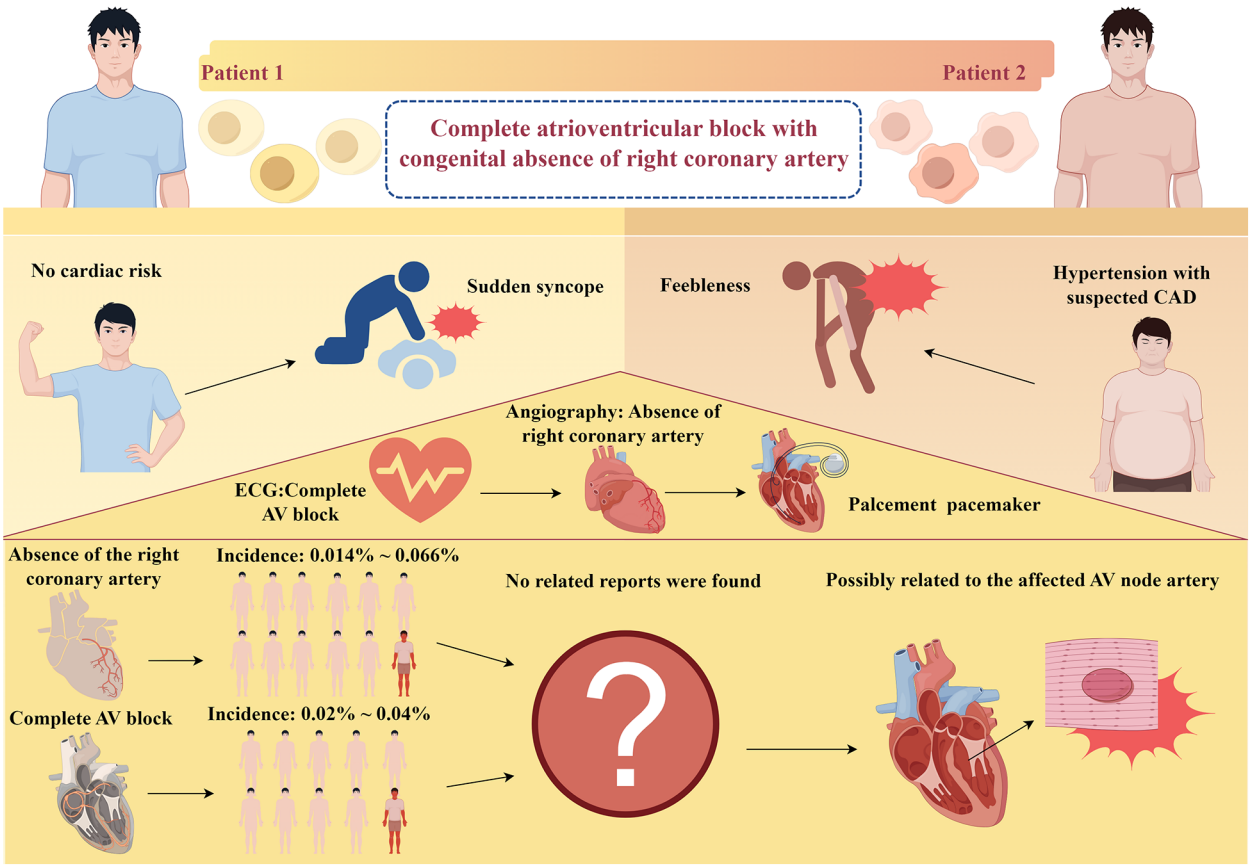
Background: Congenital absence of the right coronary artery (RCA) is an extremely rare coronary anomaly with a very low incidence in the general population. The prevalence of complete atrioventricular (AV) block also appears to be low. No previous reports have documented the coexistence of congenital absence of the RCA and complete AV block in the same patient.
Case summaries: Case 1 was a 52-year-old man with no significant past medical history who experienced syncope. The initial ECG revealed complete AV block with a non-specific ST-T segment. Coronary angiography showed mild, non-obstructive atherosclerosis in the dominant left circumflex artery (LCx), which continued along the anatomical course of the RCA. The patient underwent a dual-chamber pacemaker implantation for complete AV block. Case 2 was a 79-year-old man with a history of hypertension and coronary heart disease who presented with gradually worsening fatigue lasting 6 h. ECG showed complete AV block with a non-specific ST-T segment. Coronary angiography revealed an abnormal origin of the RCA arising from the distal portion of a dominant LCx, which retrogradely followed the course of a normal RCA to the base of the heart. The patient also underwent a dual-chamber pacemaker implantation for complete AV block.
Conclusion: These two cases represent the first reported instances of complete AV block coexisting with congenital absence of the RCA, where the LCx supplied the territory of the RCA without evidence of myocardial infarction.

KEYWORDS

congenital absence of the right coronary artery, complete atrioventricular block, coronary angiography, arrhythmia, case report

Highlights

- Rarity of congenital absence of right coronary artery: Congenital absence of the right coronary artery (RCA) is a rare form of coronary artery disease with an extremely low incidence in the general population, estimated to be approximately 0.014%–0.066%.
- Uncommon nature of complete AV block: Although atrioventricular (AV) block is relatively common, complete AV block is relatively rare with a prevalence of approximately 0.02%–0.04%.
- Novel coexistence of RCA absence and complete AV block: The two cases demonstrate the coexistence of complete AV block with an isolated single coronary artery and an absent RCA, where the LCx supplies the territory of the RCA without evidence of myocardial infarction.



GRAPHICAL ABSTRACT
Two cases represent first reported instances of complete AV block coexisting with congenital absence of the RCA, where the LCx supplied the territory of the RCA without evidence of myocardial infarction.

Introduction

Congenital single coronary artery (SCA) is a rare anomaly in which only one coronary artery originates from a single coronary ostium to supply the entire heart (1, 2). The incidence of an SCA ranges from 0.024% to 1% in various reports involving over 1.4 million patients (1, 3, 4). SCA is sometimes associated with congenital cardiac structural abnormalities, such as pulmonary artery atresia, tetralogy of Fallot, and patent truncus arteriosus (5). Congenital absence of the right coronary artery (RCA) is a form of SCA with an extremely low incidence in the general population, estimated to be approximately 0.014%–0.066% (6).

Although atrioventricular (AV) block is relatively common, complete AV block is relatively rare (7). The prevalence in the general population appears to be low, approximately 0.02%–0.04% (8). In apparently healthy and asymptomatic individuals, the incidence of complete AV block is as low as 0.001% (9).

To date, there have been no reports of the coexistence of congenital absence of the RCA and complete AV block without a reversible cause. We present two cases of complete AV block coexisting with congenital absence of the RCA without evidence of myocardial infarction.

Summary figure

Case presentation

Case 1

A 52-year-old man with no past medical history or cardiac risk factors was brought to the emergency department following an episode of syncope. Initial ECG findings indicated complete AV block with a non-specific ST-T segment (Figure 1A). The patient's cardiac troponin T was slightly elevated (0.030 ng/mL, normal reference range <0.014 ng/mL), while cardiac troponin I was within the normal range (0.026 ng/mL, normal reference range <0.034 ng/mL). His family history was negative and free of cardiac events. A physical examination revealed bradycardia but no other significant abnormalities. No edema or congestion signs were found. A transthoracic echocardiographic examination and chest x-ray showed no obvious abnormality. The patient experienced another episode of syncope due to a long RR interval and was immediately implanted with a temporary pacemaker. Suspecting acute myocardial infarction, the patient underwent coronary angiography (Figures 1B–D and Supplementary Videos 1–3). The angiogram revealed that the left anterior descending artery (LAD) and the left

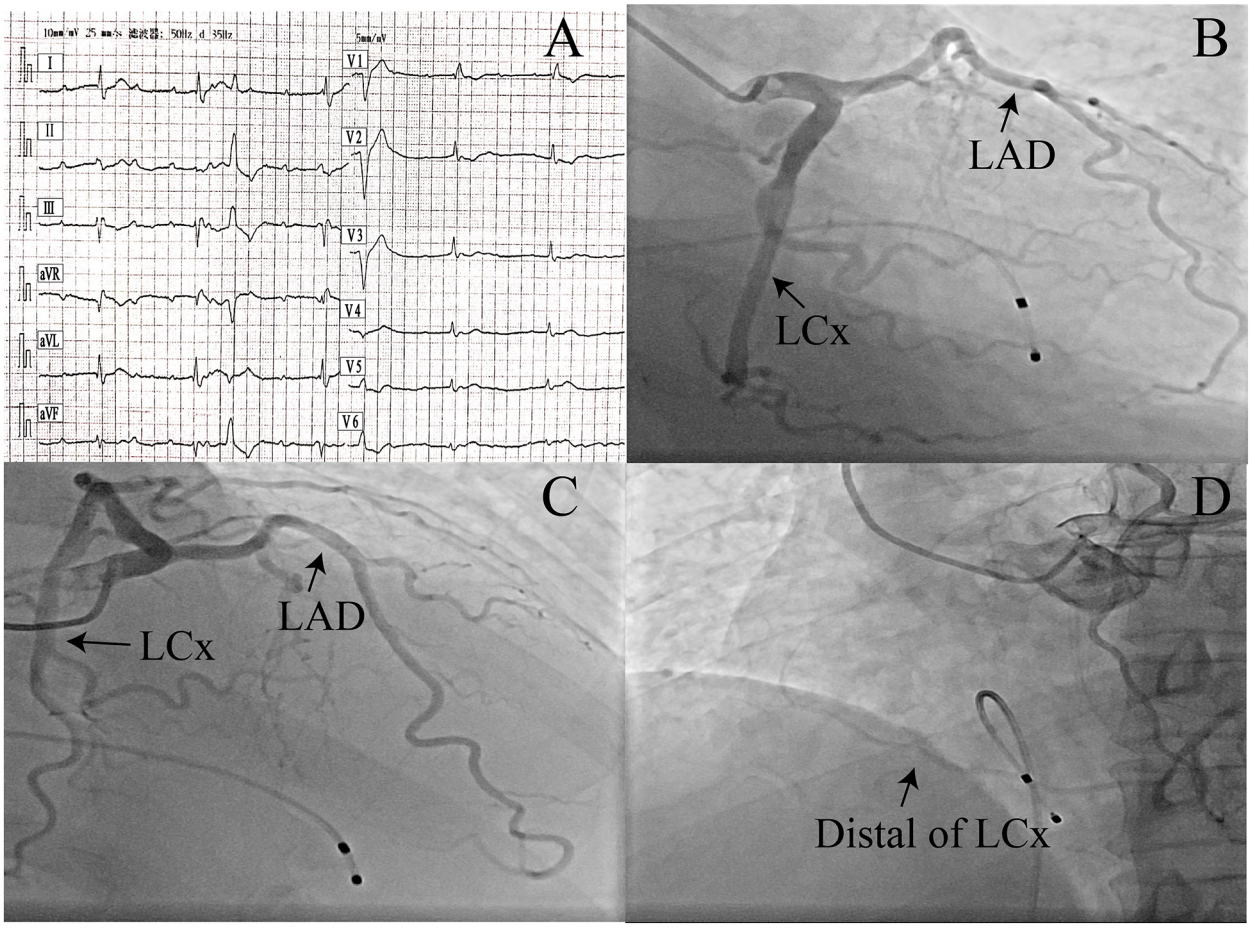


FIGURE 1
(A) Initial ECG in the emergency department: complete atrioventricular block and a non-specific ST-T segment. (B–D) Coronary angiography showing different coronary arteries and the left circumflex artery supplying the right coronary artery region (angiographic projections: B, RAO 26°/CAUD 30°; C, RAO 26°/CRAN 28°; D, LAO 38°/CAUD 3°). LAD, left anterior descending artery; LCx, left circumflex artery; RAO, right anterior oblique; CAUD, caudal; CRAN, cranial; LAO, left anterior oblique.

circumflex artery (LCx) originated from the left main coronary artery. Mild, non-obstructive atherosclerosis was observed in the dominant LCx, which continued along the anatomical course of the RCA. An injection into the right sinus of Valsalva unveiled the absence of a right coronary ostium separate from the aorta. When arriving at a diagnosis for this case, considerations of differential diagnoses, such as right coronary artery occlusion, were taken into account. No additional imaging tests, such as CT scanning or cardiac MRI, were performed, as the vessel course was clear on angiography alone. Five days later, the ECG still showed complete AV block with a low heart rate, and the patient then underwent a dual-chamber pacemaker implantation. At follow-up visits, the patient reported no discomfort.

Case 2

A 79-year-old man with a history of hypertension and coronary heart disease presented to his general practitioner clinic with gradually worsening fatigue lasting 6 h. His heart rate was 30 beats per min (bpm), and his blood pressure was 170/100 mmHg. The patient was immediately transported to the emergency room.

On admission, his vital signs showed a heart rate of 45 bpm, blood pressure of 104/42 mmHg, and a temperature of 36.5 °C. The physical examination was otherwise unremarkable. ECG showed complete AV block with a non-specific ST-T segment and a heart rate of 38 beats/min (Figure 2A). Laboratory findings, which included cardiac troponin, were within normal limits. A transthoracic echocardiographic examination and chest x-ray showed no obvious abnormalities.

Given the history of suspected coronary heart disease, the patient was scheduled for coronary angiography (Figures 2B–D and Supplementary Videos 4–6). During catheterization, only one coronary ostium originating from the left coronary cusp could be cannulated, and several attempts with different catheters to identify the RCA ostium failed. The patient had an SCA arising from the left coronary cusp. The RCA

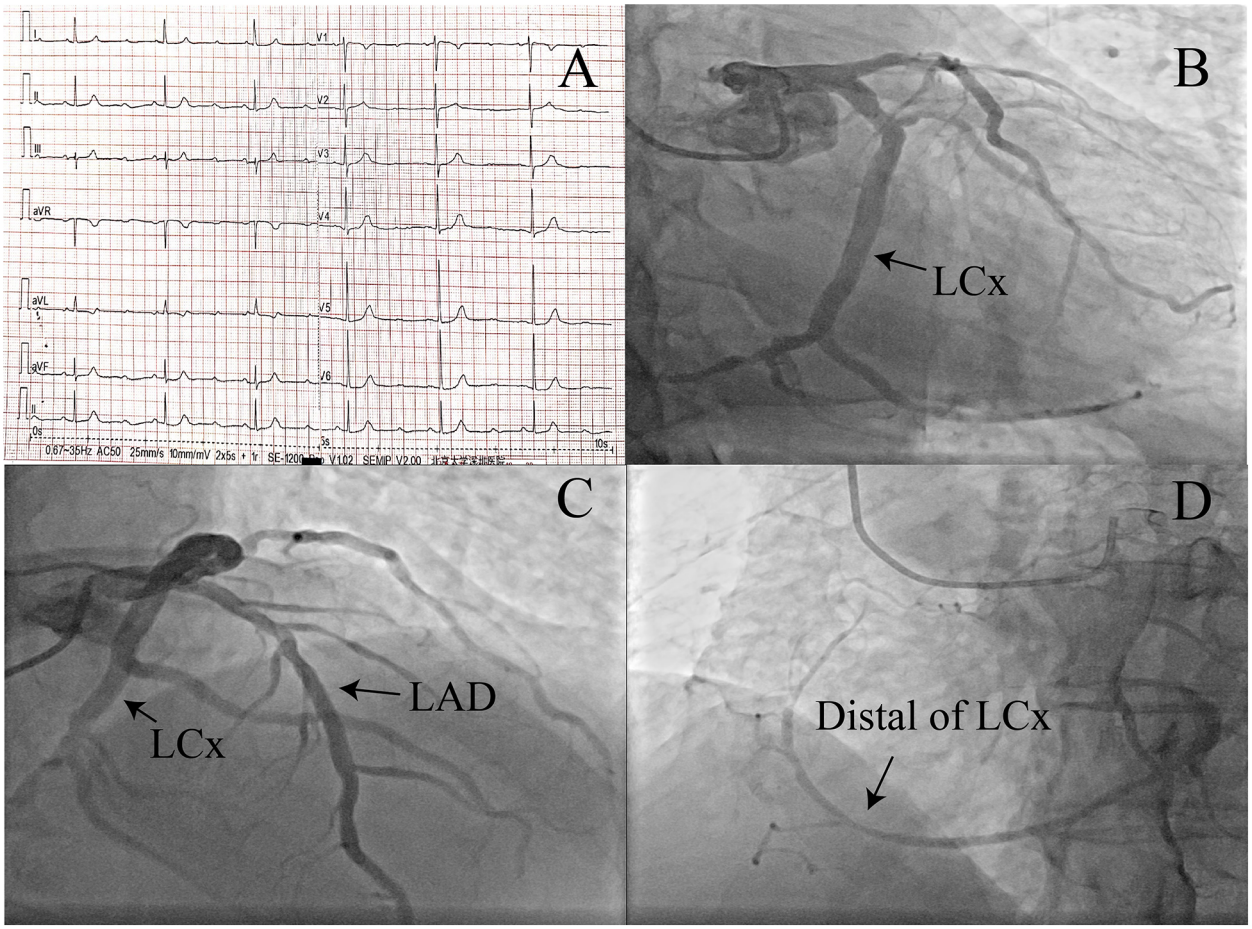


FIGURE 2
(A) ECG in the emergency department: complete atrioventricular block and a non-specific ST-T segment. (B–D) Coronary angiography showing different coronary arteries and the left circumflex artery supplying the right coronary artery region (angiographic projections: B, 0/CAUD 31°; C, RAO 2°/CRAN 36°; D, LAO 40°/CAUD 2°). LAD, left anterior descending artery; LCx, left circumflex artery; RAO, right anterior oblique; CAUD, caudal; CRAN, cranial; LAO, left anterior oblique.

had an abnormal origin from the distal end of a dominant LCx that retrogradely followed the course of a normal RCA to the base of the heart. The flow of the LCx and LAD was normal, with mild stenosis. Similar to the first patient, the ECG still showed complete AV block with a low heart rate after 5 days. The patient also underwent a dual-chamber pacemaker implantation. At follow-up visits, the patient reported no discomfort.

Discussion

We are the first to report two rare cases of complete AV block coexisting with isolated SCAs and absent RCAs, in which the distal portion of the LCx supplied the territory of the RCA.

In 1979, Lipton et al. proposed the angiographic classification of SCA (6), which was later modified by Yamanaka and Hobbs (4). SCAs can be classified into three groups (Figure 3). This classification takes into account variables such as the origin of the ostium from the sinus of Valsalva, the anatomical course of the vessel, and the course of the transverse trunk. According to this system, our patients would be classified as LI. Many patients with an SCA are asymptomatic at the time of diagnosis, and cases of SCA are often discovered incidentally during coronary angiography, as in our patients (2). The majority of patients may experience atypical chest pain or non-specific symptoms in the absence of obstructive coronary artery disease (10). Others may present with typical chest pain; sudden death, especially during exercise; syncope; palpitations; ventricular tachycardia; or myocardial infarction (11). Certain anomaly classifications, such as RI and LI, typically have a benign clinical course.

The coexistence of complete AV block and coronary disease is primarily associated with acute myocardial infarction (12). The majority of cases of complete AV block are transient following revascularization of the culprit artery (13). Patients with congenital absence of the RCA may also experience acute

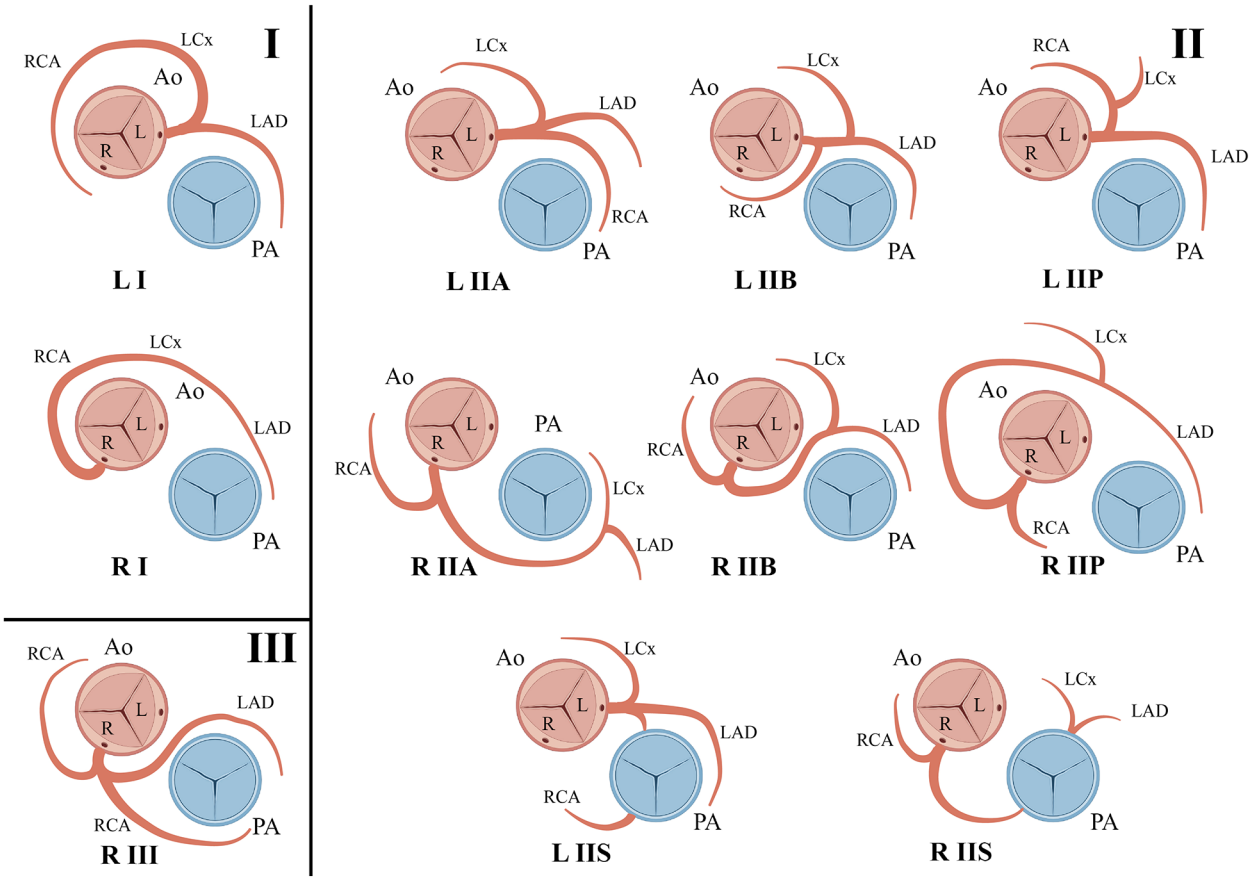


FIGURE 3
The letters R or L are used to identify the ostial origin of the vessel; the Roman numerals I, II, or III are used to represent the anatomical distribution of the vessel; and the letters A, B, P, S, and C are used to delineate the course of the vessel in relation to the pulmonary artery and the aorta.

myocardial infarction with complete AV block (14). However, there are no previous reports of complete AV block coexisting with congenital absence of the RCA in the absence of myocardial infarction. This may be due to the extremely low incidence of both SCA anomalies and complete AV block in the general population.

Degeneration and compromised blood supply to the AV nodal artery may be the most likely causes of complete AV block in the two cases. A previous case report showed an association between the coronary slow flow phenomenon and AV block (15). In that case, the patient underwent coronary angiography, which revealed a coronary slow flow phenomenon without significant stenosis. Due to persistent AV block, the patient was discharged following permanent pacemaker implantation (15). In 2018, the "FIT Clinical Decision Making" program published in the *Journal of the American College of Cardiology* reported a case of complete AV block with an anomalous RCA (16). Coronary computed tomography angiography revealed an anomalous origin of the RCA from the left cusp and a course between the aorta and the pulmonary artery (16). An electrophysiology study revealed multilevel intrahisian block and the patient underwent a dual-chamber pacemaker implantation.

Conclusion

Here, we reported the first two cases of congenital RCA absence with complete AV block in the absence of myocardial infarction. The coexistence of these two rare entities underscores the importance of anatomical and functional coronary evaluation in atypical arrhythmia presentations, expanding our understanding of the non-ischemic causes of complete AV block.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Ethics Committee of Peking University Shenzhen Hospital. The studies

were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

RL: Investigation, Software, Writing – original draft, Writing – review & editing. SS: Resources, Supervision, Visualization, Writing – original draft, Writing – review & editing. YC: Writing – original draft, Writing – review & editing. TX: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2025.1556188/full#supplementary-material

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Mediastinal hematoma following transradial percutaneous coronary intervention: case report and literature review

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Mediastinal hematoma due to transradial PCI is rare. We reported a case of chest tightness, dyspnea, progressive neck swelling after transradial PCI. Clinical examinations such as chest computer tomography were completed and identified as mediastinal hematoma caused by a rupture of the subclavian artery branch and occlude the artery under digital subtraction angiography guidance, the artery was considered to be a collateral vessel of non-bronchial arterial circulation. This case highlights the necessity of exercising extreme caution when utilizing hydrophilic-coated curved-tip guidewires during the advancement process in peripheral vascular procedures. Mediastinal hematoma is a life-threatening complication and progresses rapidly, we need timely identification and diagnosis based on symptoms and appropriate clinical examination, interventional embolization therapy is critical for patients with poor response of conservative treatment.

KEYWORDS

percutaneous coronary intervention, radial artery, complication, mediastinal hematoma, interventional embolization

Introduction

Percutaneous coronary intervention (PCI), as an effective treatment of coronary heart disease, has been widely applied in the world. With the gradual maturation and development of technology, transradial approach has gradually replaced the previous femoral artery access, benefiting from its fewer complications, better patient experience and comfortness, and shorter hospital stays, even reducing the mortality of patients with acute coronary syndrome (1–5). Currently, over 90% of PCI procedures in China are performed through the radial artery route (6, 7). Although radial artery access has many advantages, complications associated with it have gradually emerged in clinical practice (8). Mediastinal hematoma, as one of vascular rupture complications, is extremely rare in clinical practice, but can lead to serious consequences. This article describes a case of mediastinal hematoma after transraidal PCI and a series of diagnosis and treatment measures, along with a systematic review of the literature.

Case report

A 58 years old Chinese man with a history of type 2 diabetes mellitus for many years and a long-term history of smoking. In 2016, he underwent implantation of two stents in

the left anterior descending artery (LAD) due to "acute anterior wall ST-segment elevation myocardial infarction", followed by another stent implantation in the left circumflex artery (LCX) 1 month later. He has been regularly taking antiplatelet aggregation and lipid-lowering drugs after surgery. In November 2022, he experienced chest pain again, with profuse sweating, and presented to our hospital for consultation. He was diagnosed with acute non-ST-segment elevation myocardial infarction (NSTEMI). Coronary angiography (CAG) via the right radial artery showed that the original stents in the LAD and LCX were patent, the obtuse marginal branch (OM) was completely occluded, and the right coronary artery (RCA) had severe stenosis but was relatively short. One stent was implanted after opening the OM, and the patient received regular treatment with aspirin and clopidogrel dual antiplatelet therapy, along with other conventional medications. A month later, the patient still felt chest tightness and requested further treatment for the RCA lesion, leading to admission to the hospital.

Preoperative assessment showed no significant abnormalities in routine biochemical indicators such as blood routine and coagulation function. Chest CT indicated bilateral pulmonary emphysema. After a comprehensive evaluation of the patient's vascular access, a 6F short sheath (Terumo, Tokyo, Japan) was inserted through the right radial artery. Under x-ray fluoroscopy guidance, a 5F JR4.0 catheter (Cordis, Chihuahua, Mexico) was advanced with the assistance of a Hydrophilic Guide Wire (length: 180 cm, angled tip, curvature tip length: 3 cm, tip diameter 0.035″, Merit, Utah, USA) for CAG (during which inadvertent entry of the wire tip into the right subclavian artery branch occurred twice, promptly retracted without discomfort from the patient). The angiography revealed patent stents in the LAD, LCX, and OM (Figure 1), and severe stenosis in the proximal RCA (Figure 2A). With the patient's consent, intervention for the RCA was performed. A 6F JR4.0 guiding catheter (Medtronic, Minneapolis, USA) was exchanged, and a Sion guidewire (Asahi, Aichi, Japan) was selected to reach the distal RCA. A Runthrough NS guidewire (Terumo, Tokyo, Japan) was advanced to protect the OM. A 2.0 × 15 mm Sprinter balloon (Medtronic, Minneapolis, USA) was inflated to 16 atm, followed by a 2.25 × 20 mm RESTORE DEB Paclitaxel balloon (Cardionovum, Am Bonner Bogen2, Germany) at 10 atm for 60 s. Subsequent angiography revealed dissections in the proximal RCA and OM (Figure 2B). A 2.25 × 30 mm Resolute integret stent (Medtronic, Minneapolis, USA) was implanted at

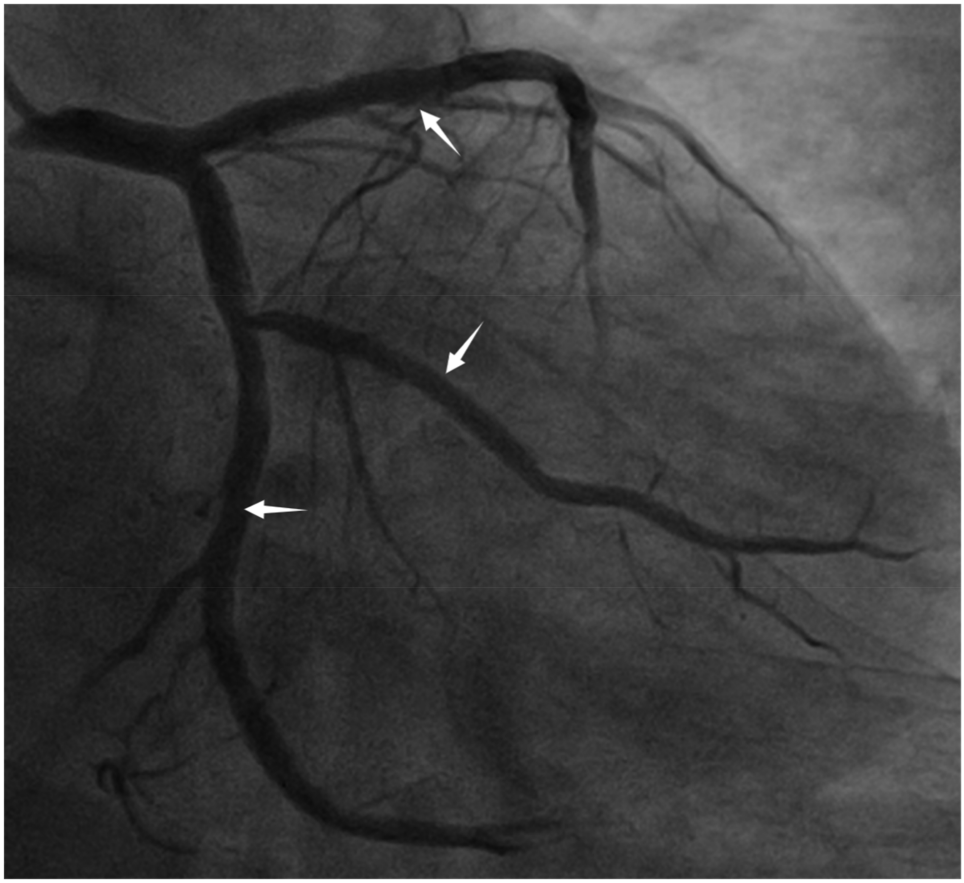

FIGURE 1
The original stents in the LAD, LCX, and OM are patent (red arrow indicates the LAD stents, white arrow indicates the OM stent, black arrow indicates the LCX stent).

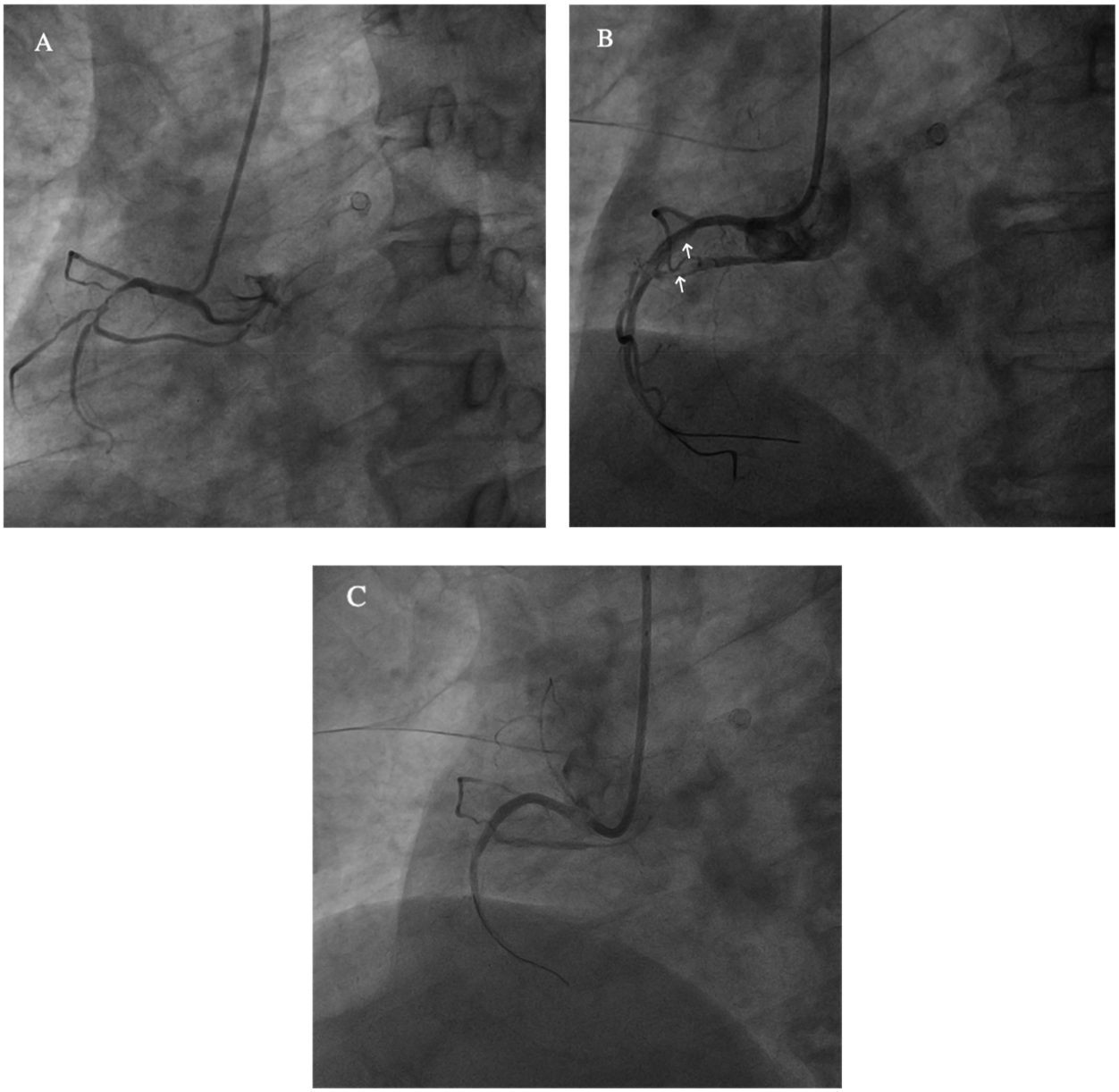

FIGURE 2
(A) The right coronary artery (RCA) is short and severely narrowed in the proximal segment. **(B)** After drug balloon dilation, coronary artery dissection is observed (white arrow). **(C)** Post-stent implantation, the stent is well-expanded, with TIMI III flow.

8 atm, followed by inflation with a 2.5 × 12 NC Sprinter balloon (Medtronic, Minneapolis, USA) to 12 atm within the stent. CAG confirmed no residual stenosis, with TIMI III flow (Figure 2C). The patient remained asymptomatic, and the procedure was concluded. The radial artery sheath was removed. The total procedure time was 77 min (CAG + PCI), and a total of 8,000 units of heparin were used.

Approximately 1 h post operation, the patient complained of progressively worsening chest pain located behind the sternum, accompanied by sweating, coughing with white sputum, wheezing in the throat, and neck swelling. His blood pressure was 144/89 mmHg, heart rate 63 bpm, and oxygen saturation 98%. Bedside electrocardiogram showed no dynamic changes in ST-T compared to preoperative findings. Emergency bedside ultrasound revealed significant soft tissue swelling in the neck, up to 23 mm thick, without evident fluid collection. Emergency consultation with an otolaryngologist revealed marked mucosal edema on the pharyngeal wall, suggesting acute pharyngeal edema. After discussion, the patient received dexamethasone 5 mg intravenous (IV) and methylprednisolone 80 mg IV, along with nebulization of budesonide. The patient's cough and sputum alleviated, wheezing disappeared, and swelling did not worsen. Further chest x-ray on the same day revealed mediastinal widening compared to preoperative images (Figure 3), which was initially overlooked due

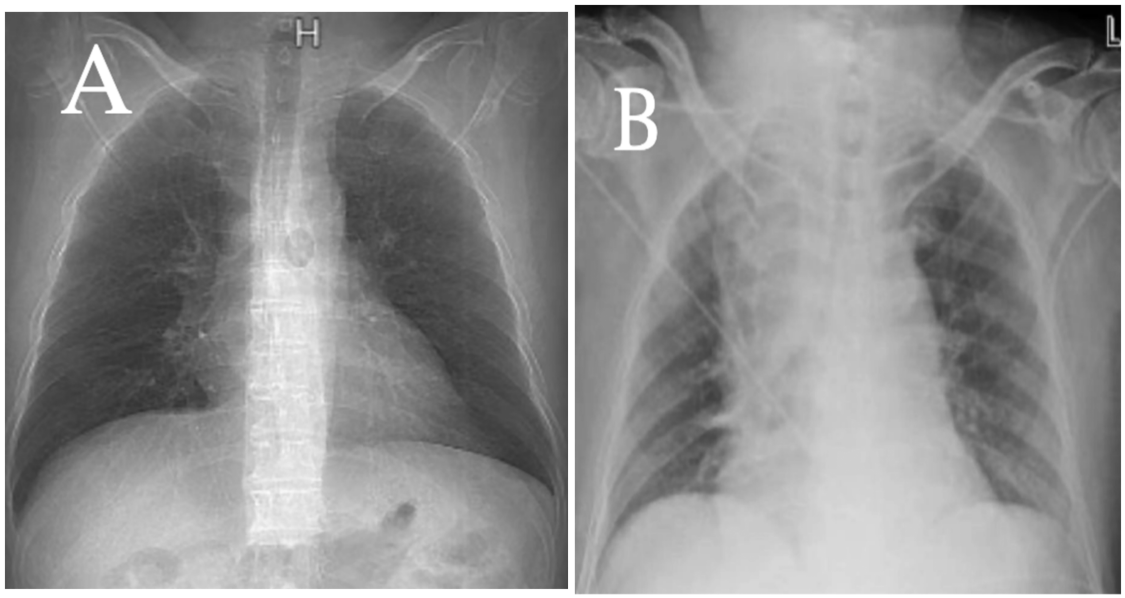

FIGURE 3
A comparison of chest x-rays taken the day before surgery **(A)** and on the day of surgery **(B)** shows a significant widening of the mediastinum in **(B)**.

to inadequate experience. Biochemical tests showed normal hemoglobin and cardiac enzyme levels. Two hours later, repeat testing showed persistent normal results. Considering the stable condition, aspirin and clopidogrel were not discontinued, and the patient was kept under conservative observation.

On the second post-PCI day, the patient experienced sudden chest tightness and shortness of breath again, with mouth breathing, but without exacerbation of neck swelling. Electrocardiographic monitoring showed sinus rhythm with a ventricular rate of 114 bpm, oxygen saturation of 92%, and blood pressure dropped to 90/57 mmHg. Oxygen therapy at 3l/min alleviated chest tightness, and 10 min later with intravenous fluids blood pressure returned to 121/71 mmHg. Repeat hemoglobin testing showed a decrease from 154 g/L to 123 g/L, with normal coagulation function. Otolaryngologic examination revealed persistent mucosal swelling and bluish discoloration, suggestive of hemorrhagic changes (Figure 4). Emergency Chest computer tomography (CT) scan showed swelling of the posterior pharyngeal wall and vocal cords, upper mediastinal hematoma, and signs of active bleeding, without evidence of aortic dissection (Figure 5). Considering the risk of further hematoma enlargement and airway obstruction, emergency digital subtraction angiography (DSA) was planned to identify the ruptured vessel after communication with the patient's family.

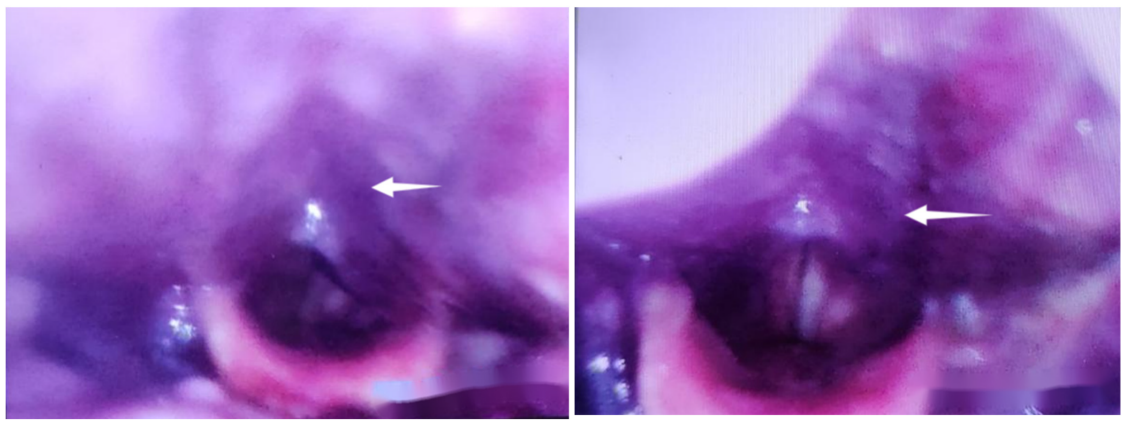

FIGURE 4
On the second day postoperatively, recurrence of symptoms, with electronic laryngoscopy revealing swelling of the pharyngeal wall accompanied by bluish discoloration.

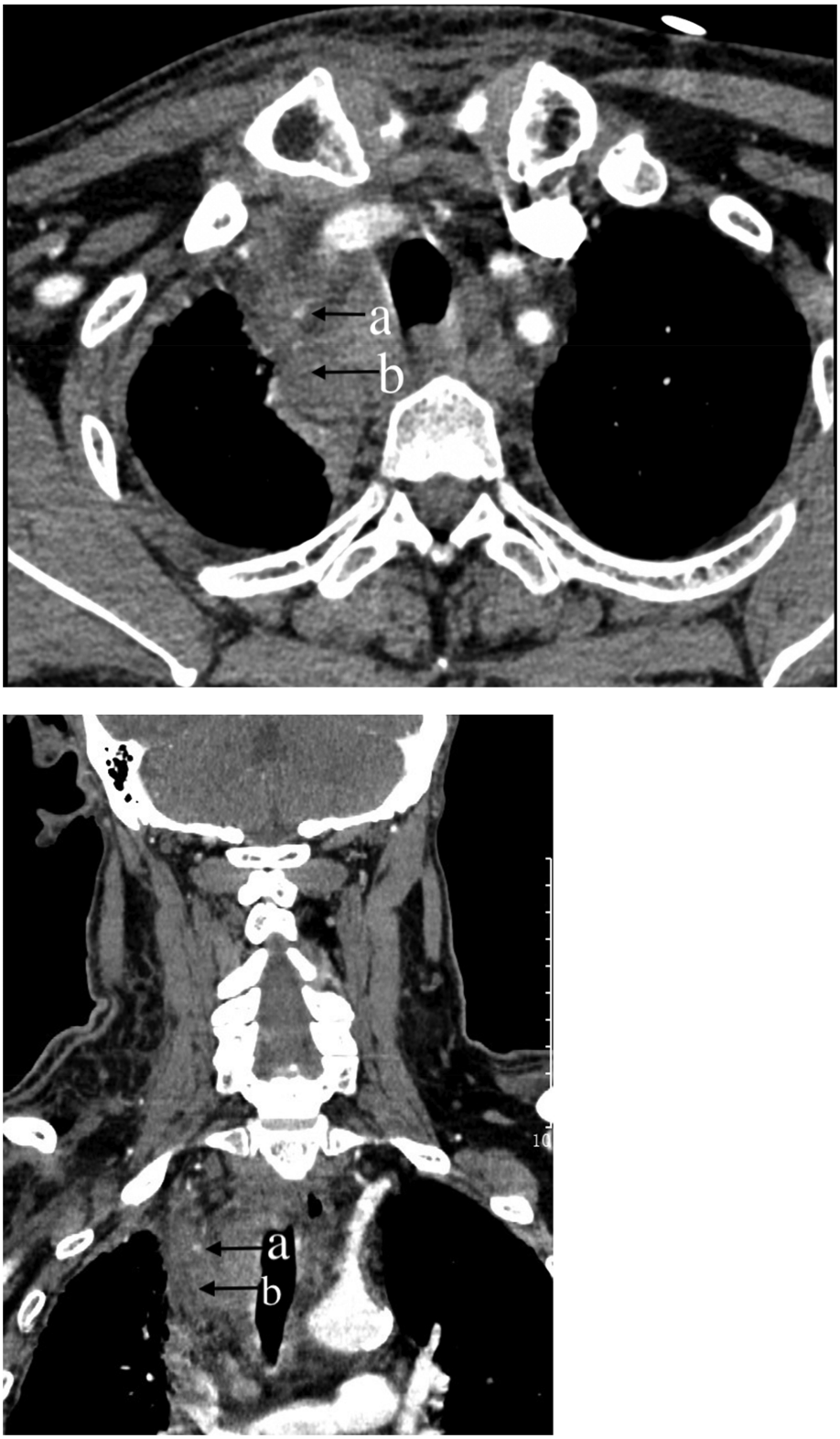

FIGURE 5
Chest computer tomography (CT) scan of the neck and chest: **(a)** Dot-like enhancement in the arterial phase, indicating active bleeding. **(b)** Mediastinal hematoma.

The patient's previous clinical records indicated occlusion of the right iliac artery. Therefore, the left femoral artery route was chosen. With a 5 F sheath, a 5 F pigtail catheter (Cordis, Chihuahua, Mexico) was advanced to the aortic arch for angiography, which showed no signs of obvious bleeding or dissection (Figure 6). Subsequently, after exchanging for a Hunter1 catheter (Cordis, Chihuahua, Mexico), a Merit Maestro microcatheter (Merit, Utah, USA) was inserted into the right subclavian artery to explore the responsible branch artery. Although the responsible artery was identified successfully, the catheter could not be secured at the opening of the responsible artery (Figure 7A). Therefore, the righr radial artery was used, and after the microcatheter entered the branch vessel, angiography showed extravasation of contrast agent, with clear visualization of the peripheral pulmonary artery vascular network (Figures 7A,B). Polyvinyl alcohol (PVA) particle embolic agents (diameter: 350–560 μm, Alicon, Hangzhou, China) and gelatin sponge particle embolic agents (diameter: 560–710 μm, Alicon, Hangzhou, China) were slowly injected through the microcatheter until the blood flow in the responsible artery completely stopped. Subsequent angiography confirmed complete embolization (Figure 7C), and the procedure was concluded.

Following the procedure, aspirin was immediately discontinued, and the patient was treated with clopidogrel alone for antiplatelet aggregation. The patient's chest tightness symptoms improved, cough and sputum production did not worsen, but significant throat pain was noted during swallowing, and neck swelling gradually decreased. Bruising was observed in the chest area (Figure 8). Dynamic monitoring of blood routine and chest CT showed a decrease in hemoglobin levels to a minimum of 103 g/L. Chest CT indicated gradual absorption of the mediastinal hematoma with secondary bilateral minimal pleural effusion. C-reactive protein (CRP) levels peaked at 147 mg/L. Symptomatic treatments for cough, sputum, and infection were provided based on the pulmonary condition. On the 7th day post-embolization, aspirin was reintroduced in combination with clopidogrel for dual antiplatelet therapy. A follow-up chest CT on the 13th day post-procedure showed almost complete absorption of the hematoma (Figure 9). The patient was discharged on the 21st day post-procedure. At 2 months post-discharge, the patient remains healthy.

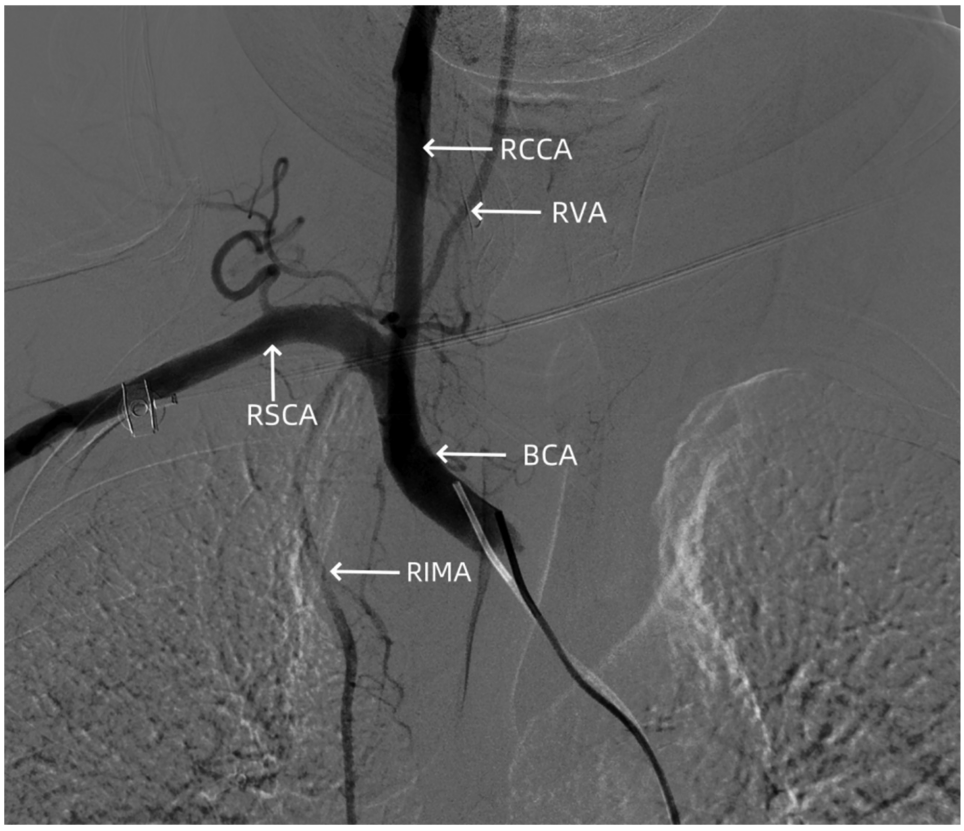

FIGURE 6
Angiography showing no signs of dissection hematoma or perforation bleeding in the brachiocephalic trunk, cervical internal carotid artery, and subclavian artery. RCCA, right common carotid artery; RVA, right vertebral artery; RSCA, right subclavian artery; BCA, brachiocephalic artery; RIMA, right internal mammary artery.

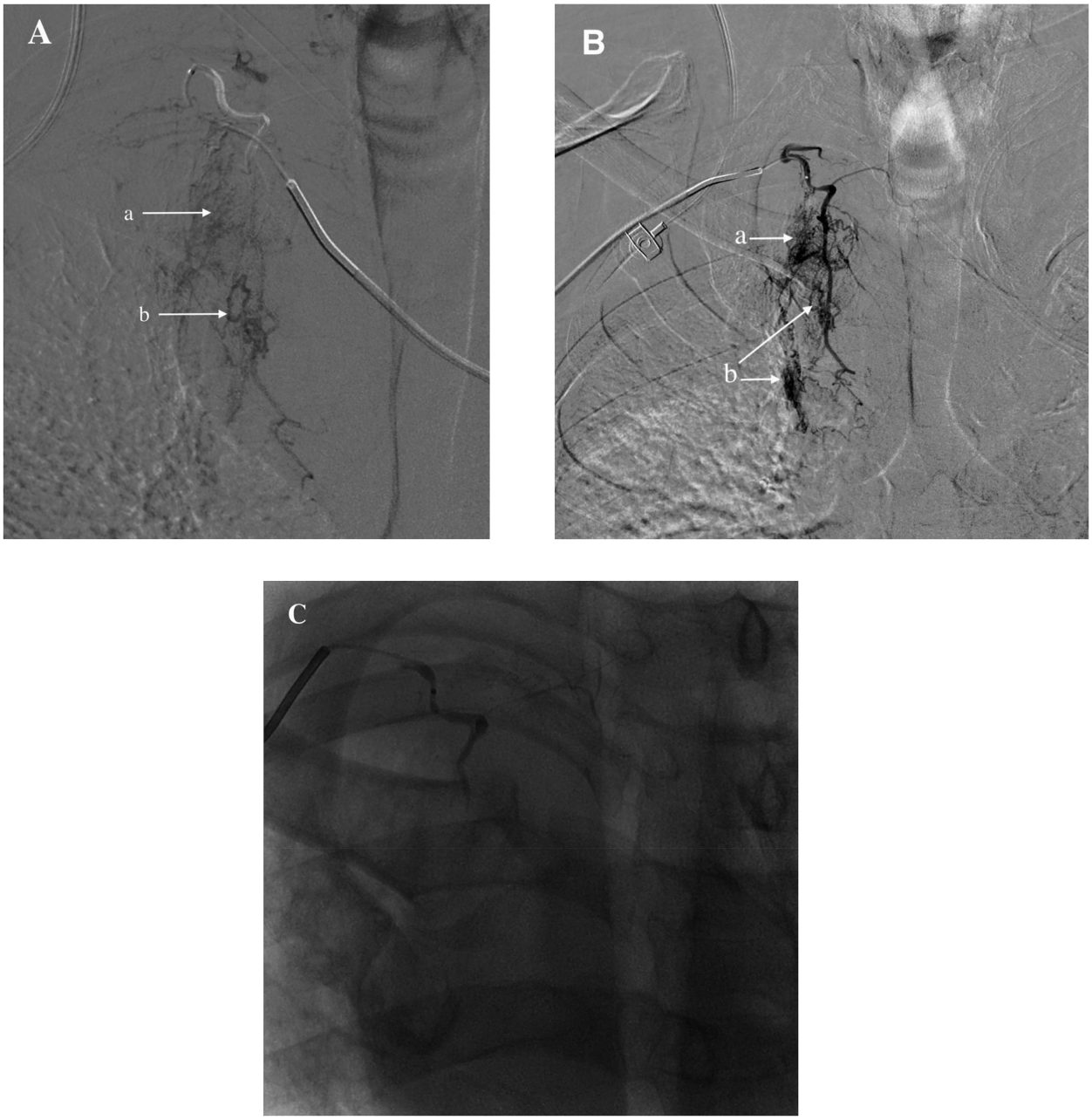

FIGURE 7
(A) Identified responsible artery via the femoral artery route, but catheter fixation was not possible. (B) Identified responsible artery via the right radial artery route. (C) Completion of embolization. (a) Diffuse extravasation of contrast agent indicating bleeding. (b) Shunt to systemic pulmonary artery.

Discussion

Coronary artery intervention via the radial artery approach has been widely recommended by numerous guidelines (9, 10). Vascular-related complications occur in only 0.4%, with most incidents happening at the puncture site or limited to the radial artery segment (11). Compared to the femoral artery pathway, this approach indeed reduces many vascular-related complications, primarily due to the decrease in complications at the puncture site (8, 12). The radial artery approach allows for prompt and effective external management of complications at the puncture site and radial artery segment. However, for intraluminal segments of arteries such as the subclavian artery and the brachiocephalic trunk, where effective external compression cannot be applied, the consequences of perforation and rupture are usually catastrophic. According to Luo et al., among 126,625 patients who underwent coronary angiography from 2006 to 2013, there were only 9 cases of mediastinal hematoma caused by radial artery access postoperatively, with an incidence rate of only 0.74% (13). To our knowledge, although there have been individual case reports of mediastinal hematomas after PCI in recent years, most have been managed conservatively, including fluid supplementation,

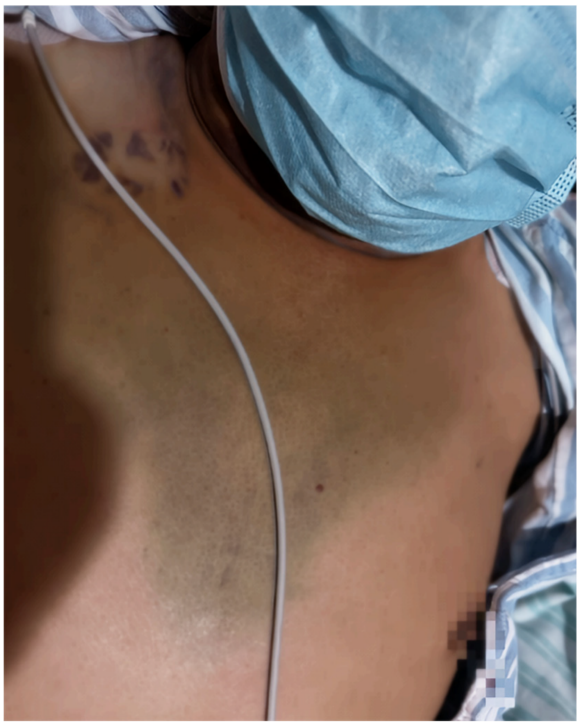

FIGURE 8
On the 6th day post PCI, bruising is visible in the chest anterior region.

adjustment of anticoagulant drugs, and maintaining airway patency. Our case has a relatively comprehensive clinical diagnosis and treatment process, and there are few reports of successful embolization of responsible arteries to treat mediastinal hematomas similar to ours. Therefore, the diagnosis and treatment of such PCI complications have significant reference value.

In this case, we used a 0.035-inch hydrophilic-coated guidewire with a curved tip. The hydrophilic coating allows it to be in a super slippery state inside the body, facilitating its passage through twisted peripheral vascular segments. However, this characteristic also makes it prone to inadvertent entry into small branch vessels. Cases of mediastinal hematoma reported by Luo et al. mostly involved the use of this type of guidewire, and other scholars have also reported vascular injuries caused by this type of guidewire (14–16). Therefore, we recommend routinely using J-shaped non-hydrophilic guidewires for radial artery access procedures to reduce the chance of entering small branch vessels. For patients where J-shaped guidewires cannot pass due to vascular tortuosity, hydrophilic guidewires of this type may be considered. However, during the procedure, the tip of the guidewire must be adequately exposed under x-ray fluoroscopy, and gentle, slow movements should be ensured, avoiding excessive flicking of the tip to reduce the chance of entering branch arteries inadvertently. If entering the same branch artery multiple times, selective peripheral arterial angiography may be performed to evaluate vascular tortuosity and assess whether perforation or other injuries have occurred. The roadmap-guided guidewire delivery through complex and tortuous artery remains a viable option. In this case, selective angiography of the responsible vessel showed signs of bleeding as well as a systemic circulation-pulmonary artery fistula. Considering the patient's pulmonary examination findings, we speculate that this vessel is a secondary collateral vessel arising from chronic pulmonary disease. To our knowledge, there have been no reports of similar vessels causing mediastinal hematoma due to rupture. Although this vessel originates from a subclavian artery branch located within the mediastinum, it continues downward through the pleura and communicates with intrapulmonary vessels. If patients develop spontaneous hemoptysis or other pulmonary diseases later on, besides investigating the usual bronchial arteries, attention should also be paid to the possibility of bleeding from such vessels (17, 18).

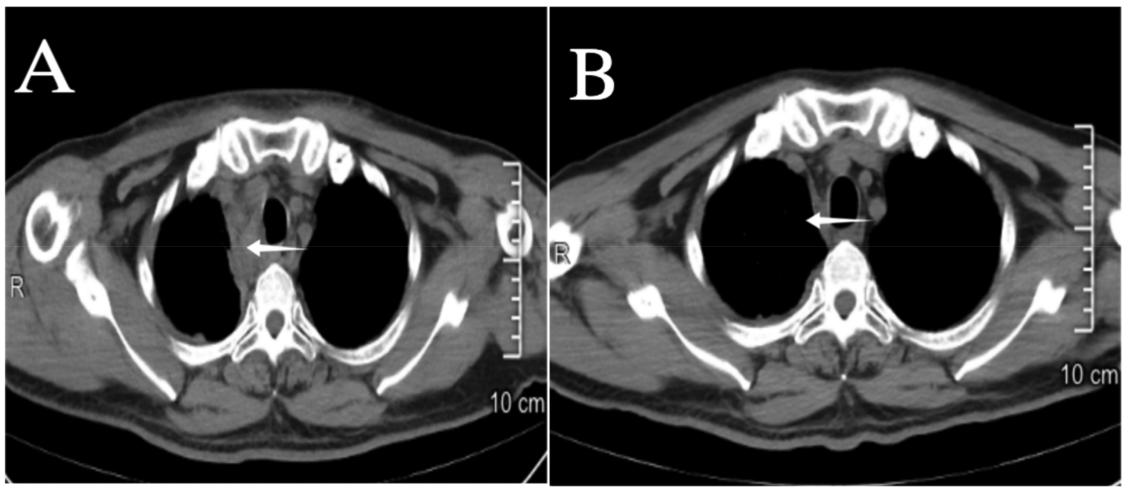

FIGURE 9
(A) 2nd day post interventional embolization; **(B)** 12th day post interventional embolization, on the 12th day the mediastinal hematoma (indicated by the arrow ←) is nearly completely absorbed, and airway compression has improved.

The patient developed symptoms approximately 1–2 h after coronary angiography. Similar symptoms related to mediastinal hematoma have been reported to occur within 2 h in other cases, with some patients experiencing symptoms immediately during the procedure (13, 15, 19). Given the rapid progression of symptoms, early recognition and detection are crucial. The symptoms observed in this patient included chest tightness, neck swelling, accompanied by difficulty breathing and wheezing. Additionally, there was decreased skin oxygen saturation, and immediate examination with electronic fiberoptic laryngoscopy revealed significant mucosal edema in the throat. Acute allergic laryngeal edema was suspected, and symptomatic treatment with steroids resulted in symptom improvement, narrowing down our diagnostic approach. We speculated that the acute inflammatory edema reaction was induced by the rapid perfusion of blood into the narrow space of the neck mucosa due to acute bleeding. Symptom relief with similar medication has been demonstrated in cases reported by Nathaniel and SeongIl, indicating the potential efficacy of steroid therapy for post-PCI neck swelling (20, 21). However, symptoms of mediastinal hematoma still lack specific clinical manifestations, requiring consideration of specific intraoperative conditions, such as whether the guidewire has entered branch vessels or if there was forceful manipulation. Additionally, prompt completion of tests such as electrocardiography, blood tests, myocardial enzyme spectrum, blood gas analysis, and cardiac ultrasound is essential for timely differentiation from postoperative acute myocardial infarction, aortic dissection, cardiac rupture, contrast agent allergy reaction, etc. Imaging examinations are the most important means of distinguishing and diagnosing mediastinal hematomas. In this case, postoperative chest x-rays already indicated significant mediastinal widening, but due to lack of experience, attention was only focused on the presence of pulmonary edema, leading to delayed diagnosis. Neck and chest CT scans are specific tools for diagnosing neck hematoma and mediastinal hematoma, respectively. CT value measurements of abnormal fluid can assess the likelihood of hematoma, but if conditions permit, direct CT with contrast medium of the neck and chest is recommended. In addition to distinguishing from aortic dissection, it can also determine the location and extent of the hematoma and identify the ruptured vessel.

Considering the large size and extremely complex distribution of branches from the subclavian artery to the brachiocephalic trunk, surgical exploration to find the responsible vessel is challenging. Therefore, early completion of peripheral vascular DSA examination for patients with active bleeding is a reliable method. Considering the possibility of secondary injury with the original access route and the surgical habits of peripheral vascular interventionists, we initially chose the femoral artery to find the responsible artery. Although non-selective aortic angiography were performed successfully, due to the long distance from the femoral artery to the brachiocephalic trunk and the upward twist angle from the brachiocephalic trunk to the right subclavian artery, the microcatheter could find the entrance of the responsible vessel selectively, but due to the mismatch in the direction of the catheter tip and the entrance of the responsible vessel, there was insufficient support for further occlusion operations. After multiple failed attempts, we switched to the original right radial route, successfully and quickly performed selective angiography, and occluded the responsible artery. Therefore, from this case, we believe that when using DSA to find the cause of hematoma, completing non-selective aortic angiography via routes such as the femoral artery to confirm the presence of aortic dissection, even rupture, and ruling out major vascular injuries, followed by progressive selective vascular angiography to clearly assess branch artery injuries, is a feasible approach. If there is deviation between the entrance of the responsible artery and the direction of the catheter, or if the responsible artery cannot be found, we still recommend selecting the original route, allowing coronary interventionists to rely on memory to further confirm the approximate path of the loach guidewire, accelerating the search for the responsible vessel, and providing reliable guidance and support for subsequent occlusion operations, thereby achieving rapid and effective treatment.

Conclusion

In summary, mediastinal hematoma, as a rare complication of transradial PCI, progresses rapidly and can have serious consequences. Caution should be exercised when using super-slippery hydrophilic guidewires during the intervention process. For patients with postoperative neck swelling accompanied by chest tightness and wheezing, the possibility of mediastinal hematoma should be considered, and prompt and thorough examination and evaluation should be performed. CT scans of the chest and neck are crucial for assessing the hematoma. Timely peripheral vascular DSA examination and occlusion embolization of the responsible bleeding vessel are necessary.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

JQ: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. WJ: Data curation, Investigation, Writing – review & editing. HX: Supervision, Validation, Visualization, Writing – review & editing. HX: Investigation, Methodology, Writing – review & editing. FS: Conceptualization, Project administration, Resources, Visualization, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Short-term recurrent coronary artery thrombosis with acute myocardial infarction in a patient with aplastic anemia–paroxysmal nocturnal hemoglobinuria syndrome: a case report

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Background: Acute myocardial infarction commonly occurs in patients with coronary artery disease, but rarely, it can develop under a hypercoagulable state. Aplastic anemia can be accompanied by paroxysmal nocturnal hemoglobinuria clones or transform into paroxysmal nocturnal hemoglobinuria with a significantly elevated prothrombotic state. These thrombotic complications predominantly arise in veins rather than in arteries. Coronary artery thrombosis in these patients, especially with short-term recurrent arterial thrombosis after initial successful treatment, is exceedingly rare.

Case presentation: A 39-year-old man with a history of aplastic anemia with paroxysmal nocturnal hemoglobinuria clones for 8 years presented with chest pain, and was diagnosed with acute inferior wall myocardial infarction on November 21, 2022. Despite standardized coronary intervention and anticoagulant/antiplatelet therapy, the patient reported intermittent chest discomfort with persistently elevated cardiac troponin and D-dimer levels 20 days after initial treatment. Repeat coronary angiography confirmed recurrent thrombosis in the right coronary artery. He underwent repeated balloon dilation and thrombus aspiration with intensified anticoagulation, which alleviated his clinical symptoms and normalized his cardiac troponin and D-dimer levels. The patient was finally confirmed to have aplastic anemia–paroxysmal nocturnal hemoglobinuria syndrome.

Conclusion: Patients with aplastic anemia–paroxysmal nocturnal hemoglobinuria syndrome can have thrombosis in arteries, such as coronary arteries, leading to acute myocardial infarction. Recurrent coronary artery thrombosis can occur after initial successful revascularization and anticoagulant/antiplatelet therapy. Close monitoring of clinical symptoms, repeated electrocardiogram and laboratory tests, coronary angiography, strengthened anticoagulation, and precautions for bleeding risks should be considered in patients with aplastic anemia–paroxysmal nocturnal hemoglobinuria syndrome.

KEYWORDS

aplastic anemia, paroxysmal nocturnal hemoglobinuria, acute myocardial infarction, cardiac troponin, myocardial injury, coronary thrombosis

Introduction

Acute myocardial infarction (AMI) describes the complete or incomplete occlusion of coronary arteries, resulting in a sudden reduction or interruption of blood supply and causing irreversible acute myocardial ischemia and necrosis (1, 2). The most common cause is coronary artery disease with atherosclerotic changes, which is often observed in older adults with multiple medical issues, such as hypertension, diabetes, and hyperlipidemia. In addition, AMI occasionally occurs in patients with a hypercoagulable state, such as those with paroxysmal nocturnal hemoglobinuria (PNH).

PNH is an acquired benign clonal disorder of hematopoietic stem cells caused by somatic mutations, and it clinically manifests as chronic intermittent intravascular hemolysis, thrombosis, and varying degrees of bone marrow failure (3, 4). PNH can evolve from aplastic anemia (AA). It was reported that more than half of patients with AA could carry PNH clones (5). Because of their proliferative advantage, PNH clones can replace bone marrow hematopoiesis, leading to the transformation of AA into PNH (6). The risk of thrombosis significantly increases after AA transforms into PNH, with venous thrombosis being more common than arterial thrombosis. Thrombosis commonly involves abdominal and intracranial veins (7–12). However, AMI with thrombosis in the coronary arteries has been occasionally reported in patients with PNH. Most of these reports were from Western countries, with a few cases identified in Northeast Asia (8). In this study, we report a Chinese patient with a medical history of AA accompanied by PNH clones. He had chest pain, and he was diagnosed with acute ST-segment elevation myocardial infarction (STEMI) and short-term recurrent coronary arterial thrombosis. We share our treatment experience regarding this patient to remind our colleagues about the extremely rare but life-threatening condition of STEMI arising from recurrent coronary arterial thrombosis in patients with AA-PNH syndrome.

Case presentation

A 39-year-old man presented to our hospital on November 21, 2022 with sudden-onset chest pain for 4 h. He reported a medical history of AA (accompanied by PNH clones) that was diagnosed at another hospital 8 years before presentation. His medications included danazol and methylprednisolone. Upon presentation, the vital signs were as follows: temperature, 36.2°C; pulse, 80 beats/min; respiratory rate, 20 breaths/min; and blood pressure, 146/85 mmHg. The patient was alert with a poor mental status, no cyanosis in the lips, bilateral coarse breath sounds without rales on lung auscultation, and regular heartbeats with no murmurs. Otherwise, his physical examination was unremarkable. Laboratory testing revealed a white blood cell count of 10.7×10^9/L, neutrophil count of 7.9×10^9/L, monocyte count of 0.6×10^9/L, red blood cell count of 3.4×10^{12}/L, hemoglobin level of 104.0 g/L, hematocrit level of 33.4%, platelet count of 148×10^9/L, high-sensitivity cardiac troponin level of 25,606.0 ng/L, and D-dimer level of 1,442 ng/ml (Table 1). The electrocardiogram (ECG) revealed sinus rhythm with ST-segment elevation in leads II, III, and aVF, suggesting acute inferior myocardial infarction. The patient was admitted into the hospital with diagnoses of acute inferior myocardial infarction and AA (accompanied by PNH clones).

Emergency coronary angiography was performed, revealing a right-dominant coronary artery system with normal openings of the left and right coronary arteries. The left main stem displayed no significant stenosis. The left anterior descending and circumflex branches featured normal openings and courses without obvious stenosis. The right coronary artery was enlarged with a normal opening and course. The posterior left ventricular branch (PLB) of the right coronary artery exhibited distal occlusion, and the first branch of the PLB displayed distal occlusion with visible thrombus (Figure 1A). Considering the patient's history of AA and significant thrombotic burden, we decided to perform coronary angioplasty without stent placement. The guidewire smoothly passed through the occluded segment (Figure 1B). Using a compliant balloon, the stenotic segment was dilated. The thrombus was aspirated. Thrombolysis in Myocardial Infarction (TIMI) 3 flow was achieved in all branches of the right coronary artery and PLB, with no significant local stenosis observed (Figure 1C). The ST segment in leads II, III, and aVF significantly decreased on cardiac monitoring. The patient's chest pain disappeared.

Postoperatively, the patient received antiplatelet and anticoagulant therapies, including oral aspirin 100 mg once daily, clopidogrel 75 mg once daily, and intravenous tirofiban at a rate of 0.15 μg/kg/min for 24 h. Subcutaneous injections of low-molecular-weight heparin sodium 0.4 ml (units) were given twice daily for 1 week. In the following 2 weeks, the patient occasionally reported mild chest discomfort. Although the repeat ECG examination did not reveal any significant dynamic changes, the patient's serum cardiac troponin I and D-dimer levels remained high after 20 days (Table 1).

We repeated coronary angiography on December 13, 2022, and no significant abnormalities were observed in the left coronary artery. However, diffuse thrombosis was present throughout the right coronary artery, in addition to occlusion of the distal PLB and its first branch (Figure 2). TIMI 3 flow was achieved after an intracoronary arterial injection of tirofiban (10 μg/kg). Postoperatively, tirofiban was continuously infused at a rate of 0.15 μg/kg/min for 24 h. The patient was subsequently prescribed long-term oral clopidogrel 75 mg and rivaroxaban 15 mg once daily. Repeated examinations revealed a significant decrease in the cardiac troponin I level, which gradually returned to normal (Table 1). He was discharged and followed up in the clinic.

In the clinic visits, the patient denied any chest pain or discomfort. Repeat testing revealed normal serum cardiac

Abbreviations

AA, aplastic anemia; AMI, acute myocardial infarction; ECG, electrocardiogram; PLB, posterior left ventricular branch; PNH, paroxysmal nocturnal hemoglobinuria; STEMI, ST-segment elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.

TABLE 1 Dynamic changes in peripheral blood high-sensitivity cardiac troponin I and D-dimer levels in this patient.

Tests	Day 1	Day 5	Day 15	Day 21	Day 27 (hospital discharge)	Two weeks after discharge	One month after discharge	Four months after discharge
Troponin I	25,606.0	9,665.3	4,454.1	1,064.5	879.2	75.0	38.4	21.1
D-dimer	1,442	868.0	1,774.0	951.0	783.0	417.0	111.0	122

Reference ranges: cardiac troponin, 0–17.5 ng/L; D-dimer, 0–232 ng/ml.

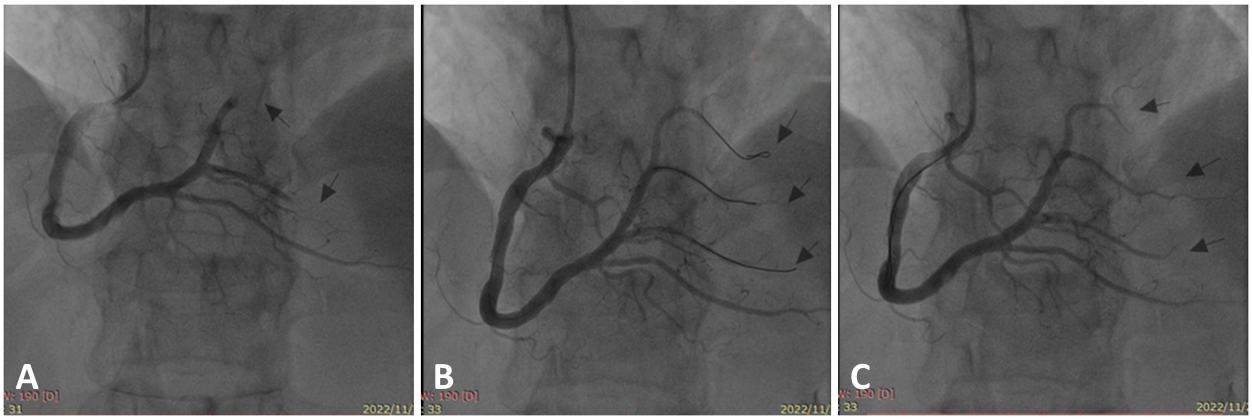

FIGURE 1
Right coronary artery under the initial coronary angiography. (A) Occlusion of the distal posterior left ventricular branch and its first branch (arrows). (B) The occluded site was opened by a guidewire (arrows). (C) After balloon dilation and thrombosis aspiration, the final angiography revealed smooth blood flow in the distal branches of the right coronary artery with no significant stenosis (arrows).

troponin and D-dimer levels. He also underwent follow-up at the hematology clinic, and he finally received a diagnosis of AA-PNH syndrome.

Discussion

AMI commonly occurs in patients with underlying cardiovascular illnesses, such as coronary artery disease with hypertension and diabetes. Rarely, AMI can arise in patients with PNH. In this study, we reported a patient with a medical history of AA accompanied by PNH. He experienced short-term recurrent thrombosis in the coronary arteries, leading to sustained myocardial injury and persistent troponin elevation, which were successfully treated with balloon dilation, thrombus aspiration, and anticoagulant and antiplatelet treatment. We have reported this case to remind our colleagues to pay special attention to patients with underlying AA-PNH syndrome because their hypercoagulable state could occasionally cause serious and recurrent arterial thrombosis, leading to life-threatening illnesses.

AA and PNH are both rare hematologic disorders involving bone marrow and blood cells (3, 4, 13). They are distinct clinical diagnoses, but they share interconnected pathophysiological mechanisms. It was estimated that 20%–40% of patients with AA might have detectable PNH clones. When patients with AA have clinical features of PNH, AA-PNH syndrome is considered. The coexistence of AA and PNH can lead to a complex clinical course and prognosis, including a high risk of thrombosis. Prompt recognition of the hypercoagulable state is vital for preventing and diagnosing life-threatening thrombotic complications. Thrombosis in patients with AA-PNH predominantly arises in the hepatic, abdominal, or cerebral veins, but arterial thrombosis with severe morbidity and mortality rarely occurs. Short-term recurrent coronary artery thrombosis with myocardial infarction is exceedingly rare. A previous case report described a 33-year-old Chinese PNH female with two episodes of AMI. However, the authors failed to provide adequate evidence (such as coronary angiography) to support that two episodes of AMI were separate events (14). Our patient, who was previously diagnosed with AA and concurrent PNH clones, likely had coexistent AA and PNH, leading to a high risk of thrombosis. Under direct visualization, the thrombus in the right coronary artery was successfully removed. Routine antiplatelet and anticoagulant therapies were administrated postoperatively. Usually, cardiac troponin levels normalize within 2 weeks after AMI treatment. However, our patient had persistently elevated troponin and D-dimer levels after 20 days of treatment. Cardiac troponin is the standard marker for myocardial injury and/or necrosis. Its concentration can serve as a quantitative marker of myocardial cell damage to assess prognosis (2, 15). D-dimer levels can reflect the presence of thrombosis and fibrinolysis. Dynamic monitoring of D-dimer levels is valuable for the diagnosis, treatment, and prognosis prediction of thrombotic diseases, including acute cerebral

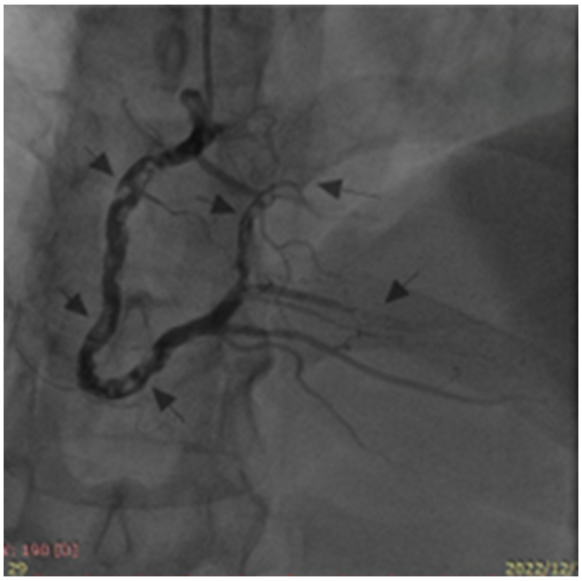

FIGURE 2
Second coronary angiography revealing diffuse thrombosis throughout the entire right coronary artery and occlusion of its distal posterior left ventricular branch and first branch (arrows).

infarction, AMI, deep vein thrombosis, and pulmonary embolism (16–18). A higher D-dimer level is associated with more severe coronary artery occlusion and a larger infarct size (19). We therefore performed repeat coronary angiography, which confirmed the presence of short-term recurrent coronary arterial thrombosis. After confirming that the coronary thrombus was the cause of the persistent elevation of troponin and D-dimer levels, we adjusted the treatment strategy, shifting the focus from antiplatelet to anticoagulation therapy. The patient has since been consistently taking the oral anticoagulant rivaroxaban. During follow-up, the patient has not experienced chest tightness or pain, and his cardiac troponin levels have remained normal. Further hematological evaluations ultimately led to a diagnosis of AA-PNH syndrome.

Our recommendation is that the possibility of arterial thrombosis with concerning clinical presentations should be eliminated in patients with a medical history of AA accompanied by PNH clones or AA-PNH syndrome. Those with chest pain should undergo appropriate diagnostic tests, including ECG and troponin level measurement. Emergency coronary angiography should be performed in patients with confirmed AMI. Balloon dilation and thrombus aspiration with follow-up enhanced anticoagulant therapy and routine antiplatelet treatment should be applied. Considering significant hypercoagulable state in AA-PNH patients, in-stent thrombosis could happen after coronary stent placement (20). Intensified anticoagulation, rather than stent placement, might be recommended in these patients. Postoperatively, close monitoring of troponin and D-dimer levels, and dynamic changes in ECG findings are crucial to detect recurrent thrombosis. Coronary angiography should be performed if there are persistent clinical symptoms of chest discomfort, abnormal ECG findings, or elevated troponin and D-dimer levels. Meanwhile, patients with AA-PNH syndrome can have an increased risk of bleeding disorders because of thrombocytopenia from AA and platelet dysfunction from PNH. They should be closely monitored for any sign of bleeding during anticoagulant and antiplatelet treatments. It was reported that thrombosis in PNH patients could be resistant to the anticoagulant treatment, The anti-C5 humanized monoclonal antibody, such as ravulizumab, could be applied to prevent recurrent thrombosis (21). In our patient here, intensified anti-platelet and anticoagulation treatments, including tirofiban, clopidogrel, and rivaroxaban, also achieved successful outcomes.

The initial coronary angiography in this patient revealed mild vascular stenosis with a heavy thrombotic burden at the distal end, indicating that the primary cause of vascular occlusion was thrombosis, with coronary artery disease being a secondary factor. Despite adequate anticoagulant and antiplatelet treatment following the diagnosis of AMI, the patient experienced recurrent thrombosis in the right coronary artery. Interestingly, two subsequent angiographies of the left coronary artery did not reveal thrombosis, suggesting that right coronary artery disease could exacerbate the risk of thrombosis in patients with AA-PNH syndrome.

Conclusions

AMI can occur in patients with AA-PNH syndrome. Despite initial successful revascularization of the coronary artery, thrombosis can return with recurrent myocardial infarction. Close monitoring of clinical symptoms, repeated ECG and laboratory testing, necessary coronary angiography, strengthened anticoagulation, and precautions concerning bleeding risks should be considered in patients with overlapping hematological and cardiovascular disorders.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Ethics Committee of Qilu Hospital of Shandong University Dezhou Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

XF: Data curation, Formal analysis, Visualization, Writing – original draft. YG: Data curation, Investigation, Methodology, Resources, Validation, Writing – review & editing. SW: Investigation, Software, Validation, Visualization, Writing – review & editing. WZ: Conceptualization, Project administration, Supervision, Writing – review & editing.

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Conflict of interest

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Publisher's note

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Multiple coronary artery perforation as a fatal complication during the management of an undeflatable stent balloon: a case report

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Background: An undeflatable stent balloon following its inflation during percutaneous coronary intervention (PCI) is a rare and unpredictable complication that can lead to serious consequences. Currently, there is no standardized protocol for managing this issue.
Case presentation: An 83-year-old man presented with chest pain. Coronary angiography showed a chronic total occlusion (CTO)-like lesion in the proximal left anterior descending coronary artery (LAD). Following stent deployment, the balloon failed to deflate and remained inflated within the LAD. Despite multiple retrieval attempts, the issue remained unresolved. As an alternative to surgical removal, we inflated the balloon beyond its rated burst pressure within the coronary artery. The balloon eventually ruptured and was successfully retrieved; However, this resulted in multiple severe coronary perforations, which were effectively sealed using covered stents.
Conclusion: Balloon deflation failure is an exceptionally rare, unpredictable, and critical complication of PCI. While various troubleshooting strategies exist, inflating an undeflatable balloon beyond its burst pressure should be considered only as a last resort, with thorough preparation for potential complications.

KEYWORDS

percutaneous coronary intervention, coronary occlusion, coronary device entrapment, complications, perforation

Background

Percutaneous coronary intervention (PCI) is a common therapeutic approach for treating coronary artery disease. Even the simplest interventional procedures can result in complications due to hardware failures, which are sometimes very challenging to manage. We report a rare complication of an undeflatable stent balloon during a PCI procedure, which led to a nearly fatal complication following the bailout approach.

Case presentation

An 83-year-old man presented with an acute non-ST-segment elevation myocardial infarction was admitted to our hospital. His medical history included hypertension, diabetes, dyslipidemia, and stage 3 chronic kidney disease.

The initial ECG showed no ST elevation or diffuse ST depression, but poor R-progression was noted. CK-MB was elevated to 9.7 ng/ml, and high-sensitivity Troponin I to 130 pg/ml. A chest x-ray revealed mild pulmonary edema with an SpO_2 91%–93%. Echocardiography detected new akinesis in the LAD territory.

Coronary angiography, performed as part of an early invasive strategy, revealed a severely calcified chronic total occlusion (CTO)-like lesion in the proximal LAD and calcified stenosis of the ramus intermedius branch (Figure 1A). Right coronary angiography showed no significant stenosis, with CC grade 1 collaterals supplying the LAD via the epicardial and septal vessels. During two days of diuresis and stabilization, the patient's chest pain and dyspnea improved, and no dynamic ST-segment changes were observed. On day 3, PCI was performed according to the patient's preference. The laboratory findings on the day of PCI showed CK-MB 82 ng/ml and high-sensitivity Troponin I 13,138 pg/ml. Both common femoral arteries were accessed for PCI. An 8 F EBU 3.5 guiding catheter (Medtronic, Minneapolis, MN, USA) was used to engage the left main ostium. The LAD was successfully wired using the antegrade wire escalation technique, a commonly used approach in contemporary CTO PCI. (Escalation from Sion BLUE (Asahi Intecc, Japan) → Fielder XT-R (Asahi Intecc, Japan) → Ultimate Bros 3.0 (Asahi Intecc, Japan), with Corsair Pro XS (Asahi Intecc, Japan) microcatheter back-up.) 7F Guidezilla™ extension catheter (Boston Scientific, Natick, MA, USA) was introduced, and lesion preparation was sequentially performed using a 2.0 mm semi-compliant balloon followed by a 2.5 mm non-compliant balloon. Intravascular ultrasound confirmed the wire was in the true lumen throughout the LAD, revealing diffuse and calcified stenosis from the proximal to the distal LAD. Subsequently, a 2.5 × 46 mm Cre8™ EVO (Alvimedica, Istanbul, Turkey) drug-eluting stent (DES) was delivered and positioned across the mid-LAD lesion without resistance. During stent deployment, the dial on the pressure gauge window did not rise appropriately despite multiple adjustments to the indeflator handle. After approximately 15 attempts, we reached the rated burst pressure of 18 atm, achieving full stent balloon expansion (Figure 1B). However, retraction of the handle failed to deflate the balloon. Despite the dial indicating zero pressure and a strong tactile sensation of negative pressure when pulling back the handle, the stent balloon remained inflated with no signs of deflation. Our initial suspicion was a malfunctioning indeflator device. Therefore, we immediately switched to a new indeflator, filling the column with normal saline alone to dilute the contrast/saline mixture in the balloon catheter through slight inflation followed by full deflation. However, this also failed to deflate the balloon. We then attached a three-way stopcock connected to a 50 cc syringe to the balloon catheter and applied strong negative suction, but this also proved unsuccessful. After all efforts to deflate the balloon using negative pressure failed, we decided to attempt intentional balloon perforation using a stiff guidewire. A 7 F Judkins Left 4 (JL 4) guide catheter was inserted via the left femoral artery. The first EBU guide catheter was slightly withdrawn, and the JL 4 guide catheter was advanced into the left main. A Turnpike® LP microcatheter (Teleflex, Wayne, PA, USA) was used to deliver the wire. We attempted to puncture the inflated balloon with both the distal and proximal end of a Conquest Pro 12 and Astato® XS 20 wire (Asahi Intecc, Japan) multiple times (Figure 1C), but these attempts were unsuccessful. As the next step, we advanced the GuideZilla™ guide extension catheter deeply and attempted forceful retraction of the trapped stent balloon, which again failed (Figure 1D). Meanwhile, the patient developed severe chest pain and ST elevation on the electrocardiogram monitoring. His hemodynamic status deteriorated, necessitating the initiation of norepinephrine and dopamine. We contacted the cardiothoracic surgeon to discuss surgical options. To avoid delays in this critical patient, we decided to attempt ultra-high-pressure inflation of the balloon beyond its rated burst pressure as a last interventional resort. At 23 atm, the pressure dial suddenly dropped, and the contrast dissipated from the balloon, indicating a rupture (Figure 2A). The balloon was then successfully retrieved into the guiding catheter and removed from the coronary artery (Figure 2B). However, follow-up angiography revealed multiple Ellis grade III perforations in the stented LAD segment (Figure 2C). A 2.5 mm semi-compliant balloon was immediately inflated in the mid-LAD to plug the perforation. Despite prolonged inflation for 15 min, the perforation remained unsealed, necessitating the deployment of 3.5 × 19 and 2.8 × 19 mm GraftMaster covered stents (Abbott Vascular, Santa Clara, CA, USA) in the proximal and distal segments of the stented LAD using the Ping Pong technique (Figures 3A,B). As the patient's hemodynamic status remained unstable, an emergency pericardiocentesis was performed. Angiography still showed persistent extravasation in the mid-segment of the stented LAD, so an additional 2.8 × 19 mm GraftMaster covered stent was deployed (Figure 3C). After successfully managing the coronary perforation, a 3.0 × 33 mm DES was placed in the stenotic proximal LAD, followed by post-dilation with a 3.5 mm non-compliant balloon. Final angiography confirmed well-expanded stents with no dissection or residual perforation (Figure 3D). Fortunately, the patient was discharged after 19 days (including three days in the intensive care unit) and remained asymptomatic for two months. We initially planned to place him on lifelong dual antiplatelet therapy, but he was later transferred to an elderly care hospital and lost to follow-up.

Discussion

Deflation failure of a stent balloon during PCI is a very rare complication (1). Several mechanisms may contribute to this issue, including kinking, twisting, or stretching of the balloon catheter during delivery or lesion crossing, which can prevent proper deflation after inflation (2). Another potential causes include acute recoil of a heavily calcified lesion or balloon entrapment within the guide catheter (3). In our case, the

Abbreviations

CTO, chronic total occlusion; DES, drug-eluting stent; JL, judkins left; LAD, left anterior descending coronary artery; PCI, percutaneous coronary intervention.

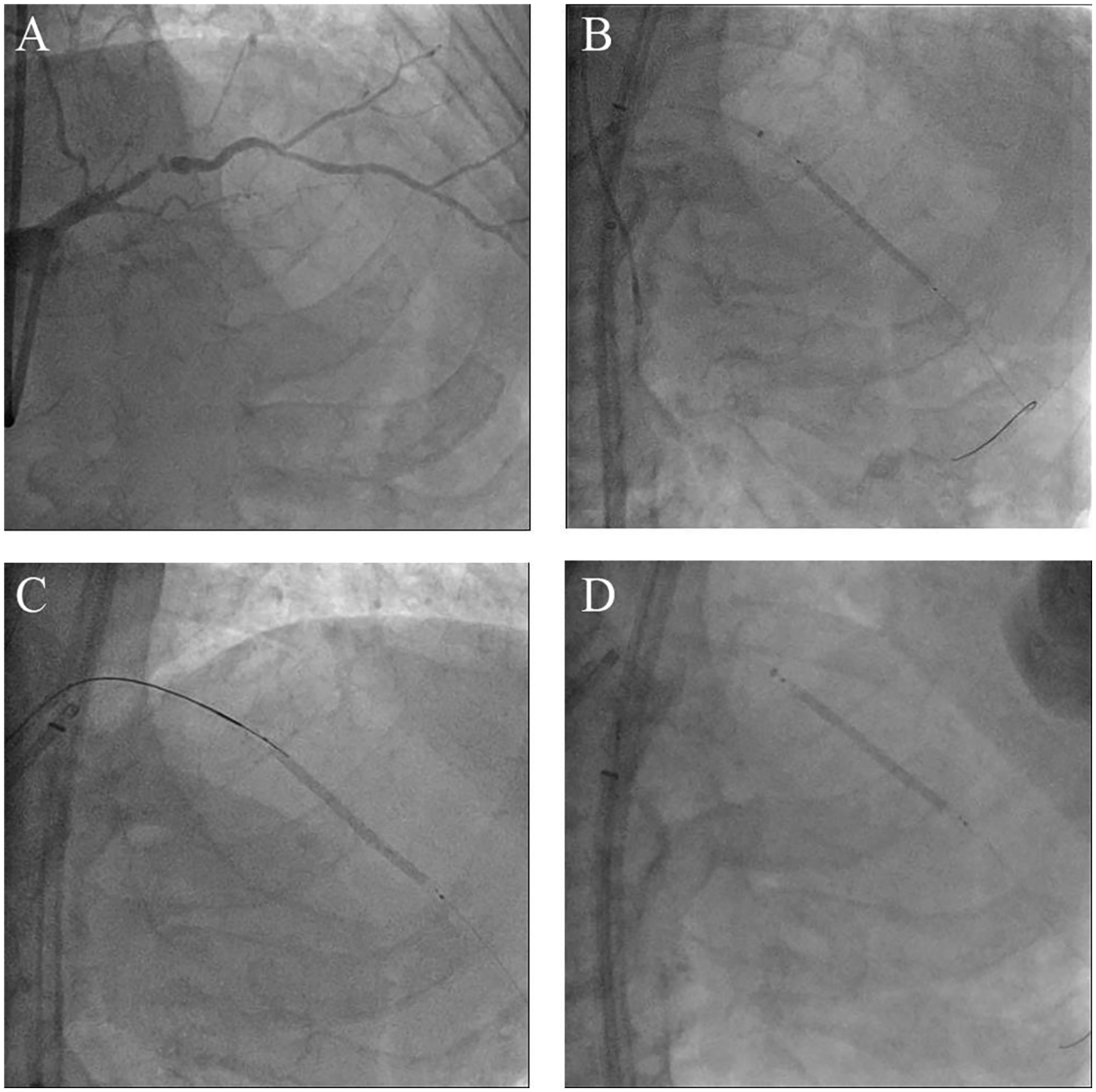

FIGURE 1
Morphology of the coronary lesions and several attempts to manage the undeflatable coronary balloon. **(A)** Coronary angiography from right anterior oblique cranial projection showing a CTO-like lesion of the proximal LAD. **(B)** Failure to deflate the stent balloon despite strong negative pressures using a saline-filled indeflator. **(C)** Attempt to perforate the undeflatable balloon using a stiff wire with microcatheter support. **(D)** Attempt to pull the undeflatable balloon back after deep intubation of the guide extension catheter; CTO, chronic total occlusion; LAD, left anterior descending artery.

difficulty was observed not only in deflating the balloon but also during initial inflation, suggesting the possibility of an unintentional kink in the balloon shaft or a manufacturing defect. When stent or balloon catheter delivery is particularly challenging, increasing the risk of hypotube compromise, a guide extension catheter may help facilitate the procedure. However, this was not applicable in our case. An inflated balloon within a coronary artery can completely block the vessel, leading to life-threatening complications such as ischemia, infarction, malignant arrhythmia, and death. Therefore, emergent rescue intervention is critical when a stent balloon fails to deflate, unlike entrapments of other interventional devices. Several techniques have been proposed in previous case reports to address an undeflatable stent balloon.

The retrieval techniques available in the catheterization laboratory can be broadly classified into those that do not require cutting the hypotube and those that necessitate cutting the hypotube. While there is no universally established order, we have outlined the techniques in a structured sequence in Figure 4.

Techniques without cutting the hypotube

First-line: Contrast dilution and negative pressure techniques.

The first-line approach involves progressive dilution of the contrast material within the balloon using saline to decrease viscosity (2). Additionally, using dual indeflators connected via a stopcock can enhance suction power and facilitate balloon deflation.

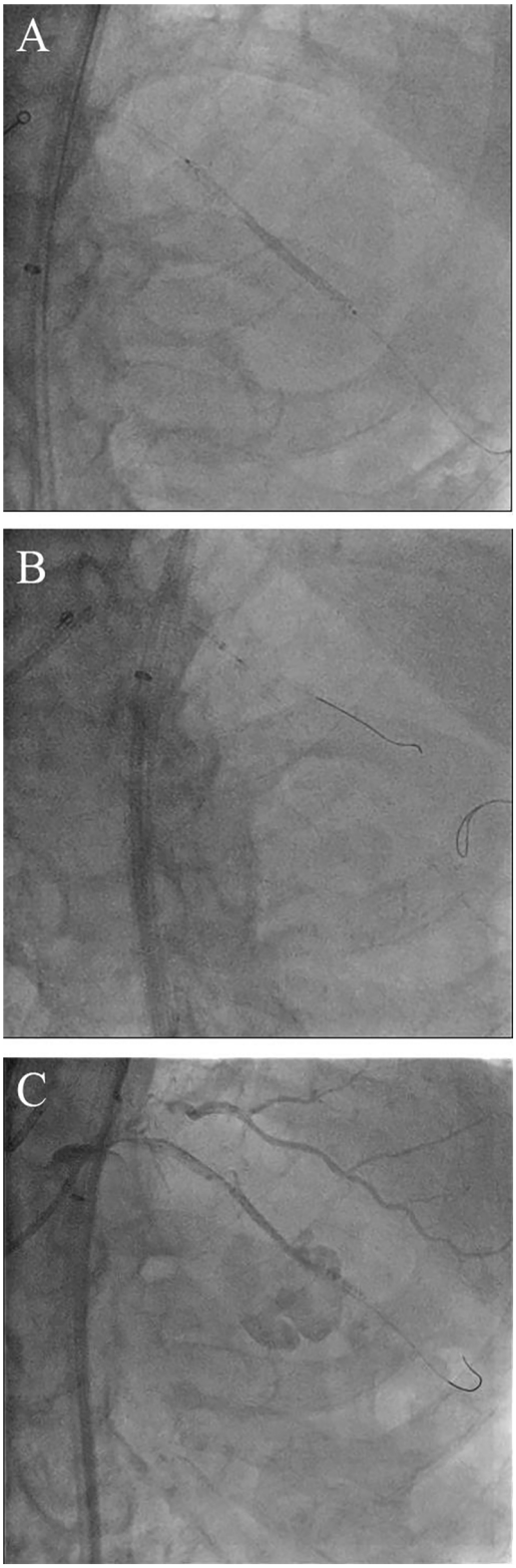

FIGURE 2
Bursting the balloon in the coronary artery with beyond-high-pressure inflation and subsequent coronary perforation. (A) Partial loss of contrast within the stent balloon following its rupture. (B) Complete removal of the ruptured stent balloon into the guiding catheter. (C) Large coronary artery perforation after the balloon burst.

Second-line: Guidewire puncture.

The distal end of 0.014″ CTO wires or the proximal end of 0.018″ wires (which are more radiopaque) can be used to puncture the balloon with microcatheter support, although this method is rarely successful (2, 4).

Third-line: Laser energy delivery.

Successful balloon deflation has been reported following laser energy delivery at 40 mJ/mm^2 fluence and 40 Hz repetition rate, applied in three cycles for a total duration of 45 s (5).

Fourth-line: Ultra-high-pressure inflation.

As a final option before cutting the hypotube, the balloon can be intentionally ruptured using ultra-high-pressure inflation. However, this carries a significant risk of coronary artery perforation and should be avoided unless absolutely necessary (1–4, 6, 7).

Techniques that require cutting the hypotube

In some cases, cutting the hypotube does not guarantee passive balloon deflation and eliminates the option of using an indeflator. However, if necessary, the following methods can be attempted:

First-line: Hole saw technique using a child guide catheter.

Cutting the distal tip of a child guide catheter (e.g., 5 Fr Terumo Heartrail) exposes its braided metallic skeleton, which can then be used to mechanically perforate the balloon by rubbing against it (6).

Second-line: Forceful retraction with guide-extension catheter support.

Forceful retraction of the balloon using guide-extension support can be attempted. However, this method carries a risk of a deeply intubated guide catheter with hypotube disruption (3, 6, 7).

Last-resort option

If all catheter-based retrieval attempts fail, surgical balloon retrieval remains a definitive option. However, due to its invasiveness and procedural delays, an interventional approach should be prioritized unless there is ongoing hemodynamic compromise (8).

Although we successfully managed the undeflatable stent balloon by inflating it beyond high pressure, this approach resulted in multiple serious coronary artery perforations. To our knowledge, this salvage procedure has never been reported as a successful intervention inside a coronary artery. Nevertheless, alternative strategies should always be considered before employing this drastic ultra-high pressure balloon bursting method.

The mechanism underlying edge perforation may be attributable to high intramural stress. Overexpanding a stent is functionally equivalent to implanting an oversized stent, which increases intramural stress, particularly at the stent edges (9). However, in this case, a mid-segment perforation necessitated the placement of an additional covered stent. Another potential cause of mid-stent perforation is pinhole balloon rupture.

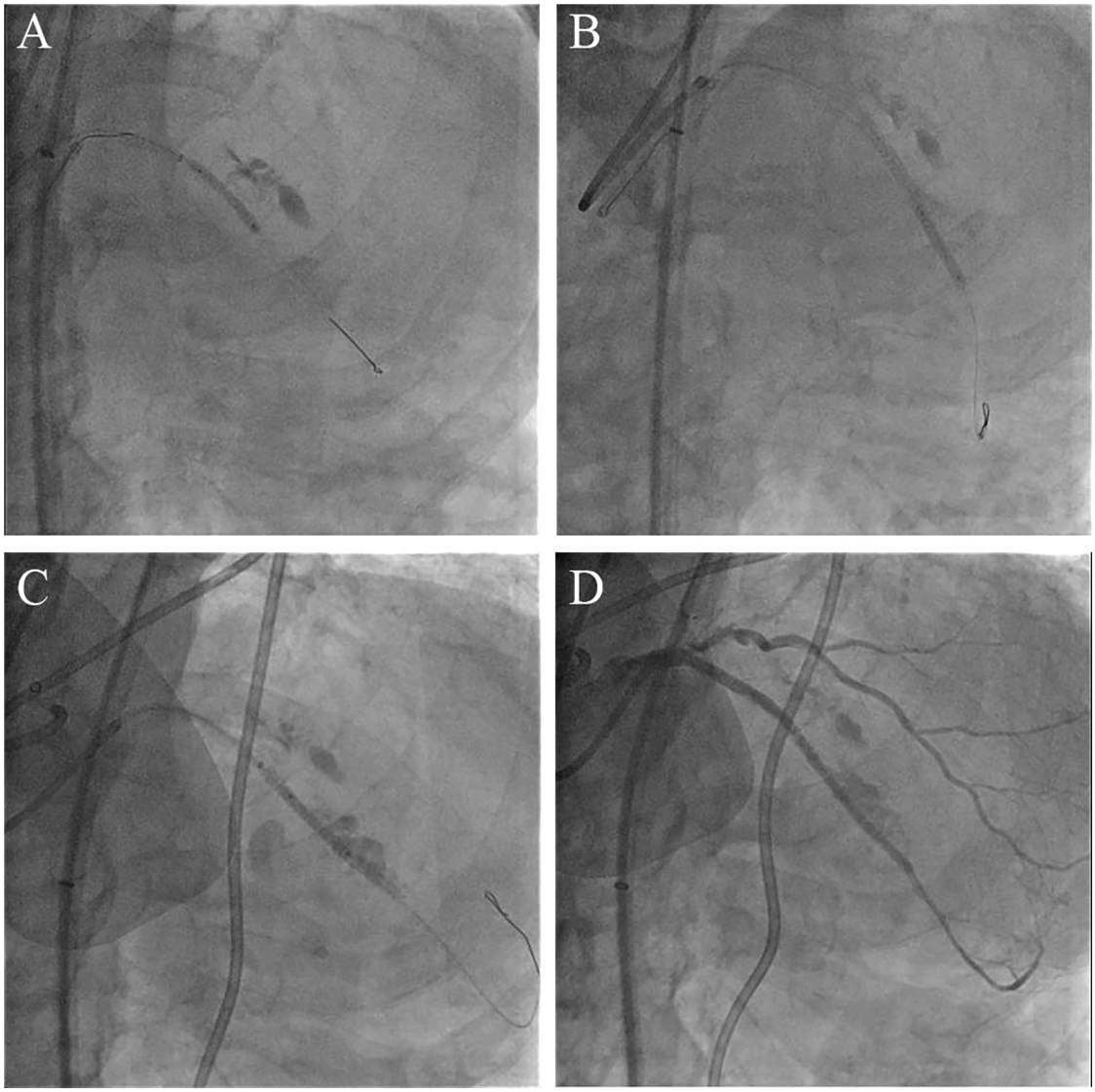

FIGURE 3
Salvage procedure for coronary perforation employing the ping-pong technique. **(A)** The covered stent deployed at the proximal segment of stented LAD. **(B)** The second covered stent placed in the distal segment of stented LAD. **(C)** Final perforation closure with a third covered stent. **(D)** Angiogram after deploying three covered stents shows complete sealing of the perforation.

A semi-compliant stent balloon generally expands to approximately 1.3 times its nominal diameter at rated burst pressure. However, specific burst pressures and pressure-burst relationships are often unspecified. Studies have shown that second-generation DES can expand beyond 50% of their nominal diameter during post-dilation with a larger balloon, though the extent of expansion varies depending on the stent design. Therefore, in our case, the mid-stented segment perforation may not have resulted solely from overdistension of the stent but could also be attributed to pinhole perforation of the balloon, as previously documented, particularly in heavily calcified lesions (10, 11). Deploying a long covered stent in the LAD inherently compromises blood flow to multiple critical branches, which can lead to a large infarct territory. However, in this patient, the presence of CTO-like chronic ischemia, compounded by acute ischemia but partially compensated by collateral circulation, helped mitigate the impact of branch occlusion. Given these risks, this approach should only be attempted as an last resort, with comprehensive preparation for potential perforation-related complications. A summary of troubleshooting techniques for an undeflatable stent balloon, along with additional case resources, is available online (12).

Conclusion

Failure to deflate a coronary balloon catheter is an extremely rare but potentially life-threatening complication during PCI. In

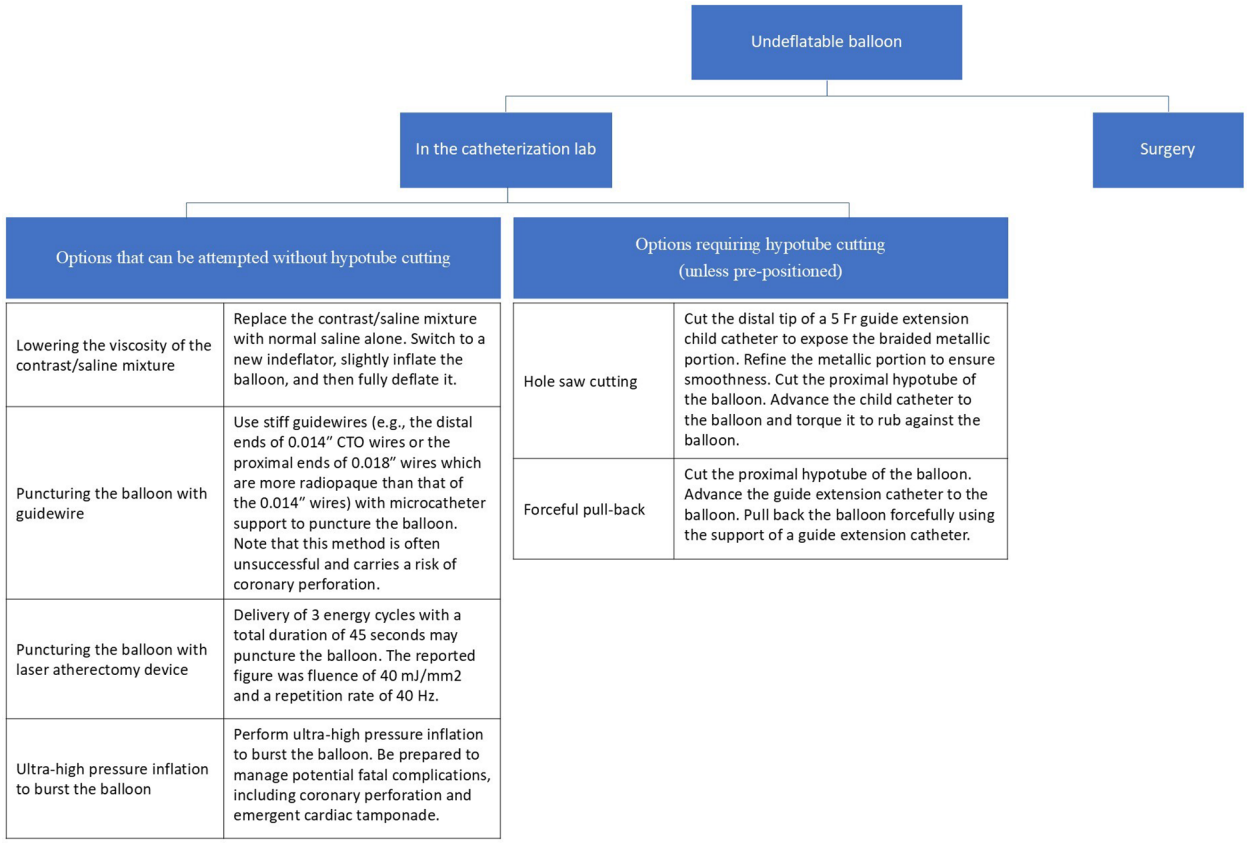

FIGURE 4
Suggested treatment options for an undeflatable balloon. The possible interventions in the catheterization room are broadly categorized into those that require hypotube cutting and those that do not.

our case, conventional retrieval techniques were unsuccessful, ultimately necessitating balloon rupture via ultra-high-pressure inflation as a last resort. While this approach successfully removed the balloon, it resulted in multiple coronary perforations requiring extensive intervention.

To our knowledge, this is the first reported case of a successful stent balloon retrieval using this extreme method within a coronary artery. However, given its high risk, alternative strategies should always be prioritized before considering ultra-high-pressure inflation.

This case highlights the importance of preparing for rare but severe complications during complex PCI procedures. Bursting an undeflatable balloon inside a coronary artery should only be attempted in exceptional circumstances, with thorough preparation for potential catastrophic events, including coronary perforation management.

Data availability statement

The original contributions presented in the study are included in the article further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Pusan National University Yangsan Hospital Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

SK: Writing – original draft. SL: Data curation, Formal Analysis, Writing – review & editing. JK: Conceptualization, Investigation, Visualization, Writing – review & editing. KC: Writing – original draft, Writing – review & editing.

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Conflict of interest

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Case Report: Kounis syndrome associated with urticaria following COVID-19 infection

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This case report describes a 58-year-old woman who sought treatment in the dermatology department after experiencing a three-day episode of widespread rash and itching, along with fever, chills, abdominal distress, and increased urinary frequency and urgency. Upon examination, she exhibited numerous erythematous patches and wheals on her face and body, devoid of blisters or erosions. Laboratory tests indicated an elevated white blood cell count, C-reactive protein, and serum amyloid A, while liver and kidney function tests were within normal limits. An electrocardiogram demonstrated sinus rhythm with T-wave alterations and a V2R/S ratio greater than 1. Subsequent nucleic acid testing confirmed the presence of COVID-19 infection, prompting the initiation of anti-allergic and supportive therapies. Despite this, the patient went on to develop chest pain, which was accompanied by electrocardiographic signs of acute extensive anterior wall myocardial infarction and elevated troponin I levels. Coronary angiography subsequently revealed mild coronary artery stenosis, with no significant blockages or stenoses in the coronary arteries, leading to a diagnosis of Kounis syndrome type II. This case underscores the significance of considering Kounis syndrome in patients with a history of infection or allergies who present with chest pain, emphasizing the necessity for thorough clinical evaluation and continued research.

KEYWORDS

urticaria, allergy, Kounis syndrome, COVID-19, acute myocardial infarction

1 Introduction

Kounis Syndrome, characterized by the development of acute coronary syndrome following an allergic reaction, was first described by Kounis and colleagues in 1991 (1). The pathophysiology of this syndrome involves the activation of mast cells and platelets, rendering it a distinct and uncommon critical condition in clinical practice. While COVID-19 is primarily known for respiratory symptoms, it can also affect multiple organ systems, including the skin and cardiovascular system. Urticaria has been identified as a notable extra-pulmonary cutaneous manifestation of COVID-19 (2). Although there are reports of Kounis Syndrome triggered by urticaria (3, 4), there is limited literature on cases associated with COVID-19-related urticaria. This case report describes a 58-year-old female patient who developed urticaria subsequent to a COVID-19 infectionand later experienced recurrent coronary artery spasms, which were suspected to have contributed to an acute myocardial infarction. The patient's condition was managed successfully with a regimen including anti-allergic, anti-vasospastic, and antiviral treatments. This case emphasizes the importance of considering cardiovascular

complications in the differential diagnosis of patients with COVID-19 who present with cardiac symptoms.

2 Case description

The patient, female, 58 years old, was admitted to the dermatology department of our hospital on August 1, 2024 due to "generalized rash accompanied by itching for 3 days and frequent urination and urgency for 2 days". Three days before admission, the patient developed generalized erythema and wheals without obvious inducement, accompanied by itching, fever, chills, abdominal discomfort. The highest recorded body temperature was 39.3 °C. There was a little nausea but no vomiting or chest tightness. She was tested negative for COVID-19 nucleic acid at Nanjing Drum Tower Hospital. Blood routine and CRP tests were normal. She was treated with ReDuNing Injection (a traditional Chinese medicine preparation) and Loratadine Tablets. The body temperature returned to normal but the rash did not subside. Two days later, the patient developed frequent urination, urgency and pain without hematuria. She was treated with "Dexamethasone Sodium Phosphate Injection" and "Levofloxacin". The rash still did not improve. She had a 20-year history of "hypertension" and usually took "Amlodipine Besylate Tablets" to control blood pressure normally. In 2014 and 2016, the patient underwent coronary CTA examination on two occasions, which revealed no significant obstruction or stenosis in the coronary arteries. She denied a history of drug or food allergy and family genetic disease. She had a history of contact with COVID-19. Physical examination: Multiple erythema and wheals on the face and body, fused into patches, without blisters or erosion. Physical examination of heart and lungs was normal. Blood routine, CRP and serum amyloid A were abnormal (Table 1); immunoglobulin E was 532 IU/ml; urine routine white blood cell count was 24.42/ul; liver and kidney function and myocardial injury markers were normal; mycoplasma pneumoniae antibody and allergens were negative. The electrocardiogram on admission showed (1) sinus rhythm, (2) T wave changes, and (3) V2R/S greater than 1 (Figure 1A); echocardiography showed a left ventricular ejection fraction (LVEF) of 63%; mild tricuspid regurgitation and decreased left ventricular diastolic dysfunction. After admission, she was given Methylprednisolone Sodium Succinate for Injection (40 mg, twice a day), Loratadine (10 mg, once a day), and Ebastine Tablets (10 mg, once a day) for anti-allergy, Omeprazole for Injection (40 mg, twice a day) for protecting gastric mucosa, Levofloxacin and Sodium Chloride Injection (0.5 g, once a day) for anti-infection, and Amlodipine Besylate Tablets (5 mg, once a day) for lowering blood pressure and other symptomatic and supportive treatments. The generalized rash and itching were alleviated. Five days later, the dose of Methylprednisolone Sodium Succinate for Injection was reduced (20 mg, twice a day). Six days later, the patient developed cough and chest tightness. The body temperature was normal. Seven days later, the nucleic acid test for six respiratory pathogens was all negative. The nucleic acid test for novel coronavirus was positive again. The patient was treated with simnotrelvir 0.75 g + ritonavir 0. 1 g (twice a day for 5 days). Nine days later, the patient felt compressive pain in the precordial area. The NRS pain score was 7 points, accompanied by profuse sweating that did not relieve continuously. Electrocardiogram indicated (1) sinus bradycardia; (2) acute extensive anterior wall myocardial infarction; (3) ST-T changes (Figure 1B); Myocardial injury marker troponin I was 0.072 ng/ml. The patient previously underwent two coronary CT angiographies, both of which

TABLE 1 Changes of inflammatory indexes during the patient's onset process.

Laboratory test (Reference range)	Jul 31	Aug 2	Aug 3	Aug 6	Aug 8	Aug 10	Aug 14	Aug 18	Aug 21	Aug 23
CTnI (ng/ml) (0.01–0.023)	—	—	—	—	—	0.072	0.093	0.052	0.011	—
WBC × 10^9/L (3.5–9.5)	11.55	12.3	14.5	16.19	22.04	—	—	13.73	9.75	8.23
CRP(mg/L) (0–6)	51.34	72.03	30.50	4.64	8.10	—	—	53.20	62.65	22.23
SAA(mg/L) (0–10.08)	474.29	528.00	531.40	59.41	64.24	—	—	—	—	—

cTnI, cardiac Troponin I; WBC, white blood cell count; CRP, C-reactive protein; SAA, serum amyloid.

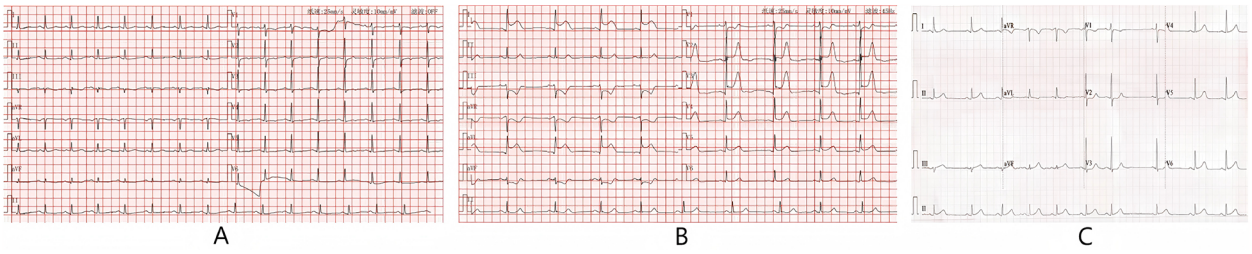

FIGURE 1
(A) ECG of the patient on admission: T-wave changes; (B) ECG at the onset of chest pain: ST segment elevation in leads I, aVL, V2–5; (C) after the patient chest pain was relieved, the elevated ST segment fell back and premature atrial contractions occurred.

showed no significant stenosis. This episode of chest pain occurred at rest during nighttime, leading us to suspect acute myocardial infarction associated with coronary artery spasm. Considering the patient's history of allergic reactions and the potential risk of contrast agents used in coronary angiography exacerbating allergic responses, coronary angiography was not performed. Instead, the patient was treated as follows: Aspirin enteric-coated tablets (100 mg, once daily) and clopidogrel bisulfate tablets (75 mg, once daily) were administered for dual antiplatelet therapy. Heparin (0.4 ml, twice daily) was used for anticoagulation. To relieve coronary artery spasm, diltiazem hydrochloride tablets (30 mg four times daily) and nicorandil tablets (5 mg three times daily) were prescribed. Additionally, intravenous methylprednisolone sodium succinate (10 mg once daily) was administered to mitigate potential allergic reactions, and isosorbide dinitrate injection (20 mg once daily) was given to further alleviate coronary spasm and improve myocardial perfusion. Following this medical treatment, the chest pain symptoms were relieved, and the electrocardiogram returnedto normal. However, atrial premature beats were observed (Figure 1C). Ten days later, reexamination of echocardiography showed no definite segmental wall motion abnormality in resting state, and LVEF was 60%. Considering the patient's allergic history, the risks associated with coronary angiography, and the symptomatic relief achieved with medication, a conservative drug treatment approach was continued. Methylprednisolone sodium succinate was gradually reduced and changed to prednisone acetate tablets (20 mg, once daily) orally to inhibit inflammatory reaction. Two weeks later, the patient had compressive pain in the chest and back again. The NRS pain score was 4 points, accompanied by radiating pain to the left shoulder and jaw. After isosorbide nitrate and papaverine hydrochloride were pumped in, the symptoms were not significantly relieved. Reexamination of electrocardiogram showed dynamic evolution of T waves in precordial leads (Figure 2), and myocardial injury marker troponin I was 0.093 ng/ml. Considering that the patient's chest pain symptoms did not relieve continuously, coronary angiography was performed on August 14, which indicated mild coronary artery stenosis (Figure 3). Continue to give antiplatelet aggregation, lipid regulation, anti-coronary artery spasm and anti-allergic treatment. Eighteen days later, reexamination of novel coronavirus nucleic acid test was negative. The rash all over the body gradually disappeared, and the patient was discharged after improvement. After discharge, the dosage of prednisone acetate tablets was gradually reduced and eventually discontinued. The patient continued to take nicorandil, diltiazem hydrochloride tablets, aspirin enteric-coated tablets and atorvastatin calcium tablets orally. At the one-month follow-up, no recurrence of urticaria or angina symptoms was observed.

3 Discussion

The main clinical symptoms of coronavirus disease 2019 (COVID-19) include fever, sore throat, fatigue, cough, and dyspnea. Some severe patients may experience respiratory failure, multiple organ dysfunction, and even death (5). With the increase in clinical cases, it is currently believed that COVID-19 can involve various systems throughout the body, including the skin and cardiovascular system. The etiology or inducement of urticaria is relatively complex. Its onset is related to infection. The specific pathogenesis may be the activation and degranulation of mast cells through immune and non-immune mechanisms (6). Literature reports that urticaria is an important part of the extrapulmonary skin manifestations of COVID-19 and can appear at different times during infection. It can precede, occur simultaneously with, or follow other symptoms. Watashi et al. reported a patient with acute urticaria as the first symptom of COVID-19 (7). There are also patients with fever and urticaria-like rashes as clinical manifestations (8). At the same time, the impact of COVID-19 on the cardiovascular system has attracted much attention. 50%–60% of patients with myocardial injury do not have severe coronary artery stenosis

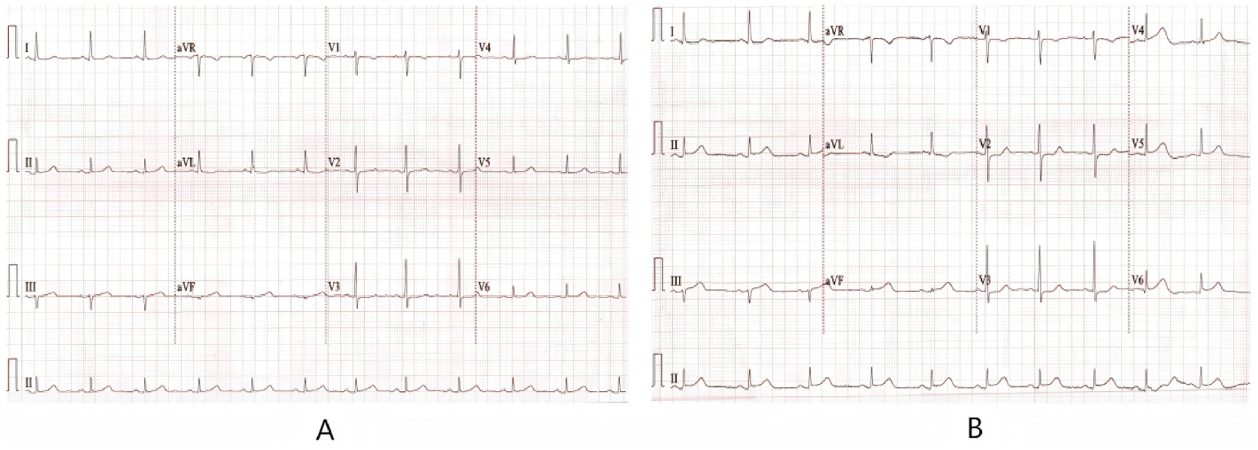

FIGURE 2
(A) When the patient has another angina attack. (B) Electrocardiogram when the pain patient has relief from chest.

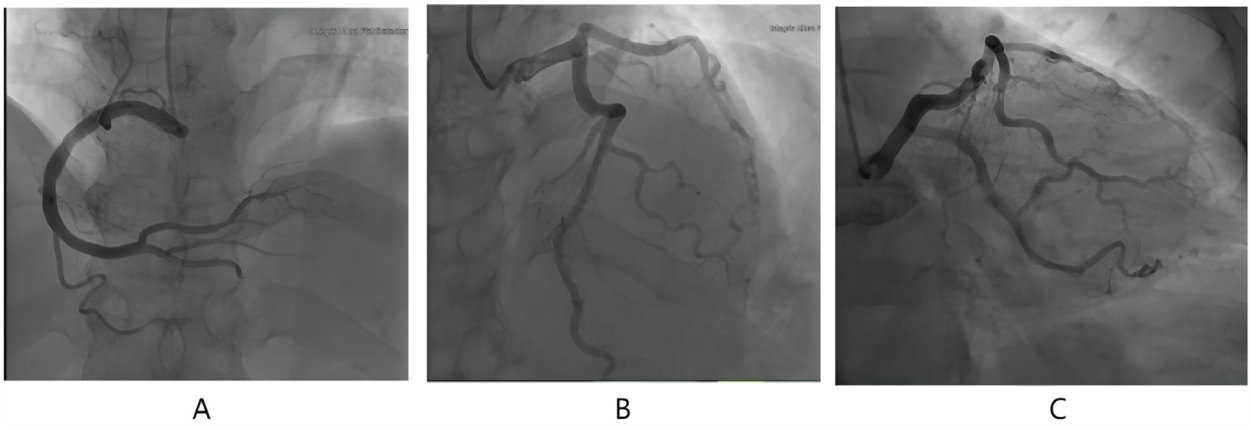

FIGURE 3
Angiographic image of this patient. **(A)** (CRA25.5+RAO1.7) the right coronary artery. **(B)** (CRA39.2+RAO3.2) the left anterior descending branch. **(C)** (CAU23.1+RAO23.6) the circumflex branch.

(9). Some scholars call this situation acute COVID-19 cardiovascular syndrome (10). COVID-19 can cause myocardial injury through various mechanisms, including direct viral infection of cardiomyocytes, excessive inflammatory responses, endothelial dysfunction, microthrombosis, plaque rupture, and hypoxemia leading to myocardial ischemia and cell apoptosis (11).

The incubation period of the new coronavirus is 1–14 days, mostly 3–7 days. Usually, nucleic acid can be detected positive 3–7 days after infection (12). This patient had rare urticaria with fever as the first clinical symptom. No special food or drugs had been taken before, so urticaria caused by food or drugs can be excluded. Although the first nucleic acid test for the new coronavirus was negative, considering that the new coronavirus may act as an allergen, induce an immune response in the body, activate mast cells to degranulate, trigger hypersensitivity reactions, release a large amount of inflammatory mediators, and cause urticaria. At the same time, inflammatory mediators will lead to endothelial dysfunction, microcirculatory dysfunction, and even damage the stability of atherosclerotic plaques to a certain extent, thereby inducing repeated coronary artery spasms. The latest literature reports (13) that Kounis syndrome is divided into four types: Type I occurs in patients with normal coronary angiography and is the most common type in clinical practice. Most cases are coronary artery spasms caused by allergic reactions. Type II is for those with coronary atherosclerosis. Inflammatory mediators induce coronary artery spasms, plaque rupture, and are often accompanied by thrombosis. Type III occurs in patients with in-stent thrombosis or restenosis of coronary arteries. Type IV occurs in patients who have previously undergone coronary artery bypass grafting. In this case, the patient was admitted to the hospital due to urticaria. The new coronavirus was positive. The immunoglobulin E level was increased. Subsequently, the patient had chest pain symptoms. The ST segment was transiently elevated on the electrocardiogram, and troponin was increased. Coronary angiography suggested the presence of coronary atherosclerosis. After giving anti-allergic and anti-spasm drugs, the symptoms were relieved. Combined with the medical history, clinical manifestations and auxiliary examinations, this patient is considered to have type II Kounis syndrome. Podder et al. (14) reported a rare case of ibuprofen-induced type 1 Kounis syndrome, with urticaria as the initial symptom, which is similar to our case where urticaria was also the primary clinical manifestation. However, the triggering factors differed between the two cases (COVID-19 infection vs. NSAID exposure). These cases highlight the importance of considering Kounis syndrome as a potential diagnosis when allergic patients present with cardiac symptoms.

Kounis syndrome needs to be differentiated from Takotsubo syndrome. The clinical manifestations and outcomes of these two diseases are similar. There are even reports that these two diseases can coexist, called ATAK syndrome (15). However, in Kounis syndrome, allergic reactions induce coronary artery spasms, plaque erosion, rupture or thrombosis. The allergic indicators in the patient's peripheral blood are often significantly increased. There may be no change in ventricular wall motion.

Takotsubo syndrome can be caused by various emotions and diseases. Current research believes that it is related to sympathetic nerve activation. The peripheral allergic indicators of patients usually do not change. Abnormal left ventricular wall motion is a necessary condition for the diagnosis of Takotsubo syndrome (16), and the local abnormal wall motion often exceeds the scope of the supply of a single epicardial vessel. In this patient, no obvious abnormal wall motion was seen on echocardiography, so Takotsubo syndrome is not considered.

In summary, allergic reactions triggered by various foods, medications, or environmental factors can induce Kounis syndrome. COVID-19, known to cause systemic inflammatory responses leading to multi-organ damage, may also contribute to this condition. When patients present with cardiac symptoms, it is crucial to recognize the importance of dynamic electrocardiogram monitoring and myocardial biomarker testing to ensure timely and

accurate diagnosis, thereby reducing the risk of missed or misdiagnosed cases. Additionally, in future clinical practice, a comprehensive evaluation of potential triggering factors for Kounis syndrome is essential.

4 Conclusions

This case report describes a rare case of recurrent coronary artery spasm triggered by urticaria following COVID-19 infection, emphasizing the importance of considering Kounis syndrome in patients with a history of infection or allergies presenting with chest pain. This underscores the need for further research and vigilant clinical assessment.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the committee of The Hospital of Jining Medical University. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Case report of severe coronary artery disease complicated by malignant arrhythmia due to inherited thrombophilia

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The principal clinical manifestation of thrombophilia is venous thromboembolism, which is also markedly linked to arterial thrombosis, including myocardial infarction. Nevertheless, patients presenting with an early-onset myocardial infarction are seldom screened for thrombophilic genes, resulting in delayed diagnosis and an unfavourable prognosis. This report presents the case of a young man who suffered an acute myocardial infarction as a result of thrombophilia. The patient had a history of deep vein thrombosis and was genetically tested to carry two thrombophilia susceptibility alleles at the PAI-1 (4G/5G) and MTHFR (C > T) loci. This ultimately resulted in severe coronary artery occlusion, myocardial scarring and frequent episodes of ventricular tachycardia, which had a significant impact on the patient's quality of life. The objective of this report was to enhance clinicians' awareness of embolism susceptibility. It is recommended that young and middle-aged patients with severe coronary artery stenosis undergo screening for embolism.

KEYWORDS

myocardial infarction, arrhythmia, thrombophilia, cardiac function, coronary artery disease, youth

Introduction

Thrombophilia refers to a pathological state in which thrombosis and thromboembolism are prone to occur due to various genetic or acquired factors (1). Thrombophilia is more common in patients with unguided venous thromboembolism (VTE), especially in those under 40 years old, with the majority being hereditary (2). Acquired thrombophilia mainly occurs in patients with various acquired diseases or acquired risk factors, due to increased levels of procoagulant proteins, decreased levels of anticoagulant proteins, and altered inflammation/autoimmune mechanisms, which increase the tendency for thromboembolism. Hereditary thrombophilia is commonly caused by mutations in genes such as antithrombin (AT), protein C (PC), protein S (PS), coagulation factor V Leiden (FVL), plasminogen activator inhibitor-1 (PAI-1), and methylenetetrahydrofolate reductase (MTHFR), leading to loss of protein anticoagulant function or enhancement of procoagulant function, ultimately resulting in thromboembolism. And thrombosis is more common in the venous system and less common in arteries (especially coronary arteries). The occurrence of acute myocardial infarction (AMI) is significantly correlated with hypercoagulability and impaired

fibrinolysis (3). Therefore, certain types of thrombophilia may also manifest as young onset acute coronary syndrome, ischemic stroke, and other arterial thrombotic events.

Plasminogen activator inhibitor-1 (PAI-1) is a member of serine protease inhibitor (SERPIN) family that acts as the primary inhibitor of two main mammalian plasminogen activators, urinary-type (uPA) and tissue-type (tPA). Research has shown that a deficiency of PAI-1 accelerates the rate of fibrinolysis and bleeding, while an increase in PAI-1 levels can easily lead to intravascular thrombosis (4, 5). The deletion/insertion polymorphism (4G/5G) within the PAI-1 locus can affect the transcriptional expression of this gene, and males with 4G allele are prone to acute myocardial infarction and coronary artery thrombosis (6–8).

Methylenetetrahydrofolate reductase (MTHFR) plays a major role in regulating homocysteine (HC) levels and increases the risk of venous thromboembolism and CAD (9, 10). In addition, genotype is associated with the bioavailability of vascular nitric oxide and the production of superoxide by uncoupling endothelial nitric oxide synthase. It is speculated that MTHFR mutations may also be a high-risk factor for myocardial infarction (11).

In summary, hereditary thrombophilia plays a crucial role in myocardial infarction in specific populations. In addition, cases of coronary thrombosis caused by carrying two susceptibility genes, PAI-1 (4G/5G) and MTHFR (C > T), are extremely rare, and there are great difficulties in screening and diagnosis, which may be related to severe complications and poor prognosis after myocardial infarction. However, there is currently no research reporting on the diagnosis and treatment of young myocardial infarction and serious complications caused by genetic thrombophilia.

This case report demonstrates the genetic testing of a young myocardial infarction patient with thrombophilia and provides follow-up information, in order to provide diagnostic and therapeutic evidence for the treatment and screening of thrombophilia.

Case presentation

A 25-year-old male was admitted to the hospital due to recurrent episodes of tachycardia. The duration of tachycardia is about 1 h, accompanied by a feeling of obstruction in the throat, sweating, and shortness of breath. It is relieved after rest, and there is no chest pain or tightness. The patient has a 10-year history of smoking. He was diagnosed with deep vein thrombosis in his right lower limb 8 years ago. After taking rivaroxaban

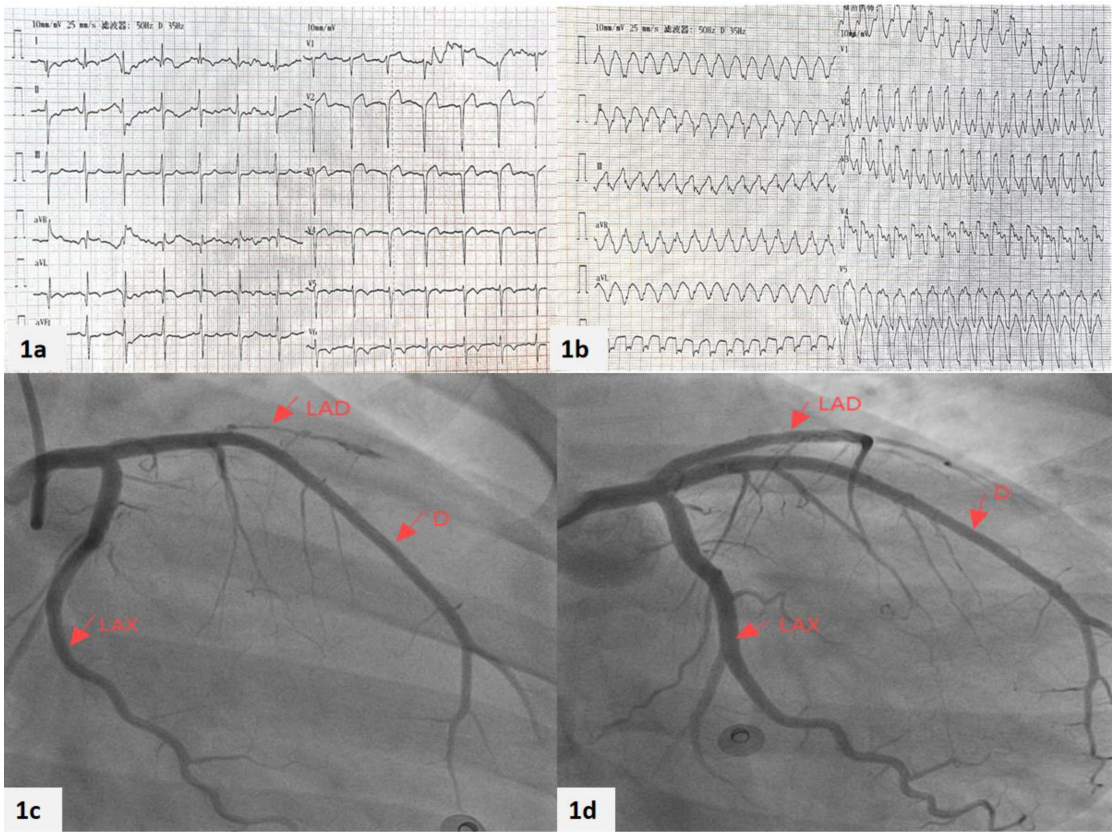

FIGURE 1
Patient's first admission electrocardiogram combined with coronary angiography and stent placement. The patient's **(a)** electrocardiogram at the time of hospital admission and **(b)** the electrocardiogram during the follow-up examination 2 months later. The results of the patient's coronary angiography **(c)** found that occlusion in the proximal segment of the left anterior descending artery (LAD). Then **(d)** stents were implanted.

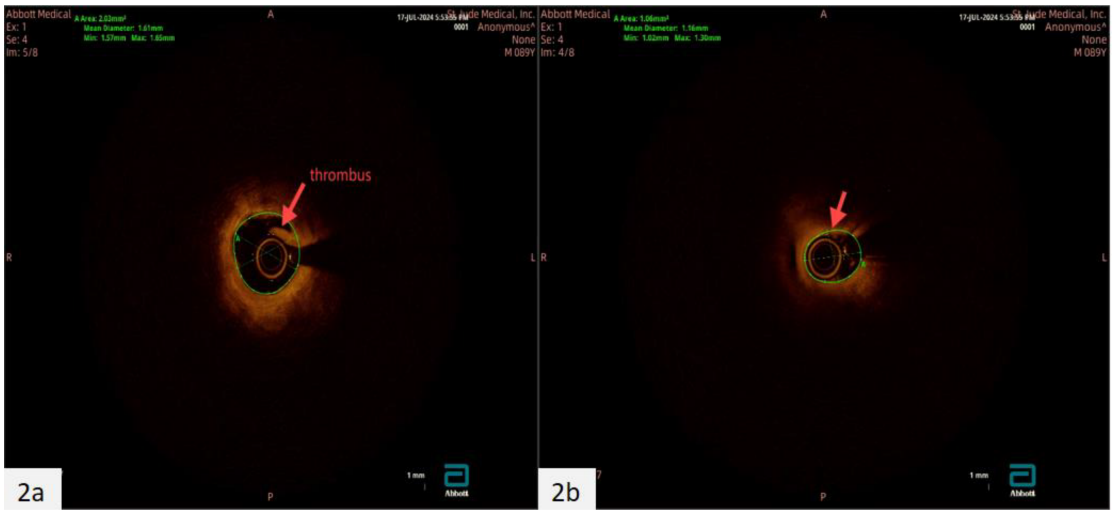

FIGURE 2
Coronary artery OCT image. There is a large amount of thrombus in the coronary artery of the patient's LAD (a), causing coronary stenosis (b) and acute myocardial infarction. The area indicated by the arrow in the figure represents the location of vascular stenosis or thrombus.

orally, the thrombosis was controlled and he stopped taking the medication on his own. In addition, the patient's father suffered from a cerebral infarction, which resulted in limb paralysis.

There were no obvious abnormalities in the physical examination upon admission. Laboratory tests indicate a significant increase in myocardial injury markers (high-sensitivity troponin: 0.149 ng/ml, normal range: 0–0.014 ng/ml, myoglobin 141.8 ng/ml, normal range: 21–72 ng/ml, creatine kinase isoenzyme 23.14 ng/ml, normal range: 0–5.501 ng/ml). Blood cell count, serum electrolytes, liver and kidney function tests, and coagulation function are all within normal ranges. Electrocardiogram shows ST segment elevation in leads V2-V4, accompanied by ST segment depression in leads II, III, and aVF (Figure 1a), suggesting acute anterior wall ST segment elevation myocardial infarction. Subsequently, the patient underwent coronary angiography and found occlusion in the proximal segment of the left anterior descending artery (LAD) (Figure 1c), while no other coronary arteries were narrowed. Optical coherence tomography (OCT) examination results showed that the LAD lumen was mainly composed of organized thrombus, with the narrowest area of 0.98 mm^2, an area stenosis rate of about 78.1%, and a diameter stenosis rate of about 53.3% (Figure 2a,b). One stent was implanted in series from far to near at the lesion site in the proximal and middle segments of the LAD (Figure 1d). At the same time, further improvements were made to lupus anticoagulants, autoantibody spectrum and ANCA, anti CCP antibodies, anti cardiolipin antibodies, and bilateral lower limb venous ultrasound, all of which were negative. We further investigated the possibility of thrombophilia. As expected, the patient carried two susceptibility genes, PAI-1 (4G/5G) and MTHFR (C > T) (Table 1). During hospitalization, the patient experienced frequent ventricular premature beats. A 24-hour dynamic electrocardiogram revealed 3,835 episodes of ventricular premature beats throughout the entire process.

TABLE 1 The patient carried two susceptibility genes, PAI-1 (4G/5G) and MTHFR (C > T).

Gene name	Genotype	Result	Reference allele	OR value
PAI-1 (4G/5G)	4G4G	–	5G	1.56
	4G5G	+		
	5G5G	–		
PROC (C > T)	CC	+	C	7.34
	CT	–		
	TT	–		
PROC (de1AAG)	DUP/DUP	+	DUP	2.71
	DEL/DUP	–		
	DEL/DEL	–		
THBD (G > T)	GG	+	G	2.8
	GT	–		
	TT	–		
MTHFR (C > T)	CC	–	C	1.75
	CT	+		
	TT	–		
APOH (T > C)	TT	+	T	1.55
	TC	–		
	CC	–		
SERPINC1 (G > A)	GG	+	G	1.2
	GA	–		
	AA	–		

Cardiac magnetic resonance imaging showed weakened cardiac motion, enlarged left ventricular chamber, thinning of the middle and apical segments of the left ventricle, and a significant decrease in corresponding motion, mainly in the interventricular and anterior walls. Echocardiography shows a significant decrease in left ventricular systolic function (Table 1). The extensive thickening rate of the left ventricular wall decreased, mainly in the basal segment anterior interventricular and apical segment lateral walls (<0%). Left ventricular function: EF: 14.76%

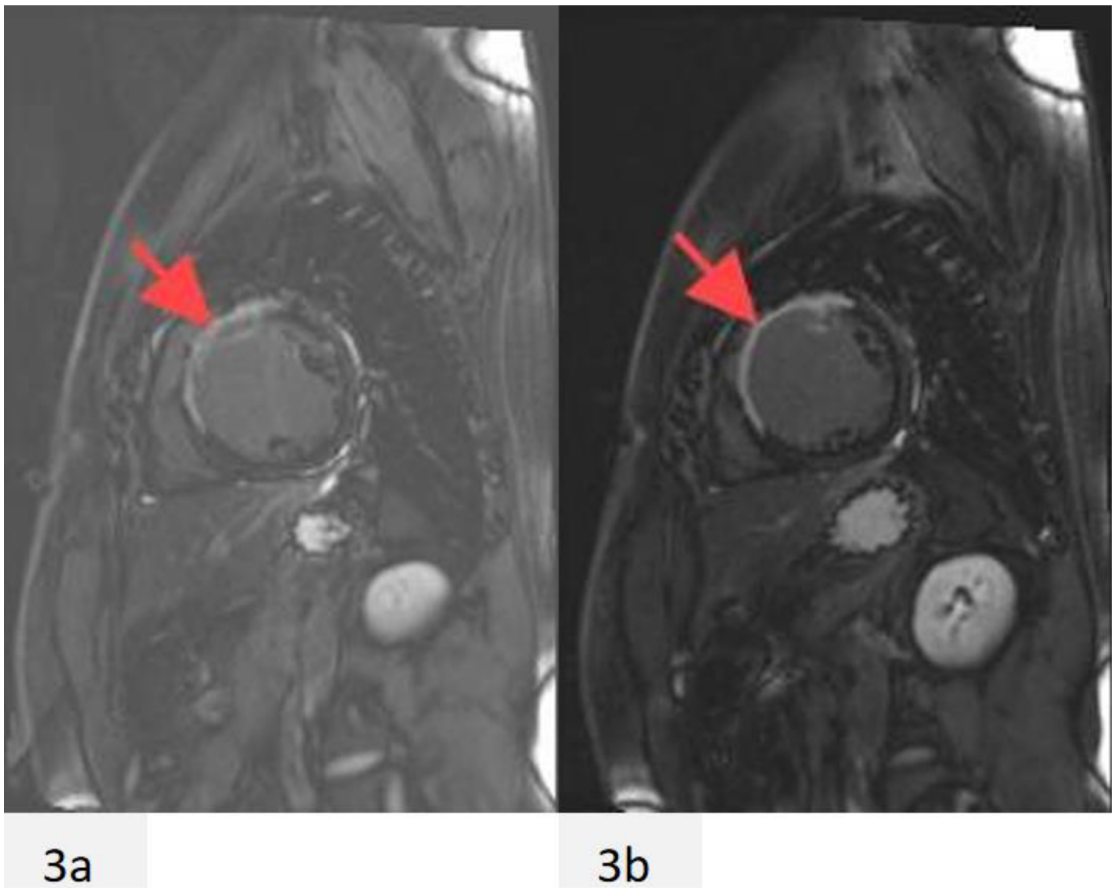

FIGURE 3
The patient underwent cardiac magnetic resonance imaging during their first admission (a,b). The area indicated by the arrow in the figure represents cardiac scars or fibrosis.

TABLE 2 Two-dimensional data from the echocardiogram.

	First admission	Second admission
LA (mm)	38	34 × 52 × 43
LVDd (mm)	74	70
LVDs (mm)	58	58
IVS (mm)	9	8
LVPW (mm)	9	8
RA (mm)	50 × 41	48 × 45
RV (mm)	24	19
LVEF (%)	41	34

LA, left atrial diameter; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-diastolic diameter; IVS, interventricular septum; LVPW, left ventricular posterior wall at end-diastole; RA, suitable atrium diameter; RV, right ventricular diameter; LVEF, left ventricular ejection fraction.

(Figure 3a,b). Subsequently, the patient received 100 mg of aspirin daily for antiplatelet aggregation therapy, 20 mg of atorvastatin for lipid-lowering therapy, and 20 mg of rivaroxaban for anticoagulant therapy.

During the 1 month follow-up after discharge, the patient still experienced recurrent palpitations, with approximately 3–4 episodes. When readmitted, high-sensitivity troponin levels were 0.038 ng/ml, normal range 0–0.014 ng/ml, myoglobin levels were 24.130 ng/ml, normal range 21–72 ng/ml, creatine kinase isoenzyme levels were 2.224 ng/ml, normal range 0–5.501 ng/ml, NT- proBNP levels were 1,976.00 pg/ml. NT- proBNP levels were significantly elevated compared to the previous admission (Table 2). The electrocardiogram showed paroxysmal ventricular tachycardia (Figure 1b), which was treated with amiodarone to control the arrhythmia. It was suggested that the patient undergo ICD implantation treatment, but the patient refused. After discharge, the patient was still treated with aspirin 100 mg, atorvastatin 20 mg, and rivaroxaban 20 mg.

Discussion

It is recommended that young and middle-aged patients with severe coronary artery stenosis undergo screening for embolism. Currently, acquired or hereditary thrombophilia can be detected in many patients presenting with venous thromboembolism (VTE), and some patients may experience severe thromboembolic disease recurrence in the short term. The patient mainly presents with non induced lower limb venous thrombosis and short-term concurrent coronary

thromboembolism, leading to acute myocardial infarction. The main causes of death in patients with acute myocardial death are malignant arrhythmia and significant decline in cardiac function due to excessive cardiac remodeling. We observed that the patient's myocardial infarction area was not large, but the heart function was extremely poor. Echocardiography shows a significant decline in cardiac function, while cardiac magnetic resonance imaging suggests severe cardiac scarring. Therefore, we speculate that thrombophilia may be an important cause of excessive cardiac remodeling leading to cardiac scars in young patients after myocardial infarction. The patient was prevented from further myocardial death due to myocardial ischemia after stent implantation treatment, but experienced irreversible serious complications. We suspect that hereditary thrombophilia may have some mechanism of action in vascular endothelial injury and endocardial damage.

The guidelines recommend indefinite antithrombotic therapy for most patients with non induced VTE. Research has shown that once anticoagulant therapy is discontinued, the risk of thromboembolic disease recurrence within 10 years after the first episode ranges from 30% to 50%. In this case report, the patient's self-discontinuation of oral anticoagulant therapy after the first occurrence of venous thrombosis may be one of the important reasons for coronary thrombosis.

Genetic thrombophilia is relatively rare in young patients with acute myocardial infarction caused by coronary artery thrombosis. Thrombophilia is not only an important pathogenesis leading to thromboembolism, but may also be a significant cause of adverse consequences after early onset of myocardial infarction. Therefore, in clinical practice, we need to be highly vigilant about the possibility of genetic thrombophilia in young patients with unexplained myocardial infarction.

Conclusion

The changes in coagulation status caused by mutations in PAI-1 and MTHFR genes are the genetic basis of the patient's myocardial infarction. After stent implantation treatment, coronary blood flow was restored, and postoperative anticoagulation therapy was continued to prevent the formation of new blood clots. But the patient experienced severe arrhythmia and cardiac dysfunction, and the mechanism is currently unclear, which may be related to genetic thrombophilia.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

JY: Writing – original draft, Conceptualization, Investigation, Visualization, Writing – review & editing. LZ: Conceptualization, Writing – original draft. CY: Data curation, Formal analysis, Investigation, Writing – original draft. XK: Resources, Writing – original draft. LL: Project administration, Resources, Writing – review & editing. XF: Methodology, Supervision, Writing – review & editing. XL: Writing – review & editing, Funding acquisition, Project administration, Writing – original draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The author(s) declare that no Generative AI was used in the creation of this manuscript.

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Case Report: a 28-year-old female with anomalous origin of the left coronary artery from the pulmonary artery syndrome presented as atrial fibrillation and pulmonary hypertension

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Anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) typically manifests in the first weeks of life. We report a 28-year-old woman with atrial fibrillation and pulmonary hypertension which were later found to be associated with ALCAPA syndrome. Despite a history free of traditional cardiovascular risk factors, her symptoms included exercise intolerance, palpitations, and an ischemic stroke. Echocardiography and further examination revealed pulmonary artery origin of the left coronary artery and extensive collateral formation between the left and right coronary arteries, contributing to her symptoms.

KEYWORDS

ALCAPA, anomalous origin of the left coronary artery from the pulmonary artery, atrial fibrillation, pulmonary hypertension, case report

Introduction

Anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) syndrome, also known as Bland-White-Garland syndrome, is a rare congenital anomaly affecting 1 in 300,000 live births (1). If untreated, ALCAPA has a high mortality rate, with most undiagnosed cases dying within the first year of life from myocardial ischemia or arrhythmia (2). If there is adequate coronary collateral between the right coronary artery (RCA) and the left coronary artery (LCA), symptoms of this anomaly may not appear until adulthood (3). However, the occurrence of ALCAPA in adults is exceedingly rare, and specific incidence data for this demographic are lacking because such cases are seldom reported. This case report describes a 28-year-old woman who presented with atrial fibrillation and pulmonary hypertension, symptoms that were later attributed to ALCAPA.

Case description

A 28-year-old female was admitted to our hospital due to atrial fibrillation and pulmonary hypertension. She first experienced palpitations at the age of 20, and an ECG confirmed atrial fibrillation. Despite treatment with amiodarone, her condition escalated from paroxysmal to persistent atrial fibrillation. She has not undergone

anticoagulation therapy. At the age of 27, her exercise tolerance notably declined, accompanied by chest pain post-activity, and suffered an ischemic stroke. The echocardiography estimated the pulmonary artery systolic pressure (PASP) at 67 mmHg. Although she was treated with oral ambrisentan, her exercise tolerance did not improve, leading her to seek further treatment at our institution. Her medical history was clear of hypertension, diabetes, hyperlipidemia, smoking, drug or food allergies, stimulant use, or any family history of cardiovascular disease. On physical examination, her vital signs were normal, with P2 > A2, irregular heart rhythm, and mild edema in both lower limbs. The patient's thyroid function, hepatic and renal function, high-sensitive troponin I were normal. The N-terminal pro-B-type natriuretic peptide (NT-proBNP) level was elevated at 2,180 pg/ml (normal range: 0–125 pg/ml). Her ECG showed atrial fibrillation with ST-segment depression in leads I, aVL and V4–V6, and poor R-wave progression in leads V1–V3 (Figure 1). Right heart catheterization (RHC) revealed the pulmonary artery systolic pressure, diastolic pressure, and mean pressure were 42 mmHg, 22 mmHg, and 30 mmHg, respectively. The pulmonary capillary wedge pressure (PCWP) was 23 mmHg, and the pulmonary vascular resistance (PVR) was measured at 1.26 Wood Units, suggesting the pulmonary hypertension was related to left heart disease (4). Her transthoracic echocardiography showed a left ventricular ejection fraction of 65%, with an enlarged left atrium with dimensions measuring 48 mm antero-posteriorly, 61 mm superior-inferiorly, and 50 mm transversely, and suspected origin of the LCA from the pulmonary artery. Additionally, the right coronary artery is dilated, and there is visible extensive blood flow communication between the left and right coronary arteries within the myocardium. Echocardiographic evaluation also revealed mild left ventricular enlargement, with left ventricular end-diastolic dimension 51.2 mm and left ventricular end-diastolic volume indexed 74.31 ml/m^2. Although no regional wall motion abnormalities were observed, the impaired diastolic function (E/e′ ratio 12) indicates chronic ischemia of the left ventricle. There are also signs of right heart dysfunction to chronic pulmonary hypertension with reduced tricuspid annular plane systolic excursion (TAPSE) 12 mm (Figure 2). Further coronary computed tomography angiography (CTA) and coronary angiography showed the left main coronary artery (LMCA) originating from the pulmonary artery, with multiple connections between the distal left and right coronary arteries, and a right coronary to left ventricle fistula (Figure 3 and Supplementary Video S1). Based on these observations, we thought that her clinical manifestations were due to anomalous coronary origin, specifically the abnormal origin of the left coronary artery from the pulmonary artery. The left atrium, mainly supplied by the left circumflex branch (LCX), suffered from prolonged ischemia, leading to structural and electrophysiological remodeling and subsequently to atrial fibrillation and heart failure with preserved ejection fraction (HFpEF), resulting in left heart failure-related pulmonary hypertension, and stroke. She underwent surgery intervention under general anesthesia with hypothermic cardiopulmonary bypass, including the LMCA repositioning and radiofrequency ablation for atrial fibrillation. Postoperative medications included warfarin and aspirin for thromboembolic prophylaxis, amiodarone for rhythm stabilization, and dapagliflozin for optimization in HFpEF phenotype. She was followed up six months after surgery. She regained sinus rhythm, demonstrated a significant improvement in exercise tolerance, and showed a decrease in NT-proBNP levels to 233 pg/ml.

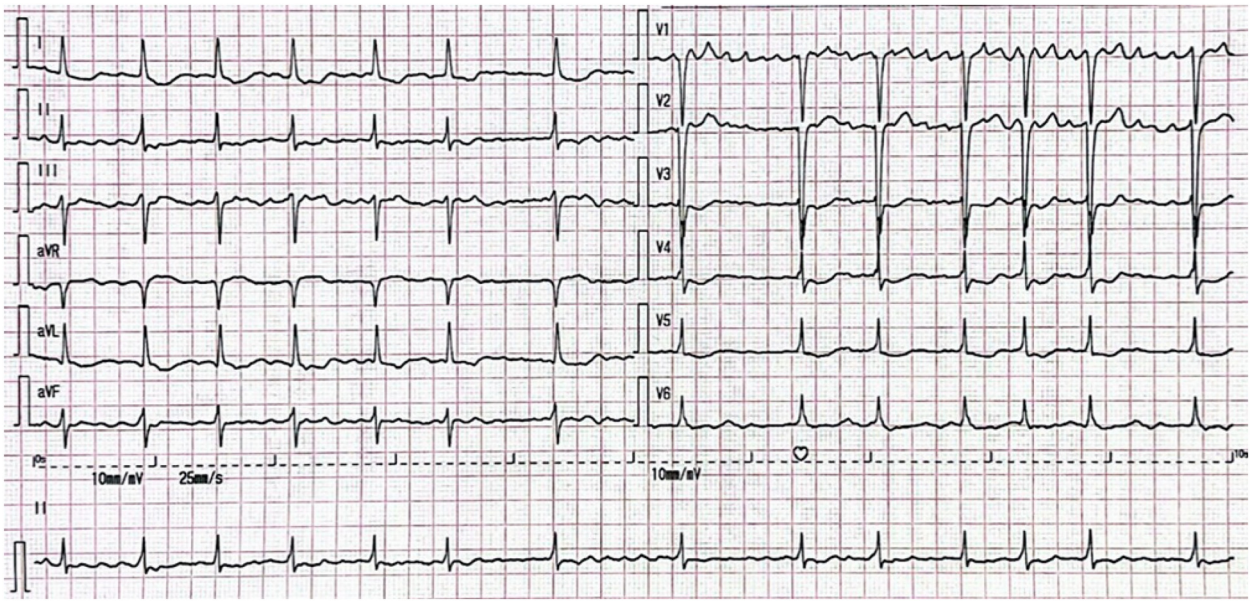

FIGURE 1
ECG. The ECG shows atrial fibrillation with a ventricular rate of 84 bpm, ST-segment depression in leads I, aVL and V4–V6, and poor R-wave progression in leads V1–V3.

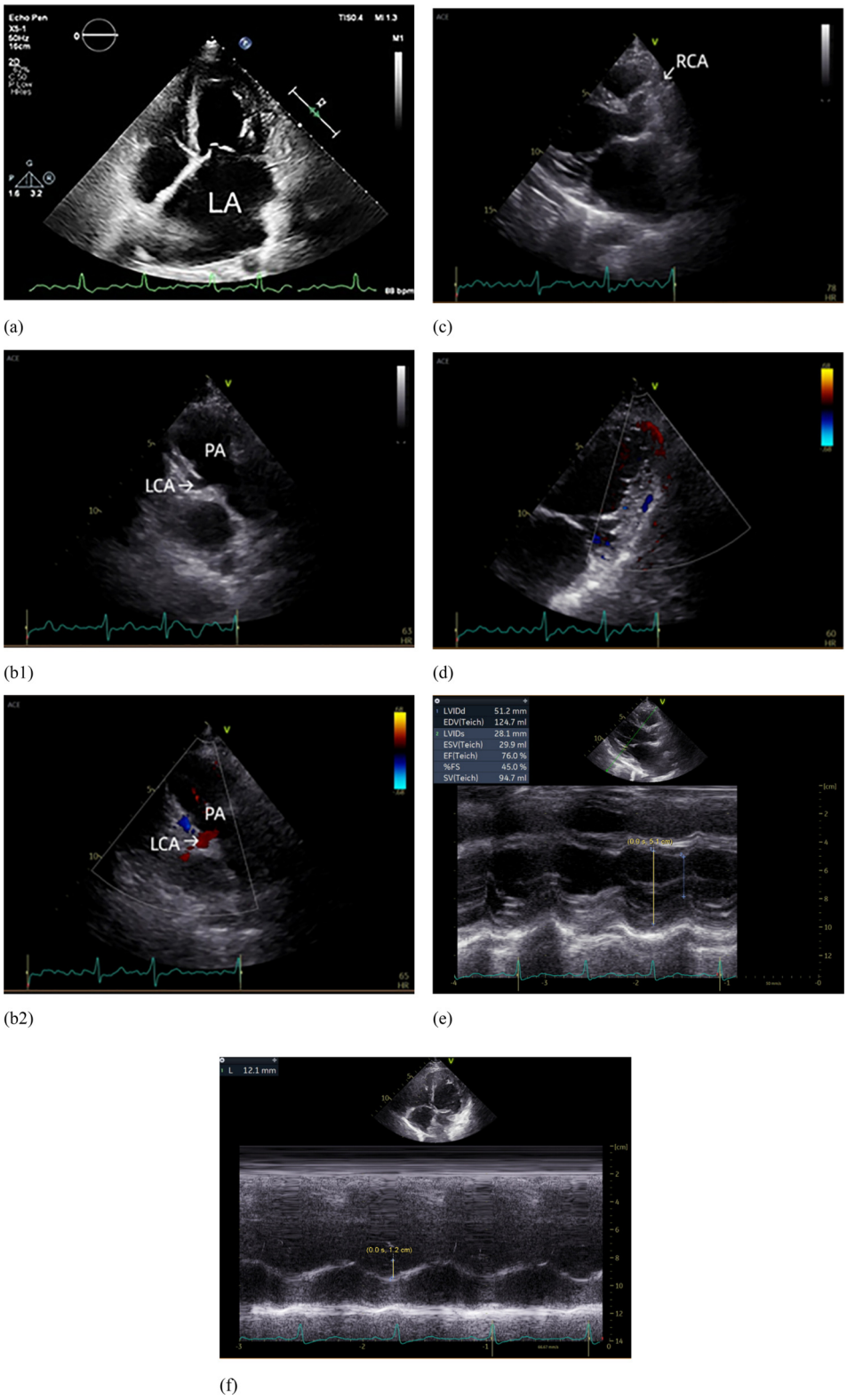

FIGURE 2
Echocardiograph. **(a)** The left atrium was markedly enlarged; **(b1)** The left coronary artery (LCA) originates from the pulmonary artery (PA); **(b2)** Blood flow from LCA to PA; **(c)** The right coronary artery (RCA) originates from the right coronary sinus and is dilated. **(d)** Intramyocardial visualization of blood flow signals between the LCA and RCA. **(e)** Dilatation of the left ventricle. **(f)** Reduced tricuspid annular plane systolic excursion (TAPSE).

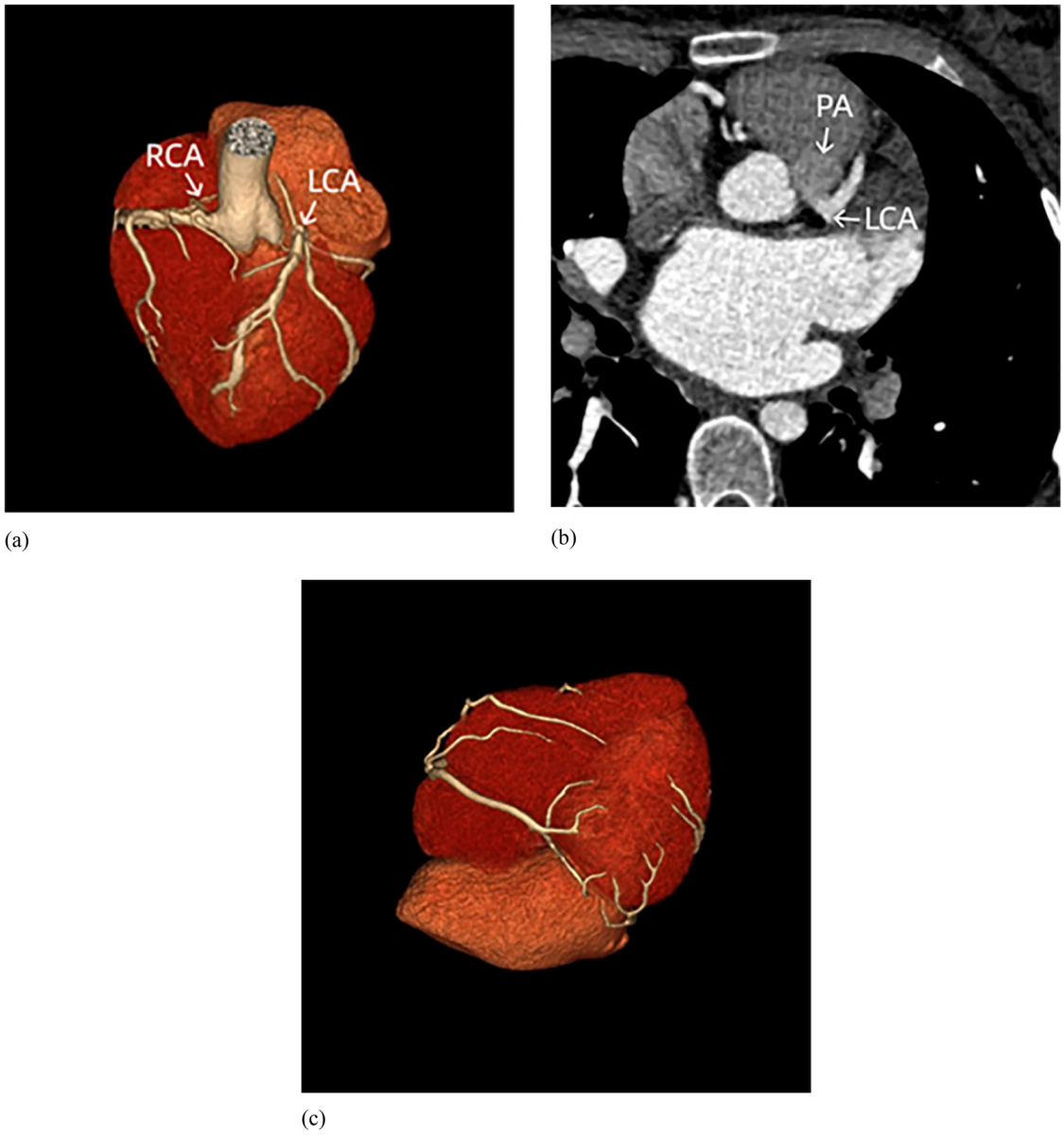

FIGURE 3
Coronary CT. **(a)** The right coronary artery (RCA) originates from the aortic root, while the left coronary artery (LCA) originates from the pulmonary artery (without pulmonary artery reconstruction). **(b)** The LCA originates from the pulmonary artery (PA). **(c)** Extensive communications exist between LCA and RCA.

Echocardiography revealed a reduction in left atrial size to dimensions of 48 mm × 61 mm × 50 mm (antero-posterior × superior-inferior × transverse diameters) and a decreased estimated PASP from 60–47 mmHg. The timeline of the diagnosis and treatment of the patient is shown in Figure 4.

Discussion

This article reports a case of an adult ALCAPA patient with atrial fibrillation and pulmonary hypertension due to left heart disease as clinical manifestations.

ALCAPA syndrome is classified into infant and adult types, each with different symptoms and outcomes (5). Infants typically suffer from myocardial infarction and congestive heart failure, with approximately 90% dying within the first year. In adults, ALCAPA is less common. Patients may present with symptoms of angina pectoris, dyspnea, syncope, and palpitations, and it can be a significant factor in sudden cardiac death (3, 6). When presented in adulthood, ALCAPA typically shows abundant interarterial collateral vessels between the RCA and the LCA (7). This was confirmed by coronary angiography and coronary CTA in this case and is the reason why she did not die at an early age.

Yau et al. summarize the clinical manifestations of adult patients with ALCAPA, noting that 66% of cases present with

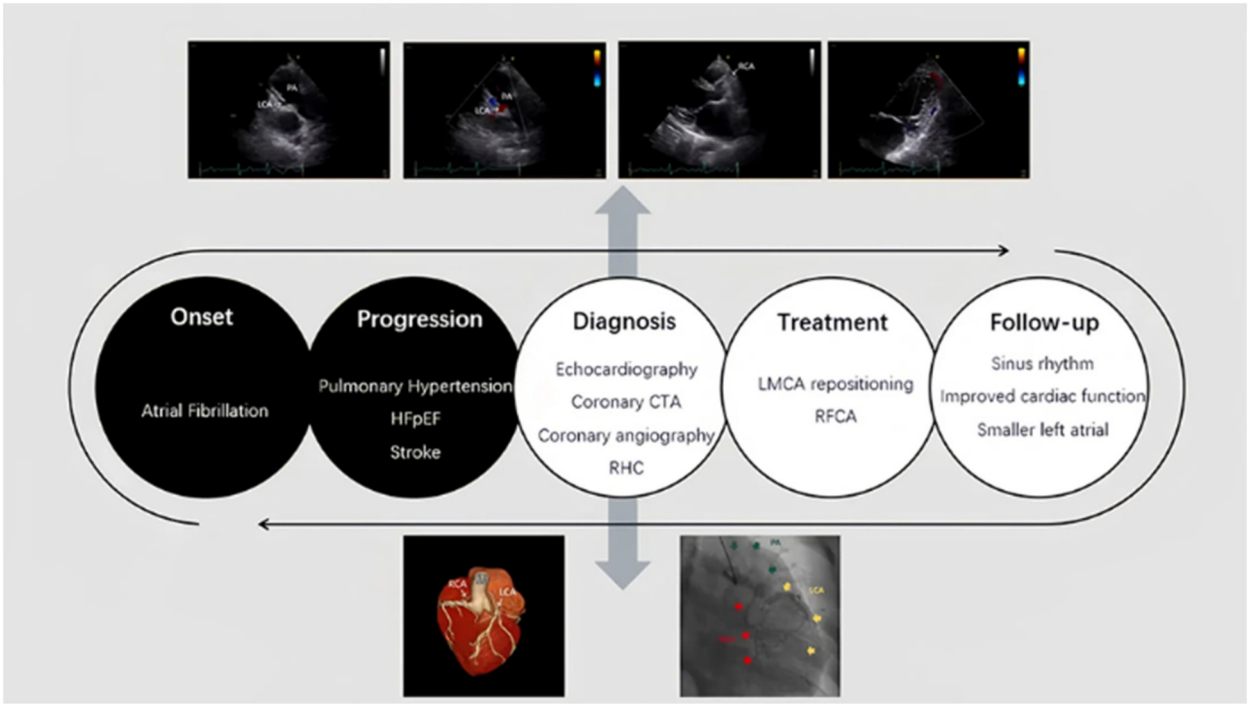

FIGURE 4
Timeline of the case. The timeline of the diagnosis and treatment of the patient.

symptoms such as angina, dyspnea, palpitations, or fatigue; 17% with ventricular arrhythmia, syncope, or sudden death; and 14% remain asymptomatic (8). However, previous studies have not clearly defined the proportion of adult ALCAPA patients presenting with atrial fibrillation or pulmonary hypertension as clinical manifestations. In this case, we observe a typical presentation with reduced exercise tolerance and exertional angina, which is consistent with documented manifestations in the literature (1, 5, 8). While cardiopulmonary exercise testing was not obtained, her exertional symptoms (NYHA Class II-III), ischemic stroke, and objective hemodynamic derangements collectively indicated significant functional impairment. However, when the patient first presented to us, her more prominent clinical manifestations were atrial fibrillation and pulmonary hypertension. She was treated with amiodarone and ambrisentan, but the therapeutic effects were poor. Echocardiography showed that her left ventricular systolic function is normal with mild mitral regurgitation and impairment in diastolic function, while the left atrium was significantly enlarged. The results of the RHC confirmed that the patient's pulmonary hypertension was left heart-related. We hypothesized that the cause was due to the origin of the LMCA in the pulmonary artery, resulting in prolonged ischemia in the left atrium, which is mainly supplied by the LCX (9). These collaterals between the LCA and RCA, although beneficial for blood supply from the LCA, do not completely alleviate the myocardial ischemia caused by the anomalous origin of the coronary artery. Long-term ischemia leads to left atrial enlargement, contributing to structural and electrical remodeling of the atrium, which plays a significant role in the development of atrial fibrillation (10). The patient also exhibited chronic left ventricular (LV) ischemia evidenced by ECG changes, LV dilation and diastolic dysfunction, and elevated NT-proBNP. While collateral circulation prevented regional wall motion abnormalities and reduced ejection fraction, the above manifestations are still important evidence of left ventricular ischemia. The pulmonary hypertension in this patient resulted from left heart disease, driven by ischemic injury to both the left atrium and left ventricle. While atrial fibrillation initially manifested at age 20—likely triggered by early left atrial hypertension from this dual ischemia—the overt pulmonary hypertension developed later as sustained left atrial overload progressively impacted the pulmonary circulation. As a result, we discontinued the use of ambrisentan. The development of pulmonary hypertension in ALCAPA may confer a paradoxical protective effect by reducing the coronary steal pressure gradient. While our patient's post-capillary PH likely had limited hemodynamic impact, this mechanism could explain her preserved systolic function despite chronic ischemia, underscoring the complex interplay between pulmonary and coronary physiology in shunt lesions.

In patients with postnatal ALCAPA, the direction of blood flow is usually left-to-right shunting, which has been repeatedly demonstrated (1, 11). Initially, both the LCA and the RCA have normal antegrade flow, because the pulmonary arterial pressure is equal to the systemic pressure (12). However, shortly after birth, the decrease in pulmonary artery pressure causes a reversal

of flow in the LCA, causing the LCA to drain oxygenated blood into the lower pressure pulmonary artery. This creates a preferential flow toward the pulmonary circulation rather than the myocardial circulation, which manifests as a left-to-right shunt known as the steal phenomenon (2, 3). This was also verified by the finding of the blood flow from LCA to the pulmonary artery on echocardiography examination (Figure 2b2).

Surgical intervention remains the cornerstone of treatment for ALCAPA to restore normal coronary anatomy and alleviate symptoms (5, 6, 13). The patient underwent the left coronary artery reimplantation and radiofrequency ablation for atrial fibrillation. These procedures significantly improved her clinical outcome.

Conclusion

This case highlights the importance of considering ALCAPA in the differential diagnosis of young patients presenting with atrial fibrillation and pulmonary hypertension.

Patient perspective

After years of unexplained cardiac symptoms, being diagnosed with the rare congenital heart defect of Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery was lifesaving for me. The care and expertise at Peking Union Medical College Hospital were pivotal in accurately diagnosing and effectively treating my condition. I am immensely grateful to the dedicated team of cardiologists whose efforts have significantly improved my quality of life.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving humans were approved by the Ethics Committee of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences; Peking Union Medical College, Beijing, China (I-25PJ1044). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

KS: Data curation, Investigation, Methodology, Writing – original draft. FG: Investigation, Writing – original draft. XX: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Writing – review & editing. YL: Conceptualization, Data curation, Methodology, Project administration, Resources, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The author(s) declare that no Generative AI was used in the creation of this manuscript.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2025.1573539/full#supplementary-material

SUPPLEMENTARY VIDEO S1
(as Listing Supplementary Material for Review). Coronary angiography showed that after the injection of contrast medium, the right coronary artery, left coronary artery, and pulmonary artery were sequentially highlighted. Extensive communication between the left and right coronary arteries was also observed.

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Case Report: Trissing balloon inflation and percutaneous coronary intervention with drug-coated balloons for the treatment of restenosis of a left main trifurcation lesion

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We report the case of a 62-year-old male with multiple cardiovascular risk factors and comorbidities who presented to our institution due to unstable angina. One year earlier, he underwent percutaneous coronary intervention (PCI) to unprotected left main trifurcation lesion involving the ostial left anterior descending artery (LAD) (Medina classification 0-0-1-0) with provisional stenting technique with single drug-eluting stent (DES) implantation from left main to LAD and PCI to LAD with single DES implantation from LAD in crossover with D1 for the treatment of LAD-D1 bifurcation lesion (Medina 1-1-0). Coronary angiography by radial approach found sub-occlusive restenosis of both jailed ostial ramus intermediate (RI) and left circumflex (LCX), with patency of DES to left main LAD and a significant in-stent restenosis (ISR) of DES to LAD at the bifurcation with D1. LAD ISR was treated with PCI with single DES implantation with optimal angiographic results. The left main trifurcation restenosis was treated by radial approach PCI with simultaneous trissing balloon inflation to left main, RI, and LCX, followed by kissing balloon with drug-coated balloons with sirolimus elution to RI and LCX, subsequent trissing balloon inflation, and final proximal optimization technique to the left main achieving an optimal angiographic result. Planned follow-up angiography at 1 year showed persistence of optimal angiographic results.

KEYWORDS

left main trifurcation, left main restenosis, left main angioplasty, in-stent restenosis, complex PCI

Introduction

The left main coronary artery can divide into three branches (trifurcation), i.e., left anterior descending artery (LAD), left circumflex (LCX), and an additional branch, usually called ramus intermedius (RI) or anterolateral branch, in 6.7% to 52.2% of cases (1–4). High variability of left main branching patterns has been found across different ethnic groups, sexes, and different body surface areas (1), with cases of quadri- or penta-furcations also (5, 6). Left main trifurcations have two carinas (between LAD

and RI and between RI and LCX) and four angles among the three branches (1). This anatomical configuration is associated with high flow turbulence and shear stress abnormalities leading to atherosclerotic plaque formation with heterogenous distribution, size, and characteristics across the different branches (1–7).

Left main trifurcation lesions can be classified using a modified Medina classification in the form of a four-digit number (e.g., 1-0-1-1 or 1-0-1-1-1) indicating significant involvement of the main branch and both side branches (8). Another classification uses a letter-based nomenclature system to indicate the diseased vessel (e.g., A, LM; B, LAD; C, LCX; and D, RI), with capital letters indicating vessels ≥3.5 mm and lowercase letters for vessel <3.5 mm (9). A stenosis is considered significant if it is >70% on angiography, according to intravascular imaging criteria, or based on functional evaluation (9).

Moreover, the complexity of anatomic configurations of left main trifurcation lesions poses challenges for interventional cardiologists owing to the risk of procedural complications, such as carina or plaque shift and side branch occlusion, and the need for more complex procedures in some cases (10, 11). Furthermore, challenges may arise when restenosis occurs following successful percutaneous coronary intervention (PCI) of left main trifurcation lesions.

We report a case of left main trifurcation restenosis successfully treated with a metal-free percutaneous coronary intervention (PCI).

Case presentation

A 62-year-old male, former smoker, with diabetes mellitus, family history of coronary artery disease, hypertension, dyslipidemia, prior orthotopic liver transplant due to HCV-related cirrhosis, and chronic thrombocytopenia and leukopenia attributed to hypersplenism and antirejection immunosuppressive drugs, underwent intravascular ultrasound (IVUS)-guided PCI to unprotected left main trifurcation lesion involving ostial LAD (Medina classification 0-0-1-0) with provisional stenting technique with single drug-eluting stent (DES) implantation from left main to LAD and PCI to LAD with single DES implantation, in crossover with D1 and overlapping stenting, for the treatment of LAD-first diagonal (D1) bifurcation lesion (Medina 1-1-0) (Figures 1A,B). A good angiographic result was achieved with minor angiographic stenosis of jailed LCX and pinching of jailed ostial D1 with TIMI 3 flow (Figures 1C,D). Clinical follow-up was uneventful until 1 year after the index procedure, when the patient started complaining of new-onset effort angina (Canadian Cardiovascular Society Class II) that rapidly progressed to unstable angina, leading to admission to our institution. Coronary angiography by radial approach found sub-occlusive restenosis of both jailed ostial RI and LCX with patency of the DES to left main LAD and a significant in-stent restenosis (ISR) of the DES to LAD at the LAD-D1 bifurcation lesion with unchanged pinching of the jailed D1 (Figures 2A,B). Blood tests showed stable and unchanged thrombocytopenia (50,000 mm^3) and leukopenia (3,500 mm^3). After the patient refused coronary artery bypass graft, revascularization was performed by PCI by a radial approach using a 7-French guiding catheter through a 7-French thin-wall introducer. LAD ISR was treated with PCI with DES implantation (3.5 × 22 mm), following lesion preparation with a non-compliant 3.5 × 15 mm balloon, achieving a good angiographic result with unchanged pinching of jailed ostial D1 with TIMI 3 flow (Figures 2C,D). The left main trifurcation restenosis was treated with simultaneous trissing balloon inflation using 3.0 × 15 mm semi-compliant balloons to left main LAD-RI-LCX (Figure 2E), followed by kissing balloon dilation with 3.0 × 20 mm DCBs with sirolimus release to left main RI and left main LCx (Figure 2F), subsequent trissing balloon dilation with 3.0 × 15 mm semi-compliant balloons (Figure 2G), and final proximal optimization technique (POT) with 4.5 mm non-compliant balloon to left main achieving an optimal angiographic result (Figure 2H). The patient was discharged home with the indication to continue dual antiplatelet therapy with aspirin and clopidogrel for 6 months followed by aspirin monotherapy. No change in platelet count throughout the follow-up was observed. At the 1-year follow-up, the patient remained asymptomatic and underwent a planned coronary angiography which showed patency of DES to left main LAD without restenosis, patency of jailed RI and LCX with no restenosis, and patency of the DES to LAD bifurcation lesion with unchanged pinching of jailed ostial D1 with TIMI 3 flow (Figure 3).

Discussion

PCI with DES is recommended as an alternative therapeutic option to coronary artery bypass graft surgery for the treatment of unprotected left main coronary artery disease in patients with low SYNTAX score and should be considered in patients with intermediate SYNTAX score (12, 13). In addition, PCI with DES to left main may also be considered in patients with multiple comorbidities and very high surgical risk or case of patient refusal for CABG.

Nevertheless, there is limited evidence on the optimal revascularization strategy with PCI for left main trifurcation lesions. Data from the EXCEL trial showed no significant differences between left main trifurcation and left main bifurcation lesions with respect to major adverse cardiovascular events (MACE) at 30 days and 5-year follow-up (14).

In our case, the left main trifurcation lesion at the time of the index procedure was a Medina 0-0-1-0 or B. Both the left main trifurcation and the LAD-D1 bifurcation lesions were treated with a simple approach consisting of a provisional single-stent strategy from the main vessel across the side branch. The decision to use a provisional one-stent strategy with wiring protection of side branches vs. two- or three-stent strategies should consider anatomical factors such as plaque burden distribution across the trifurcation, the presence of calcification or calcified nodules, the

Abbreviations

D1, first diagonal; DCB, drug-coated balloon; DES, drug-eluting stent; ISR, in-stent restenosis; IVUS, intravascular ultrasound; LAD, left anterior descending artery; LCX, left circumflex artery; MACE, major adverse cardiovascular events; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; POT, proximal optimization technique; RI, ramus intermediate; SB, side branch.

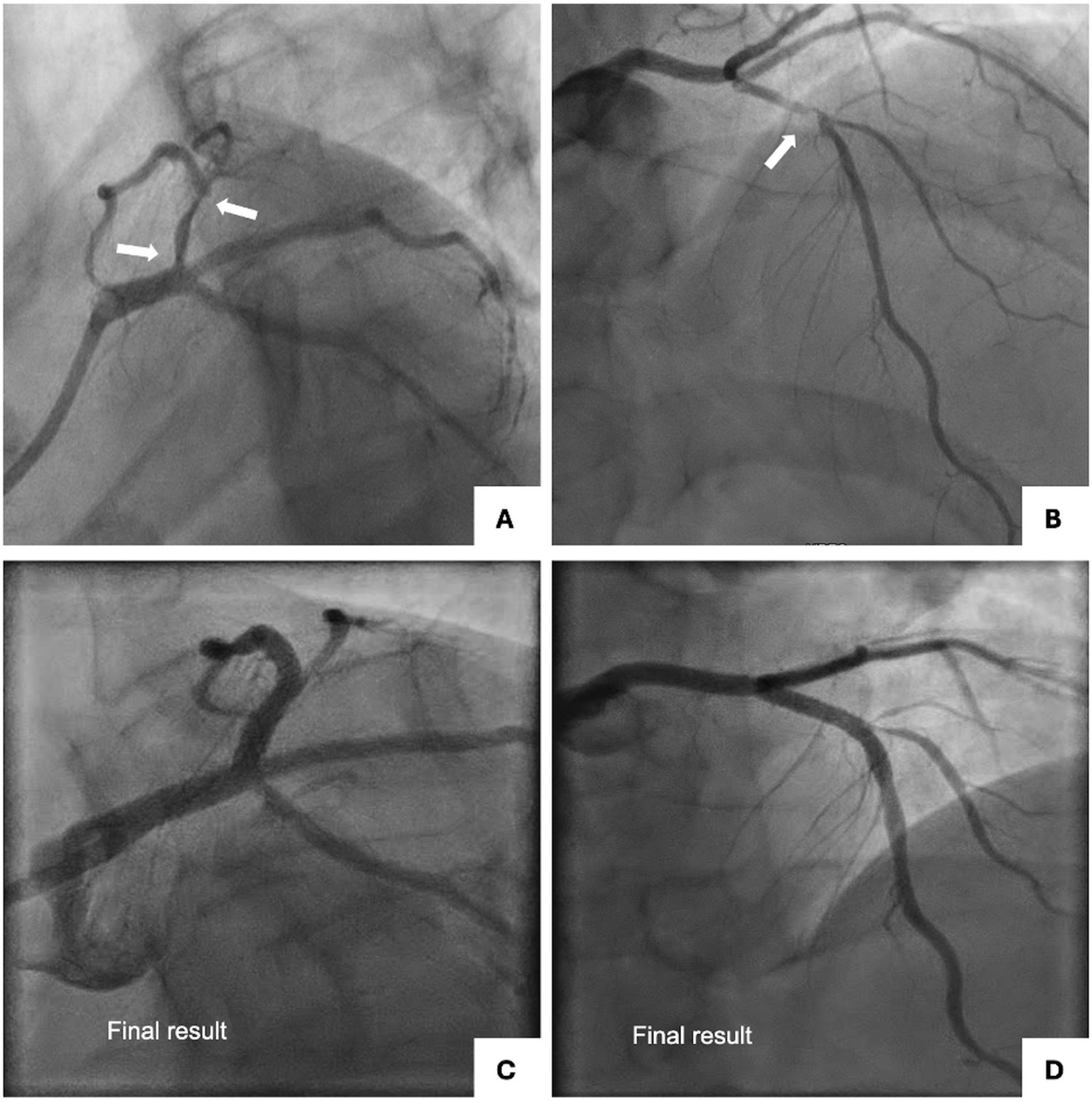

FIGURE 1
Baseline and final coronary angiography at the index procedure. **(A)** Spider view showing trifurcated LM coronary artery with severe ostial and proximal LAD (modified Medina 0-0-1-0; A, LM; B, LAD). **(B)** Right oblique cranial view showing severe LAD disease at the level of the bifurcation with D1 (Medina 1-1-1). **(C)** Spider view showing final result after provisional single DES stenting from LM to LAD. **(D)** Right oblique cranial view showing the final result after provisional single DES stenting to LAD in crossover. Pinching of jailed ostial D1 with TIMI 3 flow. D1, first diagonal branch; DES, drug-eluting stent; LAD, left anterior descending artery; LM, left main.

risk of acute side branch occlusion, and technical difficulty in recrossing very angulated side branches across stent struts after main vessel crossover stenting. Two- or three-stent strategies should be used for anticipated very complex lesions with a high risk of side branch occlusion after main vessel crossover stenting and as a bailout for flow-limiting dissections of side branches (8, 9).

The selection of the optimal treatment options for ISR following left main trifurcation-PCI remains largely undefined. The initial stenting strategy may affect the type of ISR and its subsequent management: e.g., provisional single stenting from left main to LAD vs. two- or three-stent techniques. Intravascular imaging guidance with IVUS and/or optical coherence tomography (OCT) is useful for left main PCI (15, 16) as well as for understanding the mechanisms of restenosis (17, 18). Indeed, intravascular imaging allows to diagnose stent under-expansion, strut malapposition, deformation of neocarina geometry, such as excessive protrusion of side branch stent struts into the main vessel (TAP technique), incomplete side branch ostium coverage (T stenting), ring-like pattern of restenosis at the carina (culotte technique), and protruding calcified nodules across stent struts (17, 18). OCT also

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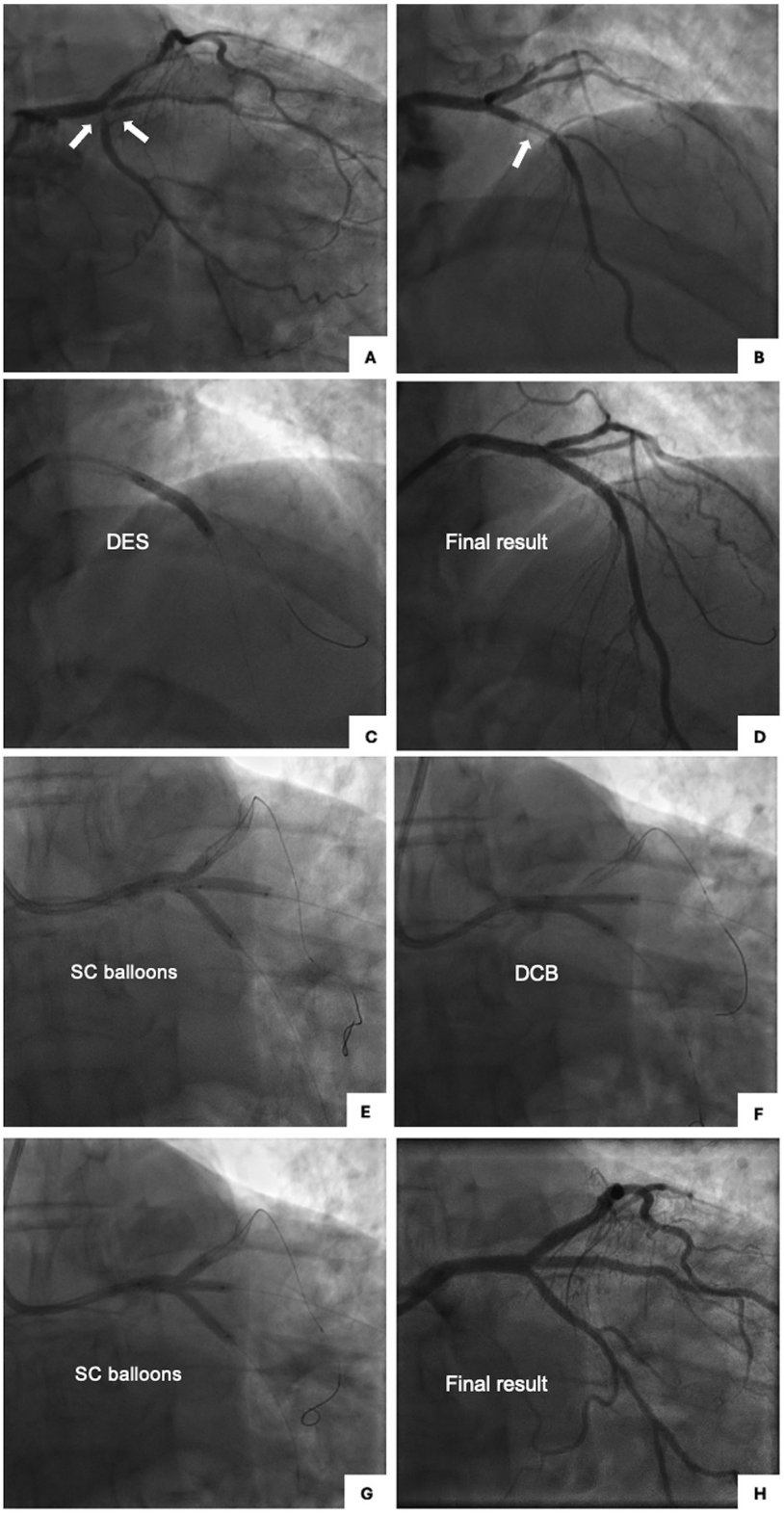

FIGURE 2
One-year follow-up coronary angiography: baseline, steps of the procedure, and final result. **(A)** Right oblique caudal view showing patency of DES to LM-LAD with severe stenosis of jailed ostial RI and LCX. **(B)** Right oblique cranial view showing significant ISR of DES to LAD, unchanged pinching of jailed ostial D1 with TIMI 3 flow. **(C,D)** Right oblique cranial view showing DES implantation to LAD, after predilation with SC 3.0 × 15 mm and NC 3.5 × 15 mm balloons for the treatment of ISR **(C)**. Final result after DES implantation **(D)**. **(E–G)** Right caudal view showing treatment of jailed ostial RI and LCX: trissing balloon using 3.0 × 15 mm SC balloons **(E)**, kissing balloon to LM-RI and LM-LCX with DCB **(F)**, trissing balloon with 3.0 × 15 mm SC balloons **(G)**. **(H)** Right caudal view showing final result after POT with NC 4.5 mm balloon. D1, first diagonal branch; DCB, drug-coated balloon; DES, drug-eluting stent; ISR, in-stent restenosis; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main; NC, non-compliant; RI, ramus intermediate; SC, semi-compliant.

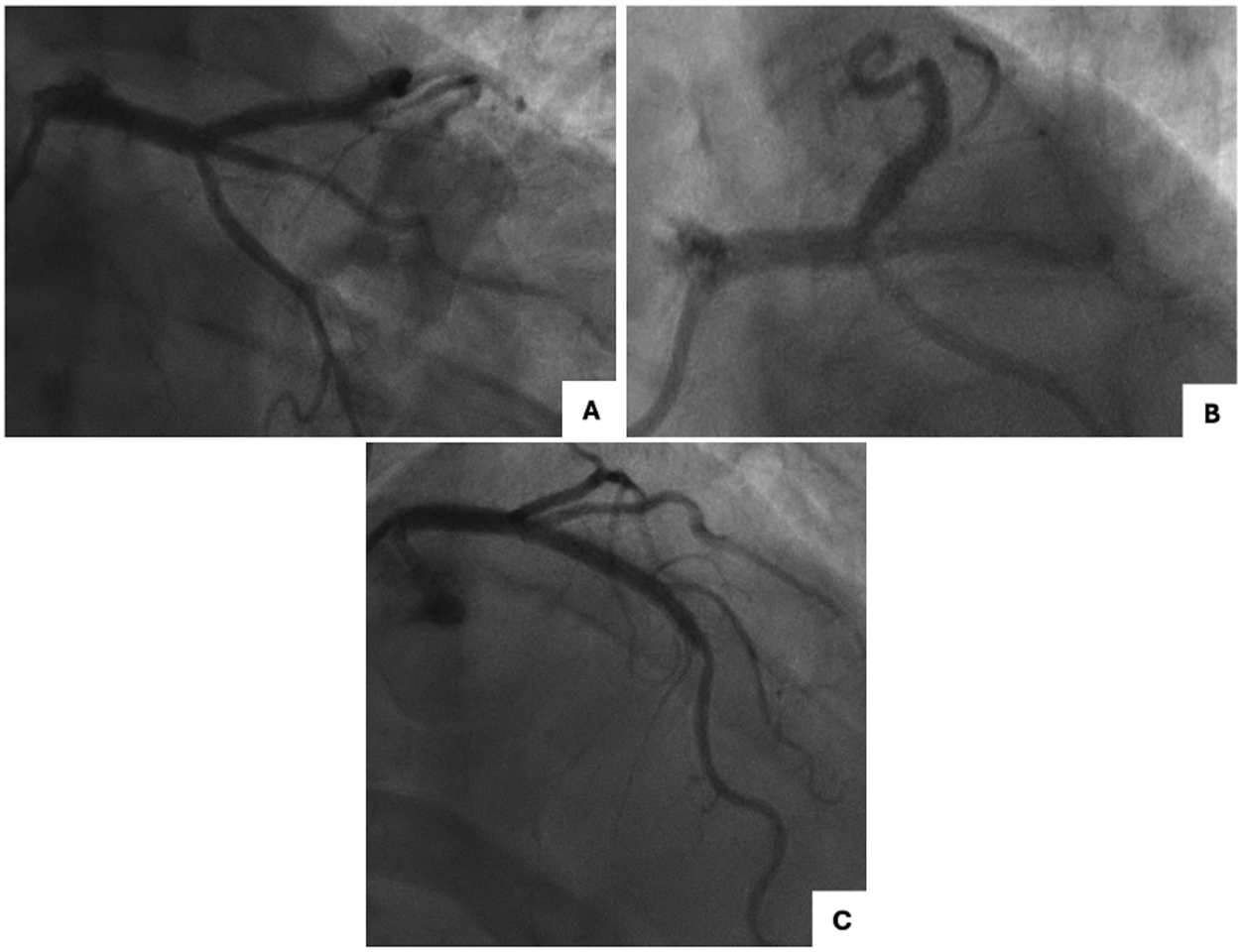

FIGURE 3
One-year follow-up coronary angiography following treatment of ISR. **(A,B)** Right oblique caudal view **(A)** and spider view **(B)** showing optimal result of DCB at the ostium of jailed RI and LCX and patency of DES to LM-LAD. **(C)** Right oblique cranial view showing patency of DES to LAD, unchanged pinching of jailed ostial D1 with TIMI 3 flow. D1, first diagonal branch; DCB, drug-coated balloon; DES, drug-eluting stent; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main.

allows the characterization of the pattern in-stent restenosis distinguishing between neointimal hyperplasia and neo-atherosclerosis as well as between aggressive ISR and stent thrombosis in cases of sub-occlusive lesions with uncertain angiographic appearance (17, 18).

The use of a metal-free PCI strategy with drug-coated balloon (DCB) for the treatment of left main trifurcation restenosis is desirable to reduce stent overlapping and minimize the risk of subsequent target lesion failure, in particular in patients treated with two- or three-stent techniques at the index procedure, such as DK-crush, TAP, or culotte stenting (19).

Evidence for the safety and efficacy of treatment of *de novo* lesions with a DCB-only strategy is rapidly growing (20, 21) and the role of DCB in the treatment of bifurcation lesions is emerging (22–25). A few studies have combined a strategy of PCI with DES to the main vessel and DCB to the side branch, reporting good angiographic results with low rates of target lesion revascularization and restenosis at follow-up (26–29). The value of PCI with DCB as compared to PCI with DES for the treatment of ISR following DES has also been shown (30). Adequate lesion preparation before DCB use is important for achieving an effective result (31). Optimal ostial side branch expansion with balloon- or non-balloon-based techniques, according to intravascular imaging, should be performed. For example, semi- or non-compliant balloons may be sufficient to expand side branch ostia across stent struts in the main vessel in most cases. However, additional techniques including cutting balloons, scoring balloons, very high-pressure NC balloons, and/or intravascular lithotripsy may be used according to intravascular imaging findings (32, 33). Nevertheless, data about the use of DCB for the treatment of restenosis of left main trifurcation lesions are lacking.

Potential advantages of DCB use for the treatment of left main ISR and restenosis of jailed side branches in complex anatomy, such as trifurcated left main, include the avoidance of additional stent implantation and strut overlap, as well as neocarina formation with imperfect strut orientation which may increase the risk of ISR and stent thrombosis (25, 34). In addition, the use of a free-metal PCI strategy may allow a safe reduction of dual antiplatelet therapy

duration, compared to double stenting techniques, which may translate into an additional clinical benefit in patients at high-bleeding risk. Furthermore, DCBs may promote positive vessel remodeling at follow-up (35, 36). Nevertheless, DCB use, compared with DES implantation, may be associated with smaller acute minimal lumen areas and carries a higher risk of acute dissections (20, 37). Despite increasing evidence about the spontaneous healing and/or the stability of most dissections at follow-up, homogenous guidelines about when to treat DCB-induced acute dissections with bailout stenting are lacking (37).

Kissing balloon inflation after stent implantation, followed by POT, is usually performed in most left main bifurcation lesions treated with a provisional single-stent technique for achieving adequate stent strut opening toward the side branch and to improve jailed side branch area, when residual stenosis is significant. In addition, it is a mandatory step for all two-stent techniques (38). For left main trifurcation lesions, the choice between trissing balloon inflation and sequential double kissing balloon inflation main vessel and each side branch is controversial. The trissing balloon inflation has some theoretical advantages such as the ability to achieve a better-rounded geometry in both stented and non-stented vessels (39, 40). Final POT is considered useful to restore the fractal geometry of the main vessel thus reducing the eccentricity index, ensuring a round LM lumen, and upsizing the stent dimension according to LM diameter (38, 41).

In our case, we used trissing balloon inflation with 3.0 mm semi-compliant balloons, which were easily accommodated in a 7-French guiding catheter, before DCB use. Trissing balloon inflation with larger size non-compliant balloons, such as 3.5 mm, for bigger side branches would have required the use of an 8-French guiding catheter, thus requiring an alternative arterial access, such as the femoral approach in most cases, or alternative techniques such as double radial access with two guiding catheters engaging the left main. We next performed kissing balloon inflation with DCB to both the jailed ostial side branches that were affected by the restenosis, followed by trissing balloon inflation to optimize the geometry of two carinas, and final POT achieving an optimal angiographic result both in the immediate phase and at follow-up.

Conclusions

Left main trifurcation lesion restenosis represents a challenge for interventional cardiologists. The use of trissing balloon inflation for carina geometry optimization, kissing balloon dilation with DCB without additional stent implantation, and final POT in the main vessel may represent a valuable therapeutic option.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements. Written informed consent was obtained from the participant/patient(s) for the publication of this case report.

Author contributions

FA: Conceptualization, Data curation, Writing – original draft. FG: Data curation, Writing – original draft, Writing – review & editing. GL: Writing – review & editing. GB: Conceptualization, Writing – review & editing. GF: Conceptualization, Data curation, Supervision, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Case Report: Anaphylactic shock and ST-elevation myocardial infarction following a bee sting: two deadly diseases in a patient with Kounis syndrome

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Kounis syndrome is an acute coronary syndrome occurring in the setting of an allergic reaction, usually caused by drug administration, food ingestion, or insect sting. We report the case of an elderly woman who presented to the emergency room suffering from an anaphylactic shock caused by a bee sting and who was diagnosed with an anterolateral ST-elevation myocardial infarction (STEMI) with moderately impaired left ventricular ejection. The patient was successfully managed with the administration of intravenous antihistaminic drugs and steroids, intravenous fluid volume resuscitation, and intramuscular epinephrine. The patient then underwent emergency coronary angiography, which showed a thrombotic subtotal occlusion of the proximal left anterior descending artery (LAD) and occlusion of the very distal apical LAD due to a spontaneous embolism. This was treated by primary percutaneous coronary intervention with thrombus aspiration and drug-eluting stent implantation in the proximal LAD, achieving a good angiographic result. Nevertheless, on day 3, the patient developed a left ventricular apical thrombosis, as assessed by cardiac magnetic resonance, requiring oral anticoagulation with rivaroxaban, de-escalation of dual antiplatelet therapy from ticagrelor to clopidogrel with acetylsalicylic acid, and finally a switch to dual antithrombotic therapy. The 3-month follow-up was uneventful. This case highlights the importance of prompt identification of Kounis syndrome in patients presenting with severe allergic reactions to allow for the timely implementation of appropriate reperfusion strategies in such high-risk patients with STEMI.

KEYWORDS

Kounis syndrome, acute myocardial infarction, thrombosis, anaphylaxis, percutaneous coronary intervention

Introduction

Kounis syndrome (KS), also known as "allergic angina," is an acute coronary syndrome (ACS) occurring in the setting of an allergic, anaphylactoid, or anaphylactic reaction and was first described in 1991 by Kounis and Zavras (1). KS can be triggered by various stimuli such as drugs, food, and insect stings, which ultimately cause mast cell degranulation, activation of the inflammatory cascade, subsequent vasospasm,

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and/or coronary plaque rupture or erosion with thrombosis (2). The incidence of KS is likely underestimated, and it has been reported to be more frequent among men (75%), with the age at onset ranging from 40 to 70 years (3). Chest pain is the most frequent symptom on admission (4). The diagnosis of ACS in relation to KS requires clinical suspicion to avoid delay in the implementation of guideline-directed therapies, and the treatment of KS may be challenging because the pharmacological interventions used to manage the allergic reaction may exacerbate coronary vasospasm (5) and reduce coronary blood flow.

Herein, we report the case of an elderly woman who experienced a severe form of KS following a bee sting.

Patient information

A 75-year-old woman with a history of arterial hypertension, dyslipidemia, obstructive sleep apnea syndrome, epilepsy, and multiple allergies to insects, penicillin, and iodinated contrast agent presented to our emergency room due to a sudden onset of general malaise following a bee sting on her left hand. The patient had a history of previous anterolateral ST-elevation myocardial infarction (STEMI) that was treated with percutaneous coronary intervention (PCI) with drug-eluting stent (DES) implantation to the first diagonal branch (D1) years earlier, and left ventricular systolic function was preserved. The patient was on aspirin (100 mg daily), atorvastatin (40 mg daily), ramipril (2.5 mg daily), and levetiracetam (500 mg twice daily). Cardiological follow-up was regular and uneventful.

Clinical findings and diagnostic assessment

On admission, the patient was drowsy, albeit responsive to verbal and pain stimuli (Glasgow Coma Scale = 14), complaining of shortness of breath at rest with a respiratory rate of 22 and oxygen saturation of 94% in room air. Her blood pressure was 70/40 mmHg, her heart rate was 110 bpm, and a large maculopapular rash was present on her trunk, arms, and limbs. She was complaining of nausea, had an episode of gastric vomiting, and was suffering from mild epigastric pain. The physical examination found normal cardiac auscultation and a diffuse reduction in lung sounds accompanied by bilateral basal rales. The arterial blood gas analysis (Table 1, upper panel) indicated type I respiratory failure coupled with metabolic lactic acidosis. Blood examinations showed blood cell count, electrolytes, renal and hepatic function, and high-sensitivity troponin I (hs-TnI) to be within normal limits (Table 1, lower panel). The patient received low-flow oxygen therapy, intravenous hydrocortisone (200 mg) and chlorphenamine (10 mg), and a fluid bolus of 500 ml saline, achieving a partial resolution of the skin rash, although no significant improvement in blood pressure occurred, and the remaining symptoms persisted. Therefore, intramuscular epinephrine (1 mg) was administered, with immediate recovery of blood pressure and improvement in her neurological status.

TABLE 1 Arterial blood gas analysis and blood examinations at admission.

Arterial blood gas analysis		
Variable	Value	Reference interval
pH	7.33	7.35–7.45
pCO_2 (mmHg)	36	35–45
pO_2 (mmHg)	58	>60 mmHg
Na+ (mmol/L)	135	135–145
K+ (mmol/L)	3.3	3.5–5
Hb (g/dl)	13.3	>12
HCO_3^- (mmol/L)	19	22–28
Lactate (mmol/L)	4.8	<2
BE (mmol/L)	−6.9	+2/−2
Glucose (mg/dl)	332	70–99
Blood examinations		
Variable	Value	Reference interval
AST (IU/L)	17	<35
ALT (IU/L)	9	<35
Bilirubin (mg/dl)	0.9	0.3–1.2
Hs-TnI (ng/L)	8.1	2.2–11.6
CPK (IU/L)	52	15–145
Mgb (mcg/L)	89	14–65
BNP (ng/L)	54	<100
Urea (mg/dl)	34	17–43
Creatinine (mg/dl)	0.92	0.5–1
Na (mmol/L)	140	135–145
K (mmol/L)	3.4	3.5–5
WBC (10^9/L)	11.58	4–10
Hb (g/dl)	13	12–16
PLT (10^9/L)	477	150–450
CRP (mg/dl)	1.2	<0.5
Glucose (mg/dl)	212	70–99

pCO_2, partial pressure of carbon dioxide; pO_2, partial pressure of oxygen; Na+, sodium; K+, potassium; Hb, hemoglobin; HCO_3^-, bicarbonate; BE, base excess; AST, aspartate aminotransferase; ALT, alanine aminotransferase; hs-TnI, high-sensitivity troponin I; CPK, creatine phosphokinase; Mgb, myoglobin; BNP, B-type natriuretic peptide; Na, sodium; K, potassium; WBC, white blood cells; Hb, hemoglobin; PLT, platelets; CRP, C-reactive protein.

Due to the persistence of epigastric pain, a 12-lead electrocardiogram (ECG) was performed (Figure 1A), showing sinus rhythm at 75 bpm with 1.5 mm ST-segment elevation in leads V5 and V6. Bedside echocardiography showed a mild reduction of left ventricular ejection fraction (LVEF) of 45%, left ventricular apical akinesia, and hypokinesia of the mid-to-distal anterior and anterolateral segments. No significant valvular abnormalities or pericardial effusion were found. A diagnosis of STEMI was made, and the patient received an aspirin loading dose of 250 mg and ticagrelor of 180 mg. Emergency coronary angiography showed a thrombotic sub-occlusion of the left anterior descending artery (LAD) involving the ostium of D1, patency of the previously implanted stent to D1 without restenosis (Figure 2A), and a spontaneous distal embolization

Abbreviations

ACS, acute coronary syndrome; ATAK, adrenaline, takotsubo, anaphylaxis, and Kounis; D1, first diagonal branch; DES, drug-eluting stent; ECG, electrocardiogram; hs-TnI, high-sensitivity troponin I; KS, Kounis syndrome; LAD, left anterior descending artery; LGE, late gadolinium enhancement; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

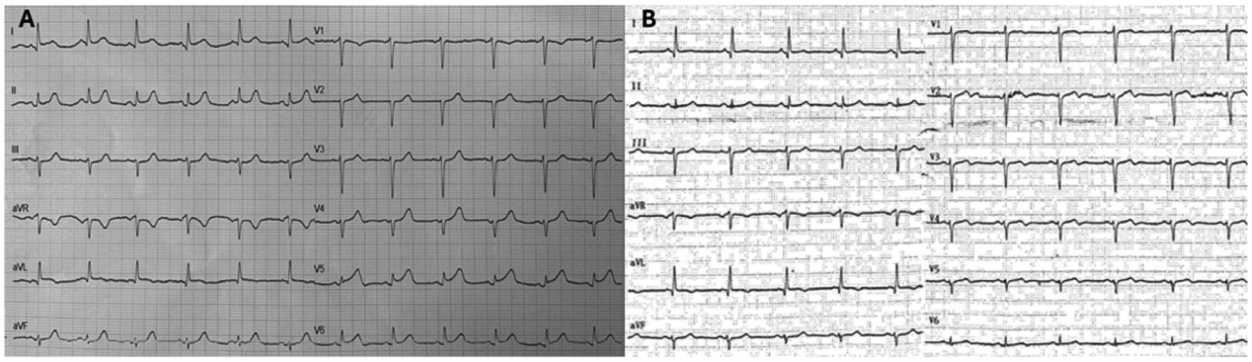

FIGURE 1
Baseline and discharge ECGs. **(A)** ECG at admission: sinus rhythm with HR~75 bpm, normal AV and IV conduction, mild left axis deviation with 1.5 mm ST-segment elevation in leads V5 and V6, and q waves in leads I and aVL. **(B)** ECG at discharge: sinus rhythm with HR~75 bpm, normal AV and IV conduction, mild left axis deviation with ST segment elevation resolution, and biphasic T waves in leads V2–V5 with persistent q waves in leads I and aVL. ECG, electrocardiogram; HR, heart rate; AV, atrio-ventricular; IV, intra-ventricular.

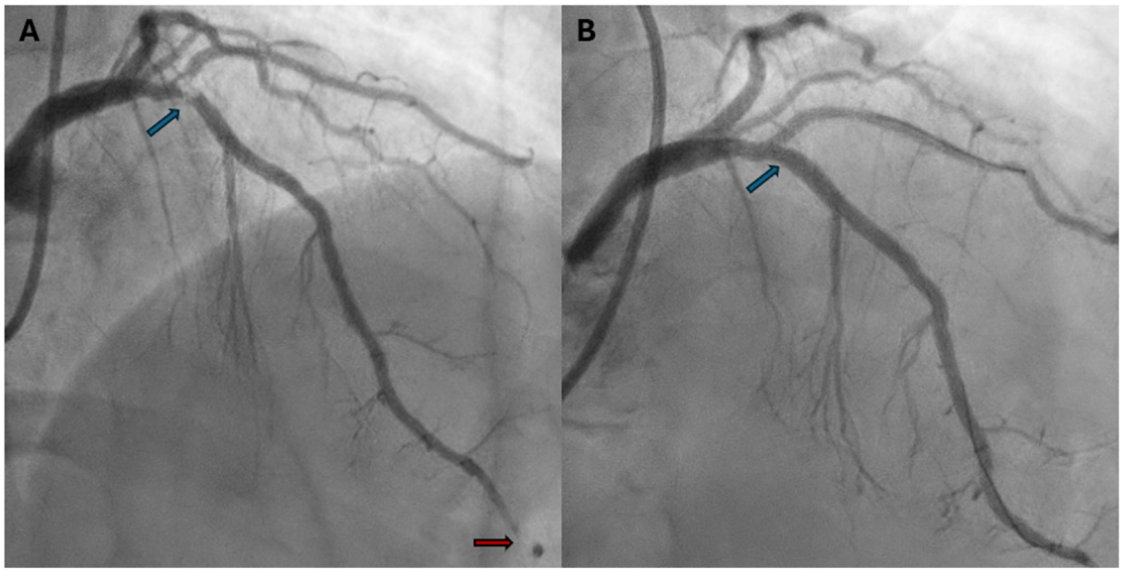

FIGURE 2
Baseline and final coronary angiography. **(A)** Baseline coronary angiography (RAO 30°, cranial 30°) shows a thrombotic subocclusion of proximal LAD with ostial involvement of D1 (blue arrow). The previously implanted DES on D1 is patent and free of restenosis. A perfusion defect in the distal LAD suggests spontaneous distal embolization (red arrow). **(B)** Final coronary angiography (RAO 30°, cranial 40°) shows a good angiographic result after PCI to LAD-D1 bifurcation with single DES implantation (3.5 × 18 mm) to the LAD, a kissing balloon with NC 3.0/2.0 mm to LAD/D1, and the proximal optimization technique with a 3.5 mm NC balloon (blue arrow). RAO, right anterior oblique; LAD, left anterior descending; D1, first diagonal; DES, drug-eluting stent; PCI, percutaneous coronary intervention; NC, non-compliant balloon.

defect of the apical LAD with thrombolysis in myocardial infarction (TIMI) 1 flow. Manual thrombus aspiration was performed to the LAD lesion at the level of the bifurcation with D1 only. It was not attempted at the very distal apical LAD because of the small caliber of the vessel. A residual tight stenosis of the LAD at the bifurcation level was treated with a 3.5 × 18 mm DES implantation to the LAD, kissing balloon inflation (3.0/2.0 mm) to LAD-D1, and the final proximal optimization technique with a 3.5 mm NC balloon. Post-procedure echocardiography showed an LVEF of 40%, with akinesia of the apex and of the mid-to-distal anterior and anterolateral segments, without evidence of mechanical complications. Blood examinations showed a peak value of hs-TnI of 19.980 ng/L at 32 h. Continuous ECG monitoring recorded frequent premature ventricular contractions and a brief episode of non-sustained ventricular tachycardia. Therefore, beta-blocker therapy with intravenous metoprolol was started. However, shortly after drug administration, the patient

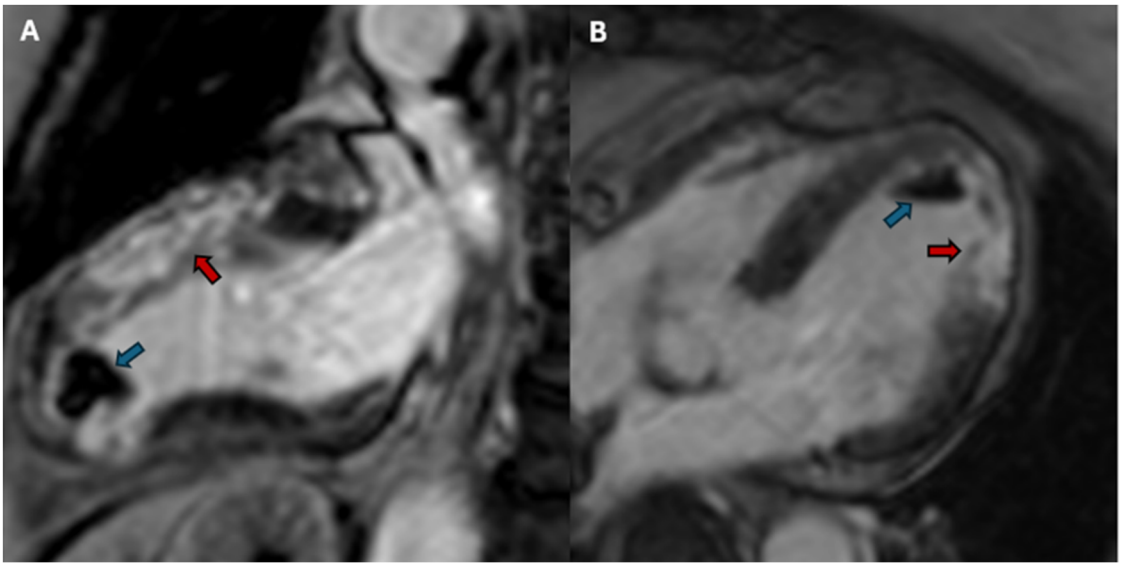

FIGURE 3
Post-PCI cardiac magnetic resonance imaging. **(A)** Post-PCI cardiac magnetic resonance 2-chamber view. LGE sequences showing an extensive transmural ischemic scar in the anterior wall (red arrow) and a large left ventricular apical thrombus (blue arrow). **(B)** Post-PCI cardiac magnetic resonance 4-chamber view. LGE sequences showing an extensive transmural ischemic scar in anterolateral wall (red arrow) and a large left ventricular apical thrombus (blue arrow). PCI, percutaneous coronary intervention; LGE, late gadolinium enhancement.

experienced a transient episode of epigastric pain that was responsive to sublingual nitroglycerin. In suspicion of drug-induced vasospasm, metoprolol was promptly discontinued with no symptom recurrence. Heart failure medications including an ace-inhibitor, a mineralocorticoid receptor antagonist, and a sodium-glucose co-transporter 2 inhibitor were started and well-tolerated. On day 3 following the index procedure, cardiac magnetic resonance imaging showed a moderate LVEF reduction (38%), akinesia in the anterior and anterolateral mid-apical regions with apical thrombosis (9×20 mm), and late gadolinium enhancement (LGE) extension wall thickness >75% in the same regions with wall motion abnormalities (Figures 3A,B). Rivaroxaban at 20 mg daily was started and ticagrelor was discontinued and de-escalated to clopidogrel, which was continued for 1 week after the index procedure. On day 7, the patient was discharged home asymptomatic on dual antithrombotic therapy with aspirin 100 mg daily plus rivaroxaban 20 mg daily. Discharge ECG showed a reduced R wave progression on the anterior leads with resolution of the ST-segment elevation (Figure 1B). At the 3-month follow-up, the patient was free from angina. She is on dual anti-thrombotic therapy with aspirin and rivaroxaban. A cardiac magnetic resonance found an LVEF of 42%, an unchanged LGE pattern, and a significant reduction in LV apical thrombus size (2×8 mm).

Discussion

KS is a rare and underrecognized cause of ACS and is associated with high morbidity and mortality. According to prior studies, KS may not be just a single-organ disease, but a complex multisystem and multi-organ arterial condition, affecting other arterial districts (mesenteric and cerebral) (6, 7). Risk factors for KS include arterial hypertension, dyslipidemia, cigarette smoking, and a history of previous allergic reactions (8). KS can be triggered by several factors, such as, most frequently, drugs (mainly antibiotics), food, and insect bites (4).

Mast cell degranulation releases vasoactive and pro-inflammatory mediators—such as histamine, leukotrienes, and proteases—which can trigger coronary vasospasm, increase vascular permeability, and promote plaque rupture or erosion, leading to thrombus formation (2).

Clinical presentation includes cardiac symptoms (chest pain, dyspnea, and arrhythmias) in the setting of overt allergic/anaphylactic reactions, which can ultimately present as systemic hypotension, shock, and/or cardiac arrest. Notably, cardiac symptoms occur in the first hour after exposure to the allergic agent in approximately 80% of cases (1).

KS can be classified into three subtypes according to its pathophysiological mechanisms: type I (the most frequent), consisting of coronary vasospasm in the absence of overt coronary artery disease; type II, caused by plaque rupture or erosion with superimposed thrombosis, and type III, the rarest form, occurring in the presence of a pre-existing coronary stent, which can be further categorized as type III-A (stent thrombosis) or type III-B (in-stent restenosis) (9, 10). Giovannini et al. have recently introduced KS type IV, which is characterized by coronary artery bypass graft thrombosis (11). Regardless of the classification, all KS subtypes share a common initial mechanism: an allergic reaction that triggers mast cell degranulation and

activates the inflammatory cascade, which may affect coronary blood flow (12).

We report a case of type II KS presenting with STEMI and angiographic evidence of a high thrombus burden likely to have been caused by plaque destabilization to the proximal LAD, and not affecting the previously implanted stent to D1. The use of intravascular imaging, such as optical coherence tomography and, to some extent, high-resolution intravascular ultrasound, may have allowed the identification of the specific coronary pathology, i.e., rupture vs. erosion (13), underlying the coronary thrombosis and the histological analysis of the coronary aspirate may be useful for detecting the presence of eosinophils and mast cells inside the thrombus, as previously reported (14).

Furthermore, intravascular imaging guided-PCI is associated with improved clinical outcomes in complex PCI, particularly for bifurcated lesions (15). Of note, the coexistence of ST-segment elevation in anterior leads and apical akinesia in echocardiography may prompt a differential diagnosis of takotsubo syndrome. Indeed, the association between takotsubo syndrome and KS has been defined as the "ATAK complex" (adrenaline, takotsubo, anaphylaxis, and Kounis) (16) and several case reports have reported the complex and challenging nature of this disease in clinical practice (17, 18). Notably, cardiac magnetic resonance imaging is an accurate imaging technique to distinguish between takotsubo syndrome and STEMI in unclear ECG patterns and allows for the assessment of the infarct size, microvascular obstruction, and complications such as left ventricular apical thrombosis following acute myocardial infarction (19, 20).

There is no formal consensus for the management of KS. Nevertheless, prior case series have highlighted the importance of simultaneous optimal treatment of the ongoing allergic reaction and the implementation of guideline-directed treatment for ACS (21). In line with these recommendations, our patient received an optimal management regimen for the allergic reaction and underwent primary PCI. Intravenous antihistamine drugs and short-acting corticosteroids, an intravenous fluid bolus, and intramuscular epinephrine were administered. Antihistamine drugs are the mainstay treatment of allergic reactions, but they have been reported to be associated with the occurrence of hypotension and worsening of coronary perfusion (22, 23). Corticosteroids appear to be safe in KS, however, it has been suggested that they could increase the risk of cardiac aneurysm and free wall rupture in patients with STEMI (24). With respect to intravenous fluid bolus and intramuscular adrenaline administration, these pharmacological interventions play a pivotal role in patients presenting with anaphylactic shock, as adequate intravascular volume expansion works synergistically with adrenaline to prevent the deterioration of the hemodynamics toward refractory shock and cardiac arrest. Nevertheless, the use of intravenous epinephrine requires careful dosing as it may worsen coronary vasospasm and it may increase the risk of ventricular arrythmias (16, 25, 26). With respect to coronary vasospasm in patients with KS, additional medications such as beta-blockers need to be used with caution (27). Nitrates and calcium channel blockers, particularly diltiazem or verapamil, are effective in preventing and terminating episodes of angina due to vasospasm. However, an optimal dosage of these drugs should be tailored according to systemic blood pressure, and caution is needed when using diltiazem or verapamil in patients with left ventricular systolic dysfunction (28).

With respect to the optimal antithrombotic therapy for the management of left ventricular apical thrombosis, there is no clear evidence from randomized clinical trials about the superiority of direct oral anticoagulants vs. vitamin K antagonists. The selection of the most appropriate drug class should take into account the patient's bleeding risk, given the presence of simultaneous single or dual antiplatelet therapy. In our case, we selected rivaroxaban in line with most recent evidence (29).

We acknowledge a number of limitations. First, we did not measure the blood levels of histamine, IgE, and tryptase. Second, we did not assess the histological composition of the thrombotic material retrieved with the thrombectomy device.

Conclusions

STEMI may occur in the setting of anaphylactic shock and may represent the clinical presentation of KS. Prompt recognition of coronary complications of allergic reactions and timely evidence-based treatment of both the allergic reaction and the ACS is mandatory to improve the patient's clinical outcome.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements. Written informed consent was obtained from the participant/patient(s) for the publication of this case report.

Author contributions

GD: Writing – original draft, Writing – review & editing, Conceptualization. CP: Writing – review & editing. FC: Writing – review & editing. GS: Writing – review & editing. GF: Investigation, Writing – original draft, Writing – review & editing, Conceptualization.

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Case Report: Recurrent acute myocardial infarction in a young woman—the importance of identifying the uncommon underlying causes

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Studies have shown that the occurrence and mortality of ischemic heart disease (IHD) in young women aged 35–54 years have increased despite improving trends globally among the general population. Common risk factors such as hypertension, hyperlipidemia, diabetes and smoking play an important role in the occurrence of IHD, but some rare causes that are easily misdiagnosed or undiagnosed should also be paid attention to. Here, we report the case of a young woman (33 years old) who suffered from recurrent acute myocardial infarction (AMI) and was ultimately diagnosed with Turner syndrome (TS) by karyotype testing. TS was identified as the cause of IHD in this patient. We then adjusted treatment strategy to include long-term estrogen-progestin therapy in addition to conventional treatment for IHD (e.g., anti-platelet, lipids-lowering). The patient has been followed up on an outpatient basis and is in good clinical condition. In this report, we highlighted the important of identifying rare causes when treating young women with IHD, and we also discussed the guideline management in such patients.

KEYWORDS

ischemic heart disease, acute myocardial infarction, young woman, Turner syndrome, replacement therapy

Introduction

Although there has been a significant decrease in the mortality of ischemic heart disease (IHD) across the general population over the past few decades, the incidence and mortality of IHD in young women aged 35–54 years continue to increase (1, 2). A observational study from The Atherosclerosis Risk in Communities study found significant trend that young women are having more heart attack (3). While the common risk factors, such as hypertension, high cholesterol, smoking, diabetes and family history of heart disease still play an important role in the development of IHD, some rare causes, such as Turner syndrome, etc., were easily undiagnosed, misdiagnosed or being diagnosed in late childhood or adolescent age, which leads to inappropriate and incomplete management for these patients (4, 5). Turner syndrome is a genetic disorder that affects females only due to complete or partial absence of the second sex chromosome (X chromosome), which occurred in 1 in every 2,000–2,500 live-born girls (5). It can cause a variety of medical and developmental problems. Heart is the most commonly affected organ in patient with TS and the main cause of the

early morbidity and mortality, including both congenital cardiovascular defect and acquired cardiovascular conditions (5, 6). Therefore, timely diagnosis is crucial which can initiate early intervention and help TS patients achieve desirable outcomes. Unfortunately, in the real world, most TS patients were diagnosed delayed in China. Here, we report a case of recurrent acute myocardial infarction (AMI) in a young woman (33 years old), the underlying cause of IHD was eventually identified as TS in second emergency hospitalization for AMI, and the patient then received estrogen-progestin therapy in addition to conventional treatment for IHD with good clinical outcome so far. In this report we highlight the importance of careful investigation of rare underlying causes of IHD in young woman and discuss the Guideline management of this rare genetic disease.

Case presentation

A 33-year-old young woman presented to the hospital with the chief complain of recurrent chest pain after exercising for the past three days. The pain was dull, localized pericardial area, accompanied with palpitation, no radiation and sweeting. The pain can be relieved by rest or nitrates. She denied cough, breathlessness, or syncope. Three months ago, the patient underwent PCI procedure [with the assistance of intra-aortic balloon pump (IABP)] due to "AMI complicated by acute left heart failure and cardiac shock, hyperlipidemia", when coronary angiography (CA) revealed left anterior descending artery (LAD) subtotal occlusion + the circumflex branch (LCX) subtotal occlusion + right coronary artery (RCA) chronic total occlusion. The patient received PCI, with two stents implanted in LAD and percutaneous transluminal coronary angioplasty (PTCA) with drug-coated balloon for LCX and proximal RCA, however, attempts at distal RCA revascularization failed. Patient was prescribed aspirin (100 mg/day), ticagrelor (90 mg/day), atorvastatin (20 mg/day), ezetimibe (10 mg/day) and followed-up in outpatient clinic. She reported compliance with her medication regimen. She denied hypertension, diabetes, family history of heart disease and any other special medical histories. Upon further inquiry, she admitted that she has no history of menstruation so far. Personal habits included drinking light amounts of alcohol and not smoking.

Upon admission, physical examination revealed normal range of blood pressure (113/79 mmHg), heart rate (88 beats/min), respiratory rate (20/min) and oxygen saturation (SO_2) level (99%, room air). Her height is 148 cm and weight is 55 kg. Cardiac and pulmonary examination revealed normal heart sounds without murmurs and clear lungs. Laboratory tests indicated that complete blood count with differential (CBC w/diff), comprehensive metabolic panel (CMP), hepatic and renal function, and several tumor markers were within normal limit, but elevated cardiac troponin (TNI) 0.287 ng/ml (normal range 0–0.0116 ng/ml) and plasma B-type natriuretic peptide (NT-proBNP) 1186 pg/ml (normal range 0–125 pg/ml). Electrocardiography (ECG) illustrated normal sinus rhythm (HR 88 beats/min) with pathological Q-wave on II, III and aVF leads, and T-wave changes on V7–V9 leads (Figure 1A). Transthoracic echocardiography (TTE) revealed normal left ventricular (LV) size (41 mm) but reduced left ventricular (LV) systolic function [LV ejection fraction (LVEF), 45%], diastolic dysfunction, and an akinesis segment in the apical region (size 36 × 13 mm) (Figure 1B). A diagnosis of "recurrent AMI without ST segment elevation (NSTEMI)" was made and the patient underwent emergency CA, which revealed proximal occlusion near the LCX stent, 95% left main (LM) coronary artery stenosis and distal RCA occlusion (Figure 1C). The patient underwent second PCI, with a stent being implanted in LM-LAD, and attempts to open the LCX and distal RCA occlusion failed (Figure 1D).

Since the patient's coronary atherosclerosis progressed rapidly despite ideal treatment of hyperlipidemia (Table 1) and there were no other significant risk factors, we speculated that some unindenting factor(s) may be involved. We then carefully reviewed the patient's physical examination, medical history and laboratory tests, we noticed that the patient was short in stature, had mild intellectual disability and absence of menstruation, the possible diagnosis of Turner syndrome (TS) was suspected. Further investigations, including imaging studies (abdominal CT and pelvic ultrasound) and hormonal tests, were then ordered. Computed tomography showed horseshoe kidneys (Figure 2A) and both CT (Figures 2B–D) and pelvic ultrasonography failed to detect the presence of uterus and ovaries. The thyroid function analysis showed free T3 level 3.03 pg/ml (normal range, 2.3–4.8 pg/ml), free T4 level 1.46 pg/ml (normal range, 0.62–1.24 pg/ml) and thyroid-stimulating hormone (TSH) level 0.01 μIU/ml (normal range, 0.38–5.57 μIU/ml). The level of serum growth hormone was 0.09 ng/ml (reference range 0.016–9.88 ng/ml), the follicle-stimulating hormone was 33.5 mIU/ml (reference range 3.5–12.5 mIU/ml), the testosterone level was <0.02 ng/ml (reference range, 0.084–0.481 ng/ml), the estradiol level <5 pg/ml (reference range 22.3–341 pg/ml), but the level of prolactin and luteinizing hormone was within in normal limit (Table 2). The patient also underwent comprehensive laboratory investigations including erythrocyte sedimentation rate (ESR), immunological workup, thrombophilia screening, anti-neutrophil cytoplasmic antibodies (ANCA), rheumatoid factor panel and anti-cardiolipin antibodies, all test results returned negative. To confirm the diagnosis, we then ordered a genetic test and the result indicated a karyotyping of "45, X" (Figure 2E), which confirmed our diagnosis of TS. We then adjusted the therapeutic strategies to include estrogen and growth hormone therapies in addition to anti-platelet and lipid-lowering therapy. The patient was followed up on an outpatient basis and remained in good clinical condition (>2 years).

Discussion

Although not completely rare, TS has an estimated prevalence of approximately 1 in 2,000–2,500 live female births (5). The clinical manifestations exhibit considerable heterogeneity, largely dependent on whether the loss of an X chromosome is partial or complete. Patients with mosaic TS may present with milder phenotypes, such as short stature and primary amenorrhea, whereas those with complete loss of an X chromosome (e.g., 45, X)

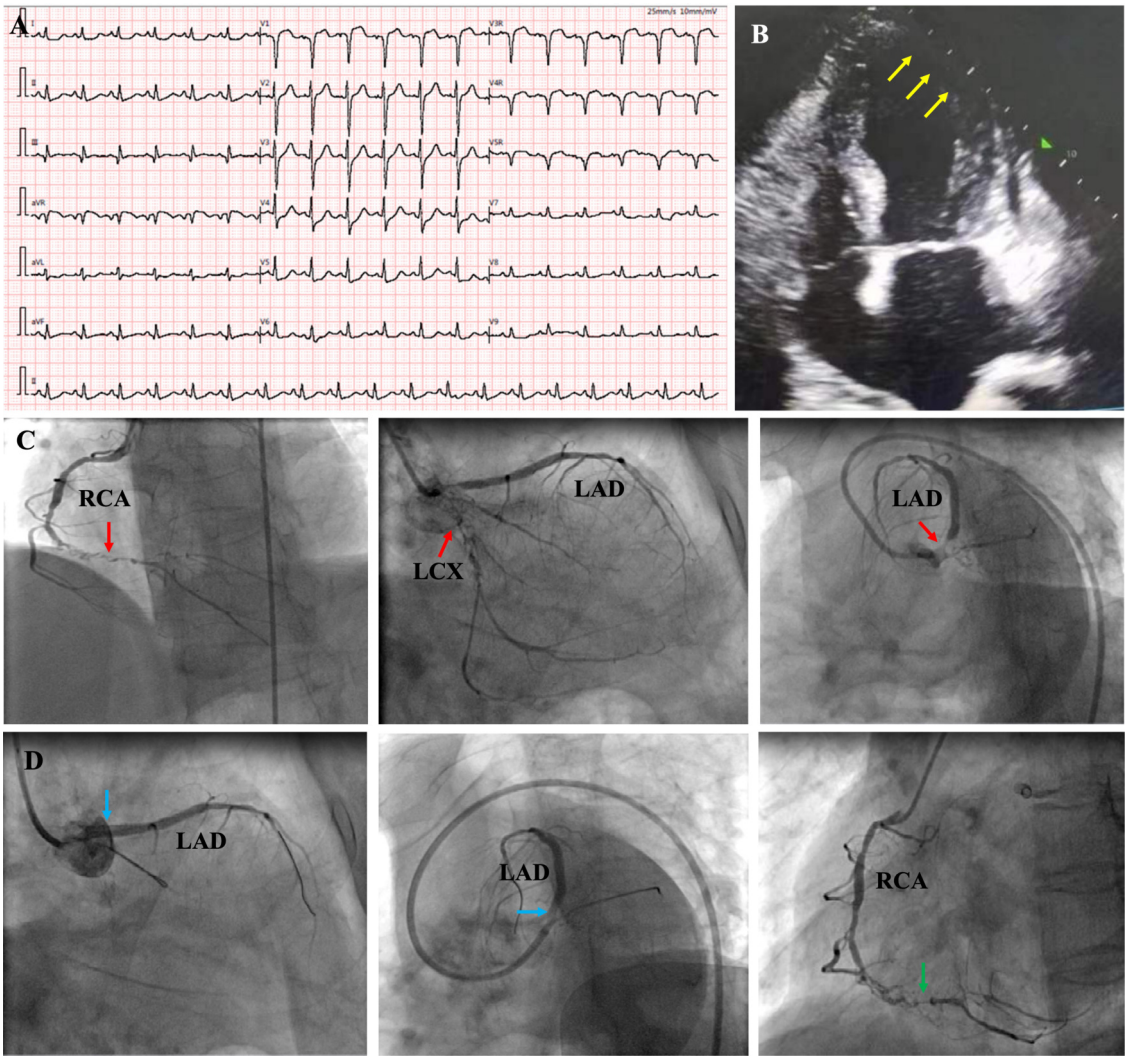

FIGURE 1
ECG at emergency room showed sinus rhythm with pathological Q-wave on II, III and aVF leads, and T-wave changes on V7–V9 leads **(A)**; echocardiography revealed normal left ventricular (LV) size but reduced left ventricular systolic function (LVEF, 45%), and an akinesis segment in the apical region (size 36 × 13 mm) [**(B)**, yellow arrows]; coronary angiography revealed chronic total occlusion of the right coronary artery (RCA) in the middle segment, and proximal occlusion near the stent in LCX, 95% stenosis in LM and [**(C)**, red arrows]; A stent was implanted in LM-LAD (blue arrow), but the attempt to open LCX and RCA failed [**(D)**, green arrow]. RCA, right coronary artery; LAD, left anterior descending; LM, left main; LCX, left circumflex.

TABLE 1 The lipid panel during hospitalization.

Lipid panel	1st hospitalization	2nd hospitalization	Normal range
TC (mmol/L)	7.05	3.93	2.80–5.20
TG (mmol/L)	2.59	1.47	0–1.70
LDL-c (mmol/L)	4.42	2.57	1.00–3.35
HDL-c (mmol/L)	1.20	1.25	0.91–2.60

Patient's lipid panel was monitored during 1st and 2nd hospitalization.
TC, total cholesterol; TG, Triglyceride; LDL-c, low density lipoprotein cholesterol; HDL-c, high density lipoprotein cholesterol.

often demonstrate more pronounced physical and psychological impairments. Characteristic clinical features include short stature, facial and oral features, premature ovarian failure and lymphedema of feet and hands (7, 8). Typical facial features include a short, broad neck with webbing, low-set ears, and down-slanted palpebral fissures with epicanthal folds (7). Oral manifestations involve a high-arched palate, hypoplastic mandible, thin enamel and decreased amount of dentin, tooth mobility, and periodontal pockets, prematurely erupted teeth, and various malocclusions (9). Additionally, TS is associated with congenital renal, cardiovascular and thyroid disease (autoimmune hypothyroidism). The most common congenital renal anomaly is horseshoe kidney (8). Girls with TS are at much greater risk for heart disease, including both

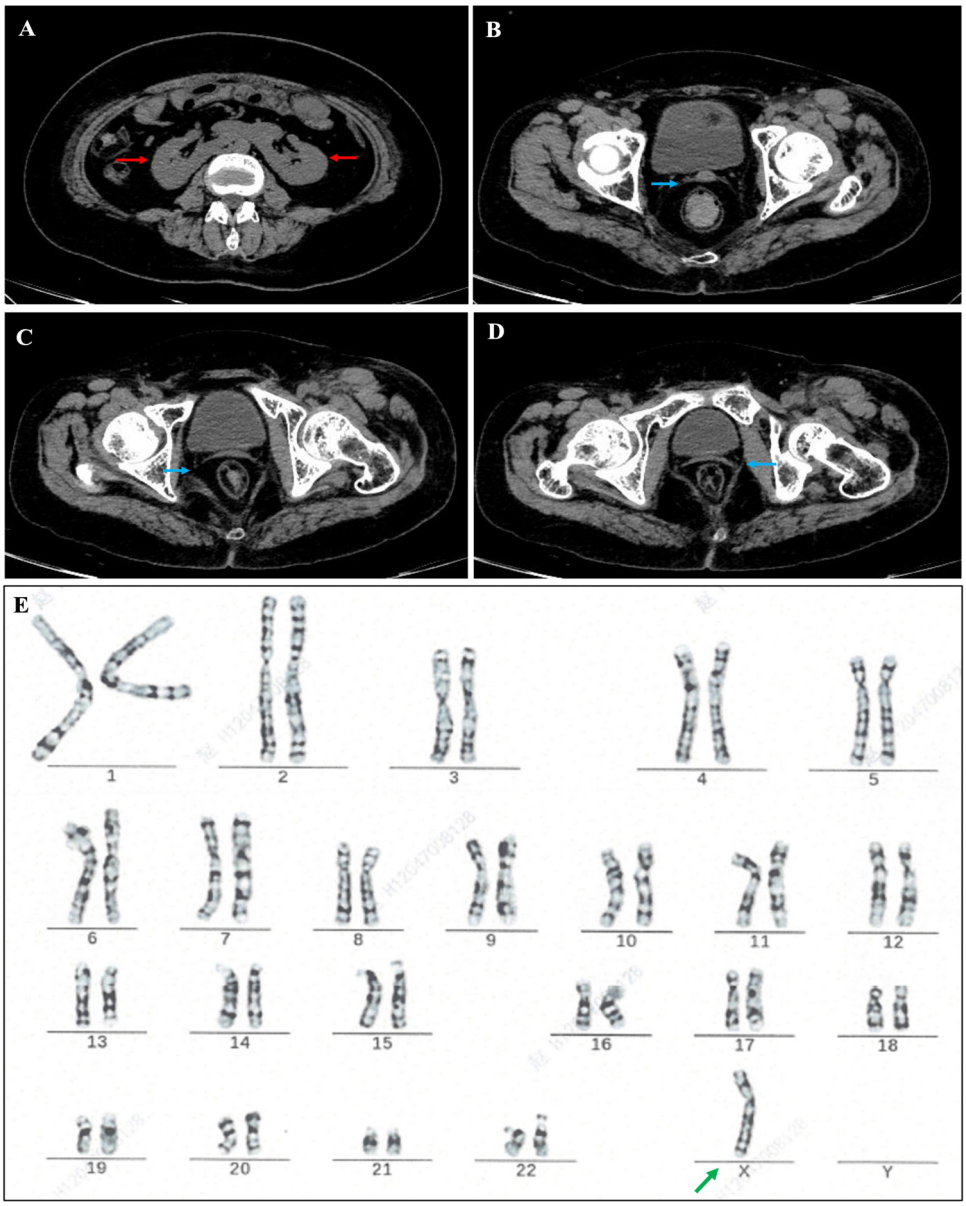

FIGURE 2
Abdominal computed tomography (CT) showed horseshoe kidney and fused kidney [(**A**), red arrow], no ovarian structure was seen, and cord-like shadow of uterus was visible [(**B–D**), blue arrow]; cytogenetic report showing a gene karyotype of 45.X [(**E**), green arrow].

congenital cardiovascular defect and acquired cardiovascular conditions. Statistics showed ~50% individuals with TS have congenital heart abnormalities, including bicuspid aortic valve, coarctation of the aorta, and thoracic aortic aneurysm (5, 10). Furthermore, TS patients face an elevated risk of metabolic and cardiovascular comorbidities, such as diabetes mellitus, obesity, dysplipidemia, hypertension (5, 6, 10) or antiphospholipid syndrome (11), all of which contribute to long-term cardiovascular morbidity. The meta-analysis by Siagian et al. (12) elucidates critical risk factors for acute coronary syndrome (ACS) in young women, including diabetes, hypertension, and hypercholesterolemia—all prevalent in TS populations. Our case aligns with these findings, demonstrating how TS-related metabolic dysfunction (dyslipidemia, thyroid disorders) synergizes with estrogen deficiency to accelerate atherosclerosis. Notably, the patient in this case exhibited a complete 45, X karyotype but displayed relatively atypical clinical features, with short stature being the sole prominent manifestation, which is a little different from other case reports (13–15). Additionally, following admission, the patient underwent comprehensive laboratory investigations including erythrocyte sedimentation rate (ESR), immunological workup, thrombophilia screening, anti-neutrophil cytoplasmic antibodies (ANCA), rheumatoid factor panel and anti-cardiolipin antibodies, all test results returned negative, therefore these findings excluded the diagnosis of vasculitides, thrombophilic disorders or rheumatological/autoimmune diseases. The absence of

TABLE 2 Thyroid function and the levels of serum sex hormones.

Hormones	Patient's level	Normal range
Thyroid function		
Free T3 (pg/ml)	3.03	2.30–4.80
Free T4 (pg/ml)	1.46	0.62–1.24
TSH (μIU/ml)	4.42	0.38–5.57
Serum sex hormones		
Growth hormone (ng/ml)	0.09	0.016–9.88
FSH (mIU/ml)	33.5	3.50–12.5
Testosterone (ng/ml)	<0.02	0.084–0.481
Prolactin (ng/ml)	5.5	4.79–23.3
Estradiol (pg/ml)	<5.0	22.3–341
Luteinizing (mIU/ml)	12.80	2.40–12.60

Patient's thyroid function was analyzed and sex hormones were measured during second hospitalization.
T3, triiodothyronine; T4, thyroxine; TSH, thyroid-stimulating hormone; FSH, follicle-stimulating hormone.

congenital heart anomalies—a hallmark of classical TS—likely contributed to the initial diagnostic oversight during her first hospitalization. Recent advances in diagnostic technologies have significantly improved the accuracy and timeliness of Turner syndrome (TS) detection. Notably, non-invasive prenatal testing (NIPT) utilizing cell-free DNA analysis enables early prenatal diagnosis, while next-generation sequencing (NGS) facilitates the identification of low-level mosaicism and structural X chromosome abnormalities with enhanced precision (16, 17).

Estrogen and growth hormone deficiency due to premature ovarian failure is a significant hallmark in patients with TS. This condition is seen in most patients with TS and may occur at birth or gradually during childhood, adolescence, or early adulthood (18, 19). Patients present as lack of growth, development of secondary sex characteristics (breast, uterine and ovaries) and primary amenorrhea (19, 20). Estrogen deficiency was thought to play a significant role in the non-congenital cardiovascular complications in TS patients. Estrogen has a number of beneficial effects on cardiovascular health. Estrogen modulates vascular function, the inflammatory response, metabolism, insulin sensitivity, cardiac myocyte and stem cell survival through communicating with estrogen receptors (21, 22). Estrogen has potent antioxidant effects and is able to reduce inflammation, induces vasorelaxation and alters gene expression in both the vasculature and the heart (22, 23). Estrogen has a very positive effect on lipoprotein profiles, lowering LDL and raising HDL (24). Conversely, estrogen deficiency disrupts the vascular homeostasis (reduces nitric oxide bioavailability, upregulates adhesion molecules and promotes monocyte infiltration into vascular walls) (21–23) and induces metabolic derangements (elevates LDL cholesterol and causes insulin resistance) (23, 24). These pathological changes contribute to the threefold increase in mortality observed in TS patients compared to the general population, with cardiovascular diseases representing the predominant cause (10). This underscores the critical importance of early diagnosis and intervention in TS management.

While no definitive cure exists for TS, comprehensive management strategies can effectively address its multisystem manifestations. The overarching goals of caring of patient with TS included long-term treatment with estrogen-progestin therapy to prevent adverse consequences of estrogen deficiency including bone loss and increased risk for early coronary heart disease, excess mortality, cognitive decline, and dementia, management of cardiovascular disorders (congenital and acquired), management of fertility issues and potential for pregnancy if desired and possible, surveillance for and management of comorbidities that may include autoimmune thyroid disease, type 2 diabetes mellitus, hearing loss, and abnormal liver enzymes (25, 26). Current therapeutic strategies for TS incorporate a multimodal approach to address growth and cardiovascular complications. The combination therapy of recombinant growth hormone (rGH) with low-dose oxandrolone has emerged as the recommended regimen, demonstrating superior efficacy in achieving final adult height compared to rGH monotherapy (4, 26). Emerging interventions include ovarian tissue cryopreservation in mosaic TS patients prior to ovarian failure, representing a potential fertility preservation strategy, along with prophylactic angiotensin-converting enzyme (ACE) inhibitors to mitigate progressive aortic dilation (4, 26).

Optimal hormone replacement therapy (HRT) follows a carefully staged protocol, with low dose start at age 11–12, gradual dose escalation to mimic physiological puberty, then transiting to full adult replacement doses by approximately 18 years of age. Comprehensive monitoring protocols mandate annual assessment of auxological parameters (height velocity), reproductive development (uterine size via pelvic ultrasound), metabolic profile (fasting lipid panel and glucose homeostasis), bone mineral density (biannual DEXA scanning), cardiovascular status (echocardiography with consideration for cardiac MRI in high-risk cases) (4, 26). In this presented case, the diagnosis was significantly delayed and no congenital heart anormalies were detected, the treatment was tailored to management of acquired cardiovascular complications, including significant dyslipidemia, thyroid dysfunction, atherosclerotic coronary arteries disease, and post-AMI. Longitudinal monitoring revealed no evidence of hepatic dysfunction or glucose intolerance. Following the implementation of estrogen-progestin replacement therapy, the patient has maintained stable clinical status for over 24 months of follow-up, demonstrating the importance of timely hormonal intervention even in atypical presentations.

Conclusion

AMI occurring in young women should be taken seriously and less common causes should be considered, such as TS. Cardiovascular disease is common in women with TS, resulting in increased mortality in affected individuals. Timely diagnosis and subsequent early intervention can improve quality of life and prognosis. Long-term treatment with estrogen and related hormone therapy can prevent adverse consequences of estrogen deficiency.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving humans were approved by The medical ethical committee of Wuhan Asia Heart Hospital, China. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

HZ: Data curation, Investigation, Methodology, Writing – original draft. CX: Formal analysis, Investigation, Methodology, Writing – original draft. HY: Investigation, Supervision, Writing – review & editing. CL: Supervision, Writing – review & editing. LL: Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Multimodality imaging and advanced calcium treatment to facilitate PCI in a rare coronary artery anomaly—case report

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Background: Coronary artery anomalies (CAAs) are a rare congenital condition and represent additional challenges in interventional treatment of coronary artery disease.
Case summary: A 76-year-old male, was admitted for elective coronary angiography due to symptoms of typical angina. CT coronary angiography (CTCA) revealed all three coronary arteries arising from the right sinus of Valsalva, where right coronary artery (RCA) and left anterior descending artery (LAD) had common ostium with significant stenosis of ostio-proximal RCA and circumflex artery (CX) coming from a separate one. Percutaneous coronary intervention (PCI) of ostial RCA was planned and intravascular ultrasound (IVUS) in both RCA and LAD was done. Due to extensive calcification, prior to intended PCI, intravascular lithotripsy (IVL) was done. Following IVL and extensive predilatation drug eluting stent (DES) was implanted. Final IVUS was used to confirm optimal stent deployment in proximal RCA and to verify that LAD ostium was not compromised with RCA stent. Six months later, due to angina and positive stress test, repeated coronary angiography revealed a restenosis of the ostial RCA so the lesion was again treated with drug-coated balloon with optimal procedural results.
Conclusion: Although rare, CAAs could be associated with coronary artery disease and usually present additional challenge for interventional treatment. Advanced imaging modalities, including CTCA and IVUS, provide good procedural guidance during complex PCI procedures in patients with CAAs.

KEYWORDS
coronary artery anomaly, intravascular ultrasound, intravascular lithotripsy, PCI, CTCA

Introduction

Coronary artery anomalies (CCAs) are a rare congenital condition and represent additional challenge in interventional treatment of the coronary artery disease (1). In the systematic review of 12.457 consecutive adult patients who underwent coronary angiography, origin of all three major coronary arteries at right coronary sinus was found to have a prevalence of 0.008% and comprised 0.89% of all congenital anomalies found in the study population (2). The intravascular ultrasound (IVUS) has already been proven to improve outcomes in complex coronary interventions (3). Compared to coronary angiography guided PCI, the use of IVUS imaging guidance to optimize stent implantation was associated with a lower risk for target vessel failure (TVF) during long

term follow-up (4). The benefits of intravascular imaging have been especially pronounced in treatment of calcified lesions which comprise substantial part of contemporary PCI (5). IVUS definitions of calcium burden allowed evaluation of new techniques to treat calcified lesions like atherectomy or intravascular lithotripsy (IVL) (6). In the Disrupt CAD III trial, the largest prospective single-arm multicenter study to date, IVL treatment prior to coronary stent implantation in severely calcified lesions was associated with lower rates of major adverse cardiac events, ischemia-driven target lesion revascularization and stent thrombosis at one-year follow-up (7).

Case report

A 76-year-old male patient, with no relevant medical history, was admitted for coronary angiography due to symptoms of typical angina. Patient underwent coronary angiography which was unable to provide enough information regarding coronary anatomy due to inability to selectively cannulate all coronary ostia. Afterwards, CT coronary angiography (CTCA) was done, which revealed the origin of all three coronary arteries from the right sinus of Valsalva. Right coronary artery (RCA) and left anterior descending artery (LAD) had common ostium and circumflex artery (CX) had separate ostium of its own and retro-aortic course. It also showed a high level of calcification in the ostioproximal segment of the RCA, which was later confirmed using intravascular imaging which demonstrated a high level of calcification occupying more than 270° of vessel circumference (Figure 1).

At repeated coronary angiography, two high grade stenoses were found in RCA, in ostioproximal and distal segment (Supplementary Videos 1, 2). The procedure was continued with PCI of the distal lesion first via radial access. The cannulation of RCA/LAD ostia was obtained using right Amplatz 2.0 7Fr catheter, which provided good support. Afterwards, two workhorse wires, *Whisper MS and BMW Universal* (Abbott Vascular International, Diegem, Belgium) were placed in distal segments of RCA and LAD, respectively. The predilatation of the distal RCA lesion was done with semi-compliant balloon 2.0 mm × 15 mm. After that, an everolimus eluting stent 2.5 mm × 20 mm was implanted in distal segment of the RCA.

Due to proximity of LAD to diseased RCA ostia, IVUS of RCA and LAD was done using Eagle Eye Platinum IVUS catheter (Philips Healthcare Andover, MA, US) (Supplementary Videos 4 and 5). At RCA ostium, stenosis was documented [minimal lumen diameter: 2.1 mm; maximal lumen diameter: 2.8 mm; lumen area (LA): 5.1 mm^2; external elastic lamina (EEL) area: 15.2 mm^2, plaque burden 66.5%] with extensive calcified plaque occupying more than 270° of vessel circumference. In the proximal segment predominantly fibro-muscular lesion (minimal lumen diameter: 3.5 mm; maximal lumen diameter: 4.1 mm; LA: 10.8 mm^2; EEL area: 28.6 mm^2, plaque burden 62.0%) was identified (Figure 2). No significant narrowing of LAD was observed. Due to extensive calcification of RCA ostium, we considered rotational atherectomy and IVL for lesion preparation. We opted for the latter one, owing to the challenges and higher risk of complications with rotational atherectomy given the proximity of the lesion to the ostium. After predilatation with non-compliant balloon 3.0 mm × 8 mm, IVL-balloon catheter 4.0 mm × 12 mm was positioned in the target lesion and inflated to 4 Atm (Supplementary Video 6). In total 9 cycles of IVL pulses were applied (Shockwave Medical, Inc, Santa Clara, CA). Following that, everolimus eluting stent Resolute Onyx 4.0 mm × 22 mm (Medtronic Inc, Galway, Ireland), was implanted in the proximal segment of RCA. Final IVUS runs were done from RCA and LAD and confirmed optimal stent deployment in RCA (minimal stent area at ostium: 8.5 mm^2; minimal stent area at proximal segment: 11.3 mm^2). There were no signs neither of dissection nor compromise of LAD ostium (Figures 3, 4, Supplementary Videos 7–10).

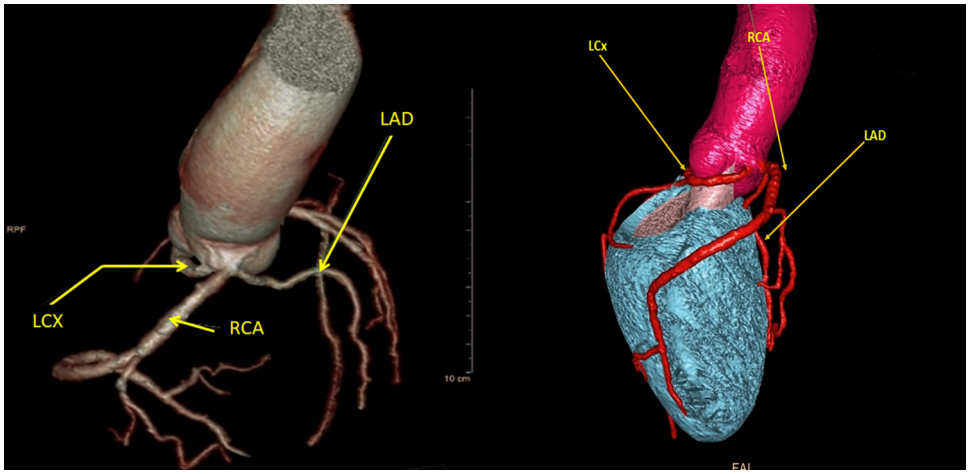

FIGURE 1
Multi-slice computed tomography (MSCT) of the coronary arteries. All three coronary arteries emerge from right sinus of Valsalva. RCA and LAD emerge from same ostium and lay in close proximity. LCX is positioned laterally and emerges from isolated ostia.

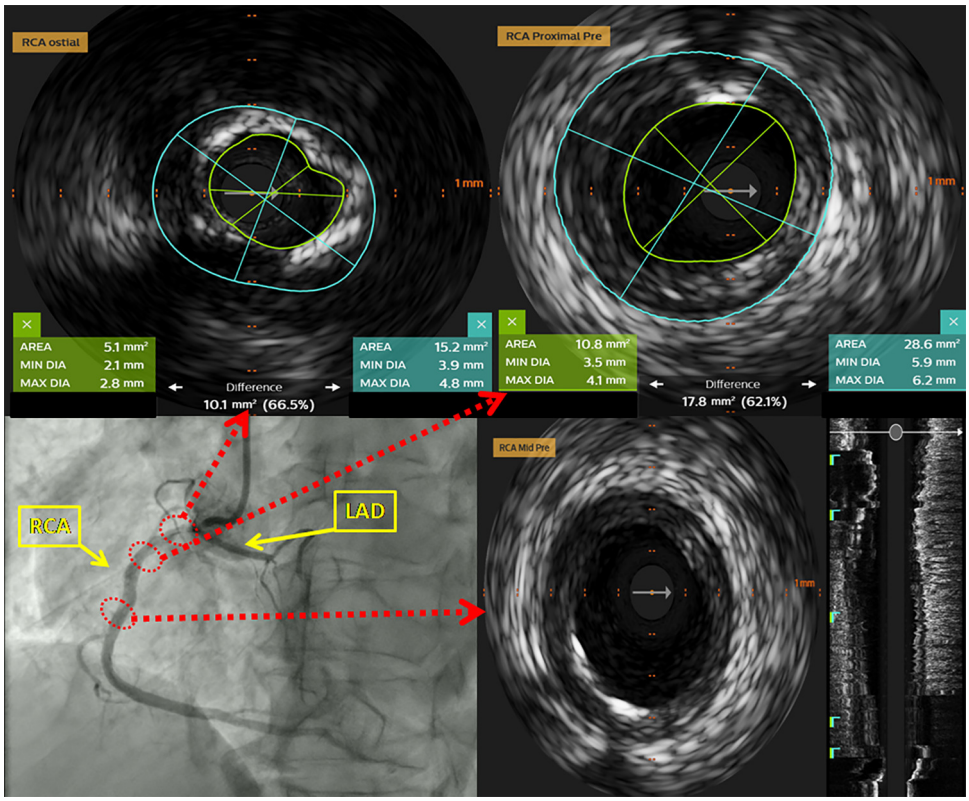

FIGURE 2
Intravascular ultrasound (IVUS) of the RCA prior to PCI. At the level of the ostial RCA segment highly calcified lesion was identified (more than 270° of vessel circumference). In the proximal segment of the RCA predominantly fibromuscular lesion was documented.

The patient was discharged on the following day on dual antiplatelet therapy including aspirin and clopidogrel. At one month follow-up visit, the patient reported doing well without angina.

However, at the next follow-up visit, six months after the initial procedure the patient reported having similar angina-like symptoms as prior to the PCI. Exercise stress test was done which showed signs of myocardial ischemia at levels of effort of 7.0 METS, with Duke treadmill score of −22 so repeated coronary angiography was done.

It revealed a significant restenosis of the ostial RCA, so the procedure was continued with repeated PCI (Supplementary Video 11). This time a Multi-Purpose 6F catheter was used, with two workhorse guidewires placed into the distal parts of the RCA and LAD. After predilatation with non-compliant and cutting ballon, the lesion was treated with a paclitaxel-coated 4.0 mm × 15 mm balloon for 60 s (Supplementary Video 12). The result was optimal and the patient was discharged from the hospital on the next day, with continuation of previously used dual-antiplatelet therapy (Supplementary Video 13).

Discussion

The widespread use of invasive and noninvasive coronary artery imaging has led to increased recognition of CAAs among adults (8). Although the data concerning impact of CCAs on clinical outcome of patients are limited, there is evidence that specific morphologies of CCAs are associated with unfavorable clinical outcomes (9, 10).

CTCA offers a detailed characterization of the anatomic features associated with high-risk CAAs. Furthermore it allows visualization of the surrounding cardiac and non-cardiac structures and their three dimensional relationships, thus representing the gold standard for CAAs (11). In our case CTCA proved to be useful in providing detailed information regarding coronary artery morphology, their relationships, and the degree of coronary atherosclerosis (12).

Due to the complex anatomy present, the myocardial territory supplied by RCA and LAD is similar to the territory of the left main trunk. Therefore, the planned PCI should be performed with utmost caution, in order to minimize the risk of complications that would jeopardize large myocardial area and ensure better clinical outcome. Due to the same reason we have considered RCA ostial lesion as significant based on IVUS findings and did not pursue functional evaluation of the lesion.

Early IVUS studies showed that an angiographically good stent result frequently conceals poorly expanded struts with edge dissections that inevitably increases the risk of acute complications. Consecutive randomized trials proved, that IVUS-

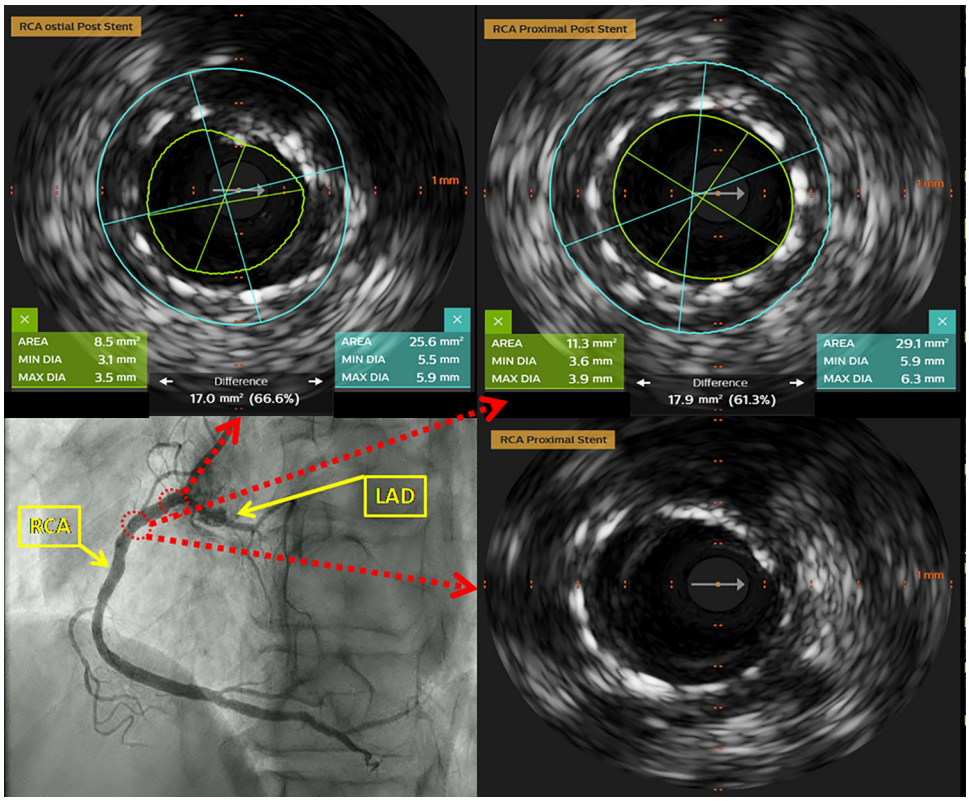

FIGURE 3
Intravascular ultrasound (IVUS) of the RCA after PCI. The optimal stent apposition without signs of dissection on proximal and distal stent edge was observed.

guided PCI provides better results than angiography guided PCI (13). Comprehensive information about the nature of the coronary plaque (calcified, fibromuscular, etc.), provided by IVUS, enables appropriate procedural decision making regarding lesion morphology and interventional strategies (14). Additionally, application of IVUS defined criteria for optimal stent implantation (plaque burden at 5 mm proximal or distal to stent edge <50%, minimal in-stent lumen area >90% of the distal reference lumen and absence of large edge dissection) provided in landmark clinical trials were associated with lower rates of MACE at one year follow-up (15, 16). Notwithstanding, optical coherence tomography (OCT) could be an alternative for plaque and lesion evaluation especially in calcified coronary arteries. OCT provides better spatial resolution and more detailed visualization of calcified lesion and can give more comprehensive information about plaque characteristics including calcium distribution, depth and volume which can be an essential information for procedural planning (17). We've opted for IVUS in this case due to ostial lesion location in both arteries of interest, RCA and LAD, due to possibility of suboptimal image quality if OCT was used due to insufficient blood clearing from the vessel.

In our case, use of combined imaging modalities of CTCA and IVUS provided important information that allowed identification of coronary anomaly type, determination of the extent and distribution of atherosclerotic plaques, as well as optimization of PCI strategy. We considered the result was good after initial PCI procedure. Although we didn't achieve 90% of stent expansion relative to the lumen diameter, we think that further attempts to optimize RCA ostium could increase the risks of RCA ostial dissection and LAD compromise.

PCI of substantially calcified lesions is associated with poor procedural success, greater complication rates, and inferior long-term clinical outcomes (18). The possible options for treatment of very calcified lesions could be rotational or orbital atherectomy, non-compliant and cutting balloons together with IVL. Rotational atherectomy can be challenging in ostial RCA lesions due to several reasons: difficulty of coaxial alignment of guiding catheter against RCA ostium, risk of laceration of the ostium and potential for embolization of rotablation debris (19). We decided to use IVL with the intention to treat calcified lesion in a more focal manner by causing localized fractures of calcified segments of ostial RCA. IVL causes fractures and local dissection even in thicker calcified segments or calcified nodules which allows better lesion preparation and stent expansion (20). Use of IVL prior to stent implantation was also associated with lower rates of major adverse cardiac events (MACE) and stent thrombosis (21). We have reported use of IVL in ostial RCA

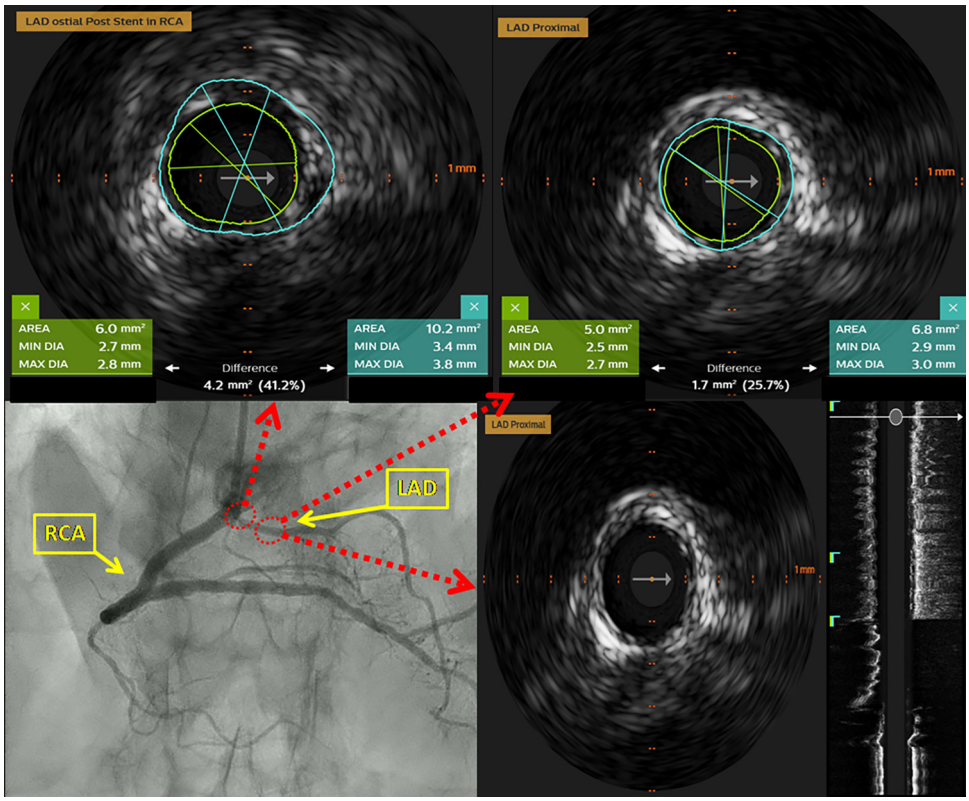

FIGURE 4
Intravascular ultrasound (IVUS) of the LAD after PCI. No signs of the narrowing of the ostial and proximal LAD after PCI of proximal RCA was documented.

lesion in a rare coronary anomaly where, in our opinion, use of IVL facilitated the lesion preparation while preventing major ostial dissection that can extend into aorta and/or ostium of LAD. IVUS guidance enabled optimal IVL balloon sizing which led to optimal lithotripsy effect and contributed to procedural success (21). Although, as previously mentioned, IVL is considered safe and potent method of lesion preparation, target-vessel revascularization still occurs in approximately 10% of patients treated with IVL (22). In our case it might be that the deep, concentrated calcium resembling calcified nodule could influence the occurrence of restenosis, despite optimal PC procedure (23). Studies have found that in-stent restenosis (ISR) can be linked to factors like patient characteristics, genetics, stent features, lesion shape, and procedural methods (24). The anatomy of the blood vessels also contributes to restenosis, particularly during PCI procedures involving bifurcation lesions (25). However, there is insufficient data regarding the impact of coronary anomalies, such as the one presented in this case. Using drug-coated balloons (DCB) for the management of in-stent restenosis was linked to lower MACE than treatment with regular, non-coated balloons, although our patient does not resemble study patients treated with DCBs in the studies that evaluated their effectiveness. However, the principles of construction of new generation DCBs seem promising even for complex patients, like ours was (26).

Conclusion

Although rare, CAAs could be associated with coronary artery disease and usually present additional challenge for interventional treatment. Advanced imaging modalities, including CTCA and IVUS, provide good procedural guidance during complex PCI procedures in patients with CAAs, while IVL provides solutions for calcified lesions, not affected by the variations in coronary anatomy. Lesion restenosis after PCI represents a challenge in everyday clinical practice, and using DCBs for treatment might be a valid option. Whether the unique coronary anatomy in this case played a part in the need for repeated revascularization remains uncertain.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

KK: Conceptualization, Investigation, Methodology, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. DO: Conceptualization, Investigation, Methodology, Resources, Supervision, Visualization, Writing – original draft, Writing – review & editing. II: Conceptualization, Methodology, Resources, Supervision, Validation, Visualization, Writing – review & editing. MD: Resources, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2025.1471211/full#supplementary-material

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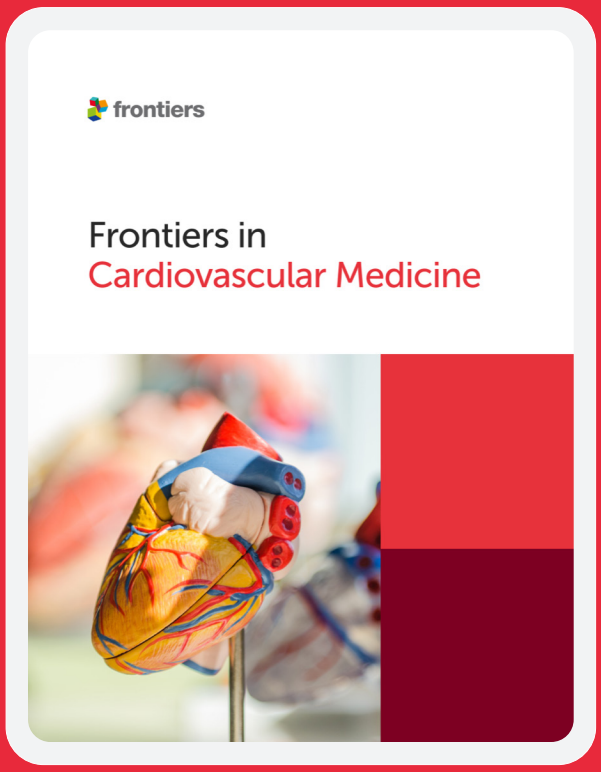

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