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Case Report: Burkitt's lymphoma with concurrent HIV, CMV encephalitis, and salmonella bacteremia

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Burkitt's lymphoma is a highly aggressive B-cell lymphoma associated with human immunodeficiency virus (HIV) infection. Despite antiretroviral therapy (ART), Burkitt's lymphoma remains diagnostically and therapeutically challenging, especially with concurrent infections. We describe a 50-year-old man presenting with constitutional symptoms and *Salmonella* bacteremia, found to have newly diagnosed HIV, stage IV Burkitt's lymphoma with central nervous system (CNS) and marrow involvement, and cytomegalovirus (CMV) viremia. His management required coordination of ART, chemotherapy, and infection treatment, complicated by CMV encephalitis and adherence barriers. This case highlights the challenges of managing overlapping malignancy and infection, emphasizing early HIV testing and patient-centered multidisciplinary care.

KEYWORDS

Burkitt's lymphoma, CMV, CMV encephalitis, HIV, lymphoma

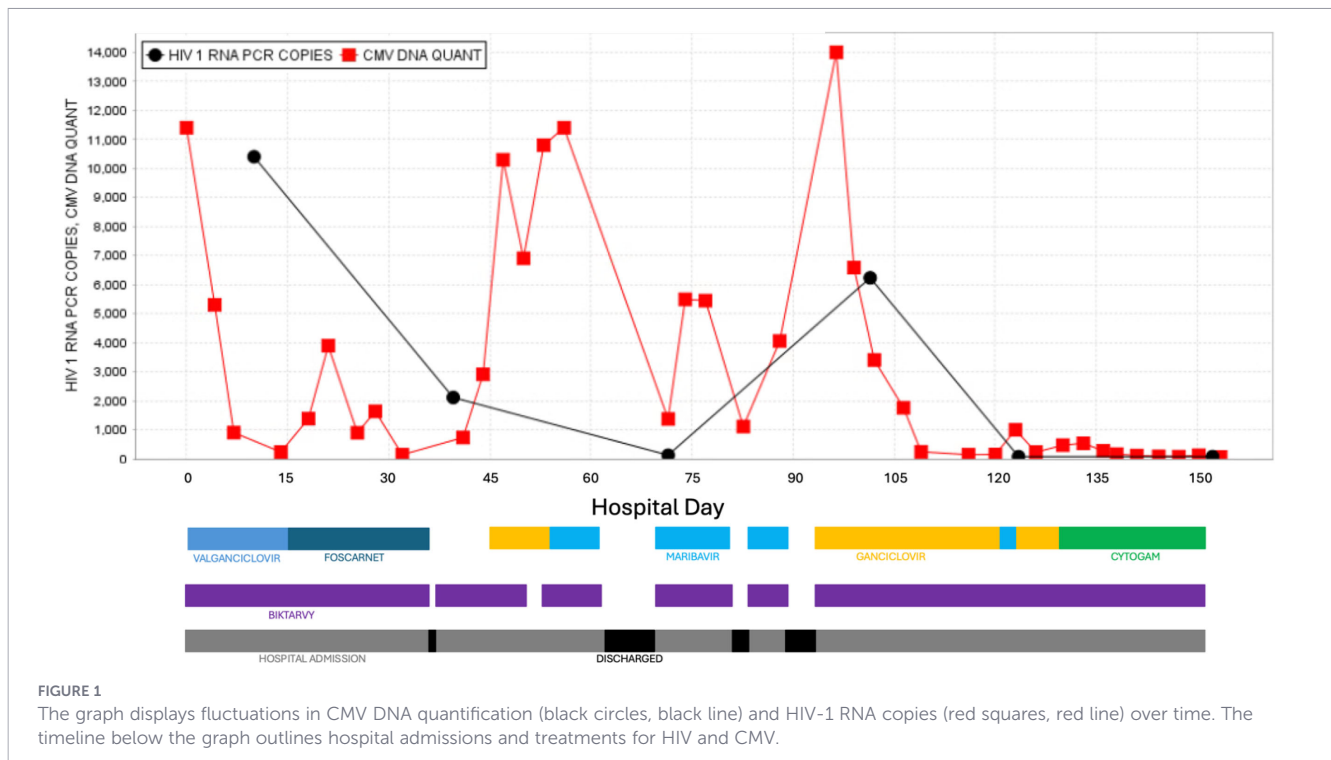
Introduction

Burkitt's lymphoma is an aggressive B-cell non-Hodgkin lymphoma with three clinical variants, including the immunodeficiency-associated subtype most often seen in patients with HIV. Compared with endemic and sporadic forms, this subtype carries a higher risk of CNS and bone marrow involvement.

The widespread use of ART has markedly reduced the incidence of HIV-associated malignancies and opportunistic infections, with HIV-related cancers declining by nearly 70% after the introduction of three-drug ART in the mid-1990s (1). Among these malignancies, however, the reduction in Burkitt's lymphoma has been less pronounced (1). Burkitt's now accounts for roughly 40% of HIV-associated lymphomas and often occurs in patients with relatively preserved CD4 counts, illustrating the complexity between immune function and oncogenesis (2). CNS involvement is reported in 20–30% of HIV-associated Burkitt's cases (3).

Despite ART, opportunistic infections such as *Salmonella* bacteremia and CMV viremia remain significant in advanced or poorly controlled HIV (4). CMV encephalitis, though rare (2–7% of advanced cases), carries a poor prognosis, with mortality exceeding 40% (5, 6). Together, these complications highlight the profound immunosuppression and overlapping morbidities that define advanced HIV.

While HIV-associated Burkitt lymphoma has been widely described, simultaneous presentation with multiple severe opportunistic infections at the time of initial HIV



diagnosis remains uncommon (3). The concurrent occurrence of stage IV Burkitt lymphoma, *Salmonella* bacteremia, and CMV encephalitis presents unique diagnostic and therapeutic challenges, particularly in the setting of profound immunosuppression and barriers to treatment adherence. This case highlights the complexity of coordinating antiretroviral therapy, intensive chemotherapy, and antiviral management in a critically ill patient while also addressing social determinants of care that impact treatment continuity. By illustrating these intersecting challenges, this report provides practical insights into the multidisciplinary management of aggressive HIV-associated malignancy complicated by opportunistic infections.

Case description

A 50-year-old man presented with two to three months of progressive night sweats, abdominal pain, fatigue, and unintentional weight loss. Two weeks prior to presentation, he had been treated for a presumed urinary tract infection, during which incidental imaging demonstrated diffuse retroperitoneal lymphadenopathy.

His past medical history was notable for septic arthritis and osteomyelitis three years earlier that required prolonged intravenous antibiotic therapy. He was not taking chronic medications and had no previously diagnosed medical conditions. He lived with his wife and daughters, was originally from Russia, and primarily spoke Russian. He reported a 10-pack-year smoking history and occasional alcohol use but denied intravenous drug use.

On presentation, he was febrile (38.9 °C) but hemodynamically stable and appeared frail. Physical examination was notable for left upper quadrant abdominal tenderness without palpable lymphadenopathy. Laboratory studies demonstrated microcytic

anemia (hemoglobin 10.2 g/dL), markedly elevated lactate dehydrogenase (1,200 U/L), mild transaminitis, and 2+ proteinuria. Blood cultures obtained at admission grew *Salmonella* species, prompting infectious disease consultation and initiation of intravenous antibiotics.

Diagnostic assessment

Computed tomography (CT) imaging demonstrated progressive retroperitoneal lymphadenopathy, hepatic cysts, borderline splenomegaly, and small bilateral pleural effusions. Given his B symptoms and rapidly enlarging lymph nodes, an underlying hematologic malignancy was suspected. Lymph node and bone marrow biopsies were obtained, and additional diagnostic testing included HIV and hepatitis serologies, CMV polymerase chain reaction (PCR), and serum protein electrophoresis.

Laboratory evaluation revealed newly diagnosed HIV-1 infection with a CD4 count of 32 cells/ μ L and an HIV viral load of 10,400 copies/mL as shown in Figure 1. CMV PCR was also positive at 6,610 copies/mL.

Histopathologic examination of the retroperitoneal lymph node demonstrated an atypical lymphoid infiltrate composed of intermediate- to large-sized lymphoid cells arranged in sheets with numerous apoptotic bodies and tangible-body macrophages, imparting a characteristic “starry-sky” appearance as shown in Figure 2. Immunohistochemical staining was positive for CD20, PAX5, CD10, and BCL6, with a Ki-67 proliferation index approaching 100%. The lymphoma cells were negative for BCL2, CD5, MUM1, CD34, TdT, cyclin D1, and CD23. Bone marrow biopsy revealed a markedly hypercellular marrow (95% cellularity) with approximately 30% involvement by lymphoma. Fluorescence *in situ* hybridization

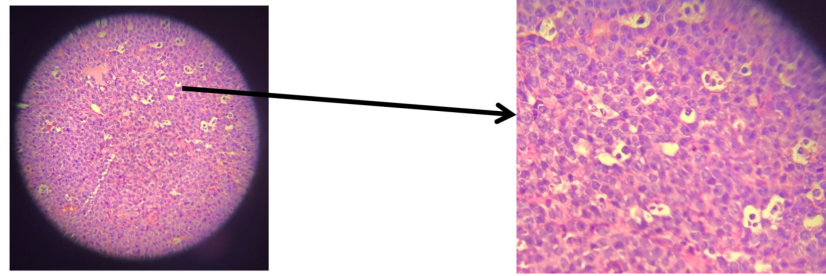


FIGURE 2
Histopathology of retroperitoneal lymph node.

identified the t(8;14) MYC translocation, confirming the diagnosis of Burkitt lymphoma. Epstein–Barr virus (EBV) evaluation by EBER *in situ* hybridization was not performed due to institutional constraints. EBV status was not assessed by EBER *in situ* hybridization in this case, which represents a limitation in fully characterizing the viral contribution to the lymphoma. EBV positivity is frequently observed in immunodeficiency-associated Burkitt lymphoma and may provide additional insight into disease pathogenesis in patients with advanced HIV infection.

Following diagnosis, the patient was transferred to a tertiary oncology center for management. Positron emission tomography (PET) imaging demonstrated extensive hypermetabolic adenopathy and diffuse osseous uptake consistent with advanced disease (Deauville score 5).

Given the aggressive nature of the malignancy and the patient's profound immunosuppression, a multidisciplinary team including oncology and infectious disease specialists coordinated treatment. Systemic chemotherapy with dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab (DA-EPOCH-R) was initiated. Dose-adjusted EPOCH-R was selected due to its demonstrated efficacy in HIV-associated aggressive B-cell lymphomas and its ability to allow dose modification based on tolerability in immunocompromised patients (3). Additionally, this regimen has been widely adopted in the management of HIV-associated Burkitt lymphoma due to favorable outcomes compared with historical intensive regimens (3). Concurrent antiretroviral therapy was started with bictegavir/emtricitabine/tenofovir alafenamide (Biktarvy). CNS prophylaxis was initiated with intrathecal methotrexate following lumbar puncture that demonstrated CNS involvement.

During early treatment, the patient's CMV viral load increased to 11,400 copies/mL, prompting initiation of valganciclovir (900 mg twice daily). Antiviral therapy was complicated by progressive cytopenias and severe mucositis, which impaired his ability to tolerate oral medications. Consequently, therapy was transitioned to intravenous foscarnet (5.4 g every 12 hours), resulting in an initial decline in CMV viral load.

Antiviral therapy was discontinued after viral load improvement around treatment day 38; however, CMV viremia subsequently rebounded to 2,910 copies/mL by day 44. Valganciclovir was restarted while maribavir was obtained from an outside facility. Resistance testing performed during this period demonstrated resistance to foscarnet. Because the patient again became unable to

tolerate oral medications, antiviral therapy was transitioned to intravenous ganciclovir. Cycle 3 of DA-EPOCH-R was initiated during this period. Once available, maribavir therapy was started.

The patient's hospitalization was prolonged and complicated by multiple medical issues, including pulmonary embolism, pneumonia, severe mucositis, and chemotherapy-associated cytopenias requiring repeated transfusions. After approximately 50 days of hospitalization, he was discharged but was readmitted within hours due to recurrent fever and fatigue, necessitating an additional month of inpatient care. A follow-up PET scan demonstrated a mixed response to chemotherapy as shown in Figures 3A, B.

Two weeks following discharge, he required readmission for diarrhea and neutropenic fever. Evaluation revealed *Clostridioides difficile* colitis, recurrent *Salmonella* bacteremia associated with *salmonella* enteritis, perianal abscess, cystitis, and a subdural hematoma. At this stage, he had completed four cycles of DA-EPOCH-R and two intrathecal chemotherapy treatments.

Four days after his subsequent discharge, the patient presented again with worsening confusion, generalized weakness, and poor oral intake. Magnetic resonance imaging (MRI) of the brain demonstrated ventricular enhancement as shown in Figure 3C. Lumbar puncture revealed cerebrospinal fluid positive for CMV by meningoencephalitis PCR panel, confirming CMV encephalitis. Cytology was negative for malignant cells.

Although CMV immunoglobulin (Cytogam) was recommended at this time, treatment was delayed due to insurance authorization barriers. Intravenous ganciclovir was initiated because there was concern for treatment failure with maribavir.

During this admission, significant barriers to outpatient management became apparent, including challenges with medication adherence related to language barriers and complex medication regimens. After further evaluation, maribavir therapy was briefly resumed; however, given its limited central nervous system penetration, antiviral therapy was transitioned back to intravenous ganciclovir once CMV encephalitis was confirmed.

Following insurance approval, Cytogam was initiated at a dose of 200 mg/kg every other day for one week, followed by weekly dosing for two weeks and then every two weeks for six additional doses.

Despite these interventions, the patient's clinical condition continued to deteriorate. Progressive encephalopathy and severe malnutrition ultimately necessitated initiation of total parenteral nutrition (TPN). After approximately five months of treatment, he had completed five cycles of DA-EPOCH-R and two intrathecal

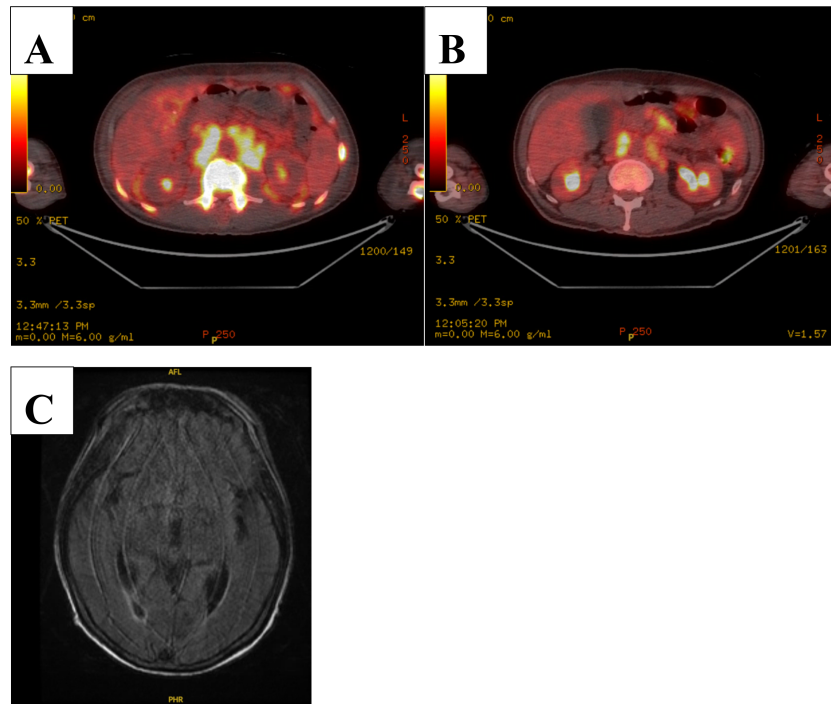


FIGURE 3

(A) Baseline PET/CT scan prior to initiation of therapy for Burkitt lymphoma demonstrating a Deauville score of 5. (B) Follow up PET/CT performed approximately 45 days later after two cycles of systemic therapy, including intrathecal chemotherapy, showed a mixed metabolic response, overall remaining consistent with Deauville score 5. (C) Brain MRI with and without contrast demonstrating ependymal enhancement along the surface of the lateral ventricles and aqueduct of Sylvius, findings characteristic of CMV encephalitis.

chemotherapy doses (methotrexate and cytarabine). However, he remained encephalopathic, dependent on TPN, and unable to tolerate further chemotherapy.

Although Cytogam therapy was eventually administered, his CMV encephalitis persisted, and neurologic recovery did not occur. Given his poor prognosis and progressive clinical decline, goals-of-care discussions were initiated with his family, and hospice care was ultimately pursued.

Discussion

Managing simultaneous acquired immunodeficiency syndrome (AIDS)-defining illnesses and an aggressive malignancy presents profound clinical challenges. Burkitt's lymphoma, a recognized HIV-associated cancer, rarely occurs concurrently with *Salmonella* bacteremia and CMV encephalitis at the time of initial HIV diagnosis. To our knowledge, this is the first reported case in which all three conditions presented simultaneously. In this patient, the initial *Salmonella* bacteremia obscured the underlying lymphoma, highlighting how opportunistic infections can mask or coexist with malignancy in advanced immunodeficiency. Clinicians should therefore maintain a high index of suspicion for underlying malignancy in immunocompromised patients and prioritize rapid diagnostic evaluation alongside multidisciplinary coordination of care (7).

Managing aggressive cancer in the setting of advanced HIV and concurrent infections requires careful coordination of ART, cytotoxic chemotherapy, and antiviral therapy. Patients with

advanced HIV undergoing DA-R-EPOCH present unique therapeutic challenges because several components of the regimen overlap with ART in terms of metabolism, bone marrow toxicity, and immunologic recovery. Agents such as etoposide, doxorubicin, and vincristine are metabolized via CYP3A4, raising the potential for drug–drug interactions with ART regimens containing ritonavir- or cobicistat-boosted protease inhibitors. These interactions may increase chemotherapy exposure and toxicity. Conversely, integrase strand transfer inhibitors (INSTIs), which are commonly recommended in the modern era, have minimal CYP3A4 interactions and are generally preferred when treating lymphoma in people with HIV. In our patient, ART selection and timing were guided by the need to minimize pharmacokinetic interactions and avoid compounded cytopenias during DA-R-EPOCH. Additionally, maintaining viral suppression during chemotherapy is associated with improved oncologic outcomes, but this must be balanced against periods of intolerance, mucositis, and treatment-related cytopenias that can limit ART adherence. Although concurrent ART and chemotherapy are recommended, this case highlights the real-world difficulty of implementing such regimens amid infection, frailty, and organ dysfunction.

CMV encephalitis further worsened this patient's prognosis. Despite appropriate valganciclovir, viral reactivation occurred, emphasizing the aggressiveness of CMV in immunosuppressed hosts and the consequences of nonadherence. Delays in obtaining CMV immunoglobulin further exemplify systemic barriers that can affect timely management of opportunistic infections, even in well-resourced settings.

Equally important are the social determinants of care. Language barriers and health literacy gaps also significantly impacted adherence and care coordination. The patient's limited English proficiency contributed to misunderstanding complex medication schedules for HIV, CMV, and lymphoma. This highlights the importance of professional interpreters, simplified regimens, and caregiver involvement to ensure safe and effective care for patients with limited English proficiency.

Finally, early palliative care involvement is critical in cases with competing morbidities and high symptom burden. Despite aggressive multimodal therapy, this patient experienced recurrent hospitalizations, functional decline, and limited tolerance of curative-intent treatment. Early integration of palliative care may help align therapy with patient goals and improve quality of life (8).

Several limitations must be acknowledged. As a single case, the findings are not generalizable to all patients with HIV-associated Burkitt lymphoma. In addition, EBV status was not assessed using EBER *in situ* hybridization, limiting full virologic characterization of the lymphoma. Therapeutic decisions in this case were also influenced by the patient's profound immunosuppression, concurrent opportunistic infections, and challenges with treatment adherence, which may not reflect standard management in more controlled clinical settings. Despite these limitations, the case highlights the real-world complexity of managing aggressive lymphoma in patients with advanced HIV infection and overlapping infectious complications.

This case highlights several important clinical lessons relevant to the management of advanced HIV-associated malignancy. Burkitt lymphoma may present as the initial manifestation of undiagnosed HIV, often in the setting of profound immunosuppression, underscoring the need for rapid evaluation and multidisciplinary care. Opportunistic infections can mask underlying malignancy, making vigilant assessment essential in immunocompromised patients. Simultaneous management of ART, chemotherapy, and antivirals requires careful consideration of drug–drug interactions, overlapping toxicities, and treatment timing. CMV encephalitis remains a severe complication in advanced HIV, highlighting the importance of prompt recognition, tailored antiviral therapy, and attention to systemic barriers. Finally, this case underscores the significant impact of social determinants of health—including language barriers and treatment adherence challenges—on the successful outpatient management of complex oncologic and infectious diseases. Recognizing and addressing these barriers is critical to optimizing outcomes in vulnerable patient populations.

The interplay of biological complexity, treatment challenges, and social factors in this patient highlights how outcomes in advanced HIV-associated disease are shaped by more than clinical interventions alone. Success requires not only careful coordination of ART, chemotherapy, and antiviral therapy, but also attention to social determinants, adherence barriers, and timely palliative support. Clinicians must remain vigilant for underlying malignancy in immunocompromised patients, anticipate and manage drug interactions and overlapping toxicities, and implement culturally sensitive, multidisciplinary care to optimize both survival and quality of life.

Data availability statement

Ethics and privacy prevent the dataset from being made public. Requests to access these datasets should be directed to elinor.barsh@healthonecares.com.

Ethics statement

The studies involving humans were approved by HCA Institutional Review Board and Ethics Committee. The studies were conducted in accordance with the local 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. Written informed consent was obtained from the participant/patient(s) for the publication of this case report.

Author contributions

EB: Conceptualization, Investigation, Visualization, Writing – original draft, Writing – review & editing. MB: Resources, Supervision, Writing – original draft, Writing – review & editing. DS: Resources, Supervision, Writing – original draft, Writing – review & editing.

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The author(s) declared that generative AI was not used in the creation of this manuscript.

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