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Seronegative Disseminated Visceral Leishmaniasis with Secondary Hemophagocytic Lymphohistiocytosis in Advanced HIV Infection: A Case Report

İleri Evre HIV Enfeksiyonunda Seronegatif Yaygın Visseral Leishmaniasis ve Sekonder Hemofagositik Lenfohistiyositoz: Bir Olgu Sunumu

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Abstract

Visceral leishmaniasis (VL) is a life-threatening infection endemic to the Indian subcontinent and may be associated with atypical and severe manifestations in patients with human immunodeficiency virus (HIV) infection. Secondary hemophagocytic lymphohistiocytosis (HLH) is a rare but serious complication of VL. We report a 51-year-old man with advanced HIV infection due to poor adherence to antiretroviral therapy (ART) who presented with prolonged fever, melena, hepatosplenomegaly, and pancytopenia. A series of laboratory investigations ruled out common opportunistic infections. VL with secondary HLH was diagnosed based on the identification of *Leishmania donovani* and hemophagocytosis on bone marrow examination, despite a negative rK39 antigen test. Upper gastrointestinal endoscopy with subsequent biopsy revealed *Leishmania* infiltration, confirming disseminated involvement. The patient was treated with conventional amphotericin B deoxycholate, continuation of ART, and a short course of corticosteroids, resulting in clinical and hematological recovery. This case highlights the diagnostic challenges of seronegative VL in advanced HIV infection and underscores the importance of early tissue diagnosis and targeted therapy in patients presenting with fever, cytopenias, and organomegaly in endemic regions.

Keywords: Visceral leishmaniasis, hemophagocytic lymphohistiocytosis, HIV/AIDS, rK39 antigen test, amphotericin B deoxycholate

Öz

Visseral leishmaniasis (VL), Hint alt kıtasına özgü, yaşamı tehdit eden bir enfeksiyondur ve insan immün yetmezlik virüsü (HIV) enfeksiyonu olan hastalarda atipik ve şiddetli belirtilerle ilişkili olabilir. Sekonder hemofagositik lenfohistiyositoz (HLH), VL'nin nadir ancak ciddi bir komplikasyondur. Antiretroviral tedaviye (ART) uyumsuzluğu ve ileri evre HIV enfeksiyonu olan ve uzun süreli ateş, melena, hepatosplenomegali ve pansitopeni ile başvuran 51 yaşında bir erkek hastayı bildiriyoruz. Bir dizi laboratuvar incelemesi yaygın fırsatçı enfeksiyonları ekarte etti. Negatif rK39 antijen testine rağmen, kemik iliği incelemesinde *Leishmania donovani* ve hemofagositoz saptanması temelinde sekonder HLH ile birlikte VL tanısı kondu. Üst gastrointestinal endoskopi ve ardından yapılan biyopsi, yaygın tutulumu doğrulayan *Leishmania* infiltrasyonunu ortaya çıkardı. Hasta, konvansiyonel amfoterisin B deoksikolat, ART'nin devamı ve kısa süreli kortikosteroid tedavisi ile tedavi edildi ve klinik ve hematolojik iyileşme sağlandı. Bu vaka, ileri HIV enfeksiyonunda seronegatif VL'nin tanısız zorluklarını ve endemik bölgelerde ateş, sitopeni ve organomegali ile başvuran hastalarda erken doku tanısı ve hedefe yönelik tedavinin önemini vurgulamaktadır.

Anahtar Kelimeler: Visseral leishmaniasis, hemofagositik lenfohistiyositoz, HIV/AIDS, rK39 antijen testi, amfoterisin B deoksikolat



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Introduction

Visceral leishmaniasis (VL) is an endemic and potentially fatal protozoal infection in the Indian subcontinent, classically presenting with prolonged fever, hepatosplenomegaly, and pancytopenia^[1,2].

Coinfection with HIV alters the natural history of VL, leading to a higher parasite burden, atypical organ involvement, poor serological responses, and frequent relapses^[3,4].

Gastrointestinal dissemination of leishmaniasis, which may manifest as ulcerative lesions and bleeding, is uncommon in immunocompetent individuals but is increasingly recognized in patients with advanced immunosuppression^[5,6].

One of the severe and potentially fatal complications of VL is a hyperinflammatory state known as hemophagocytic lymphohistiocytosis (HLH), characterized by persistent fever, cytopenias, hyperferritinemia, and multiorgan dysfunction^[7,8]. Infection-triggered HLH is well described, and VL is an important but often underdiagnosed precipitating factor^[9,10].

The coexistence of advanced human immunodeficiency virus (HIV) infection, disseminated VL, and secondary HLH presents a significant diagnostic and therapeutic challenge because of overlapping clinical features. We describe a case of disseminated VL presenting with gastric ulcers and secondary HLH in a patient with advanced HIV infection.

Case Report

A 51-year-old migrant worker from Bihar presented to the emergency department with complaints of high-grade fever ($>101^{\circ}\text{F}$) associated with chills for three weeks. During this period, he also reported 1-2 episodes of vomiting and melena daily. He complained of diffuse, cramping-type abdominal pain and noted progressive abdominal distension. In addition, he experienced dysphagia, severe generalized weakness, and myalgia.

The patient was a known case of HIV infection and had been receiving antiretroviral therapy (ART) consisting of tenofovir, lamivudine, and dolutegravir (300 mg/300 mg/50 mg) once daily for the past 10 years. He had been under regular follow-up at an ART center in his hometown; however, for the past year, he had poor adherence to ART and irregular follow-up because of migration to our city. His last CD4 count, measured one year earlier, was 482 cells/ μL (reference range: 500-1,500 cells/ μL).

On presentation to the emergency department, the patient was febrile, with a temperature of 102°F . He appeared severely undernourished and cachectic, with a body mass index of 16.4 kg/m^2 . On examination, he had a systolic blood

pressure of 90 mmHg and a heart rate of 116 beats/min. He had severe pallor and mild bilateral pitting pedal edema. Abdominal examination revealed grade 2 splenomegaly and hepatomegaly, with a liver span of 18 cm. The remainder of the systemic examination was unremarkable. The patient was admitted to the medicine ward, and initial laboratory investigations were performed.

A complete hemogram revealed pancytopenia, and the peripheral blood smear showed normocytic, normochromic anemia with leukopenia and thrombocytopenia. No hemoparasites were detected.

Initial laboratory investigations demonstrated severe hypoalbuminemia, elevated transaminases, with aspartate aminotransferase levels higher than alanine aminotransferase levels, euolemic hypotonic hyponatremia, severe hypocalcemia, and severe vitamin D deficiency. The laboratory findings are summarized in Table 1.

The CD4 count was 157 cells/ μL , and the HIV viral load was elevated at 30,000 copies/mL.

Given the advanced immunosuppression, investigations to rule out opportunistic infections were performed. Cryptococcal antigen, cytomegalovirus (CMV) polymerase chain reaction (PCR), and urinary histoplasma antigen tests were negative. Fundus examination showed no evidence of CMV retinitis. The rK39 antigen test for leishmaniasis was also negative.

Routine stool microscopy was positive for occult blood, with no ova or cysts identified. Stool examination using modified acid-fast staining for *Cryptosporidium*, *Isospora*, and *Cyclospora* was negative. Stool culture showed no growth.

Blood cultures for aerobic and anaerobic bacteria, as well as fungal cultures, were also negative.

The patient was started on empirical intravenous ceftriaxone and antipyretics. He received transfusions of two units of packed red blood cells and platelet concentrates. Intravenous calcium gluconate was administered along with vitamin D₃ supplementation.

Despite treatment, the patient continued to experience persistent fever spikes, pancytopenia, hyponatremia, and worsening liver function tests. Serum ferritin, fibrinogen, and triglyceride levels were measured because of suspected HLH and were markedly abnormal. The findings are shown in Table 2.

Under aseptic precautions, bone marrow aspiration and biopsy were performed because of persistent pancytopenia. Samples were sent for microscopic examination, Ziehl-Neelsen (ZN) staining, histopathological examination, and cartridge-based nucleic acid amplification testing (CBNAAT).

Table 1. Laboratory investigations.

Investigation	Result	Reference	Investigation	Result	Reference
Haemoglobin	7.30 gm/dL	13.2-16.6 gm/dL	Total bilirubin	0.80 mg/dL	0.22-1.20 mg/dL
Haematocrit	30.4%	38.0-48.60%	Direct bilirubin	0.50 mg/dL	Upto 0.5 mg/dL
Mean corpuscular volume	77.8 fL	78.2-97.9 fL	Indirect bilirubin	0.30 mg/dL	0.1-1.0 mg/dL
TLC ¹	770/ μ L	4,000–10,000 / μ L	AST ²	207 U/Lt	8-48 U/Lt
Neutrophil	70%	40-80%	ALT ³	76 U/Lt	7-55 U/Lt
Lymphocyte	22%	20-40%	ALP ⁴	313 U/Lt	40-129 U/Lt
Eosinophils	0%	0-6%	Serum protein	5.10 g/dL	6.4-8.30 g/dL
Monocyte	9%	2-10%	Serum albumin	1.80 g/dL	3.5-5.2 g/dL
PLT ⁵	31,000 / μ L	150,000–410,000 / μ L	Sodium	122 mmol/Lt	136-145 mmol/Lt
Vitamin B12	194 pg/mL	187-883 pg/mL	Potassium	3.92 mmol/Lt	3.50-5.10 mmol/Lt
Lactate dehydrogenase	972 U/Lt	120-246 U/Lt	Serum osmolality	259.2 mOsmol/kg	275-300 mOsmol/kg
Dengue NS1 Ag/IgM/IgG	Negative		Ionized calcium	0.8 mmol/Lt	1.12-1.32 mmol/Lt
Rapid malaria antigen test	Negative		Vitamin D	9.30 ng/mL	20-50 ng/mL
HBsAg	Non-reactive		Urea	42 mg/dL	17-49 mg/dL
Anti-HCV	Non-reactive		Creatinine	0.77 mg/dL	0.6-1.35 mg/dL

TLC¹, total leukocyte count; AST², aspartate aminotransferase; ALT³, alanine aminotransferase; ALP⁴, alkaline phosphatase; PLT⁵, platelet.

NS1, non-structural protein 1; Ag, antigen; IgM, immunoglobulin M; IgG, immunoglobulin G; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus.

Table 2. Laboratory findings.

Investigation	Result	Investigation	Result
Hemoglobin	7.10 gm/dL	Total bilirubin	3.09 mg/dL
TLC	600/ μ L	Direct bilirubin	2.58 mg/dL
PLT	24,000/ μ L	Indirect bilirubin	0.5 mg/dL
Sodium	123 mmol/L	AST	599 U/L
Ferritin	9,491 ng/mL (21.8-274.6 ng/mL)	ALT	227 U/L
Triglycerides	282 mg/dL (<150 mg/dL)	ALP	1,579 U/L
Fibrinogen	240 mg/dL (238-498 mg/dL)		

TLC, total leukocyte count; PLT, platelet count; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase.

Samples were also sent for bacterial, fungal, and mycobacterial cultures, including culture on Lowenstein-Jensen medium.

Bone marrow examination revealed a normocellular marrow with trilineage hematopoiesis and evidence of hemophagocytosis. Numerous intracellular kinetoplast-containing organisms consistent with *Leishmania donovani* bodies (LD bodies) were identified within macrophages, as well as within erythroid and myeloid precursors, confirming the diagnosis of VL (Figures 1 and 2).

Bone marrow aspirate samples were negative on ZN staining and CBNAAT, as well as on bacterial, fungal, and mycobacterial cultures, ruling out tuberculosis and other infectious etiologies.

The patient fulfilled six of the eight HLH-2004 diagnostic criteria: (1) fever, (2) splenomegaly, (3) cytopenias involving all three hematopoietic lineages, (4) hypertriglyceridemia,

(5) hyperferritinemia, and (6) evidence of hemophagocytosis in the bone marrow. The remaining criteria included hypofibrinogenemia, which was not present because the serum fibrinogen level was within the normal range, and low or absent natural killer cell activity and elevated soluble interleukin-2 receptor (sCD25) levels, which were not assessed because these tests were unavailable at our institution. Thus, a diagnosis of secondary HLH due to VL was made.

The patient was initiated on intravenous amphotericin B deoxycholate at a dose of 1 mg/kg body weight (50 kg), according to the National Institutes of Health Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV, because liposomal amphotericin B was unaffordable. ART was reinitiated, and cotrimoxazole (trimethoprim-sulfamethoxazole) 160/800 mg once daily was started for prophylaxis.

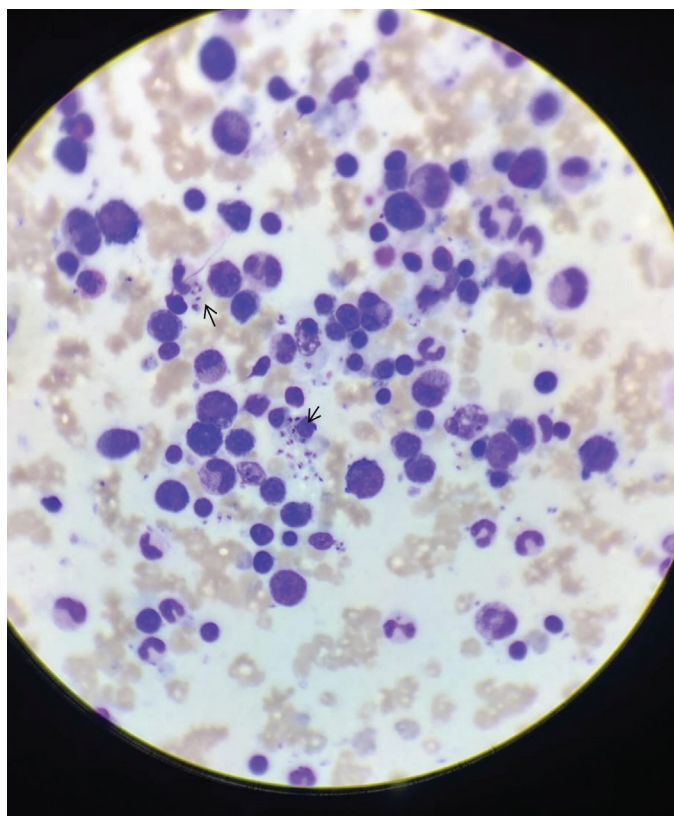


Figure 1. Bone marrow aspirate smears stained with Leishman stain ($\times 40$, oil immersion) showing numerous intracellular and extracellular *Leishmania donovani* amastigotes (arrows).

Low-dose corticosteroids were administered for 5 days (intravenous dexamethasone, 8 mg once daily), followed by gradual tapering, as adjunctive therapy for HLH management.

In view of the melena and dysphagia, upper gastrointestinal endoscopy was performed. Endoscopy revealed a large excavated ulcer measuring approximately 4 cm, with regular margins and slough, in the prepyloric region. Another ulcer measuring approximately 2 cm and covered with an adherent blood clot was also noted in the prepyloric region (Figures 3-5).

Histopathological examination of biopsy samples from the gastric ulcers demonstrated benign gastric ulcers with multiple intracellular and extracellular *Leishmania donovani* bodies, further supporting the diagnosis of VL.

Intravenous amphotericin B deoxycholate was continued for 30 days with close monitoring of renal function and electrolyte levels, along with appropriate premedication to prevent infusion-related reactions. From the sixth dose onward, the patient developed persistent hypokalemia, requiring daily potassium supplementation; however, renal function remained normal throughout therapy.

The patient showed significant clinical improvement after 10 days of treatment, with defervescence and improved appetite.

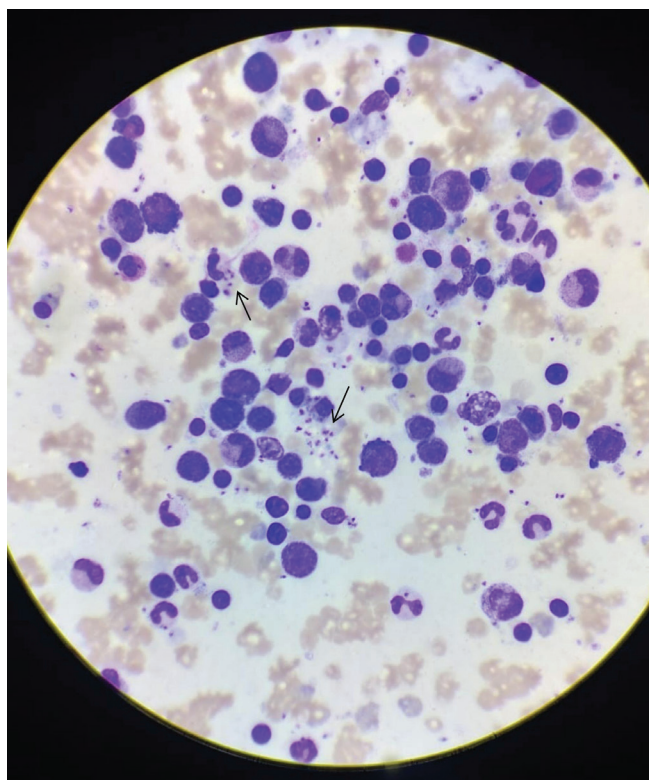


Figure 2. Bone marrow aspirate smears stained with Leishman stain ($\times 40$, oil immersion) showing numerous intracellular and extracellular *Leishmania donovani* amastigotes (arrows).

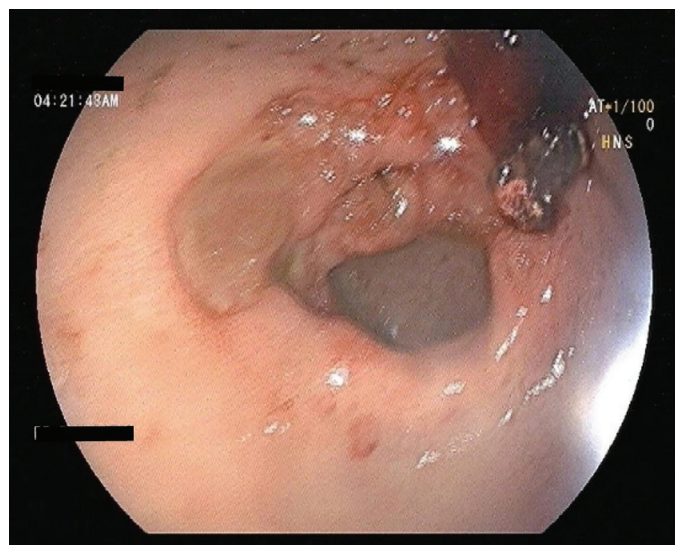


Figure 3. Upper gastrointestinal endoscopy showing gastric ulcers.

Symptoms, including vomiting, dysphagia, melena, and abdominal pain, resolved. There was marked regression of hepatosplenomegaly, and repeat ultrasonography on day 20 showed a normally sized liver and spleen.

Pancytopenia resolved by day 20, with progressive improvement in the hemoglobin level, leukocyte count, and platelet count.

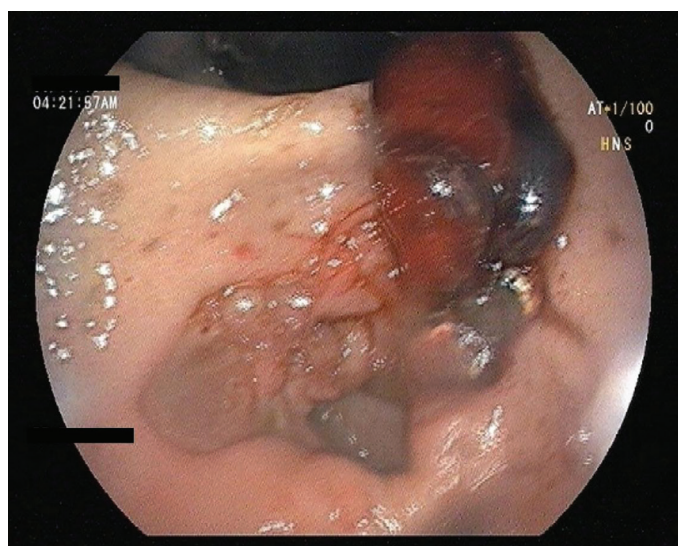


Figure 4. Upper gastrointestinal endoscopy showing gastric ulcers. Liver function tests normalized.

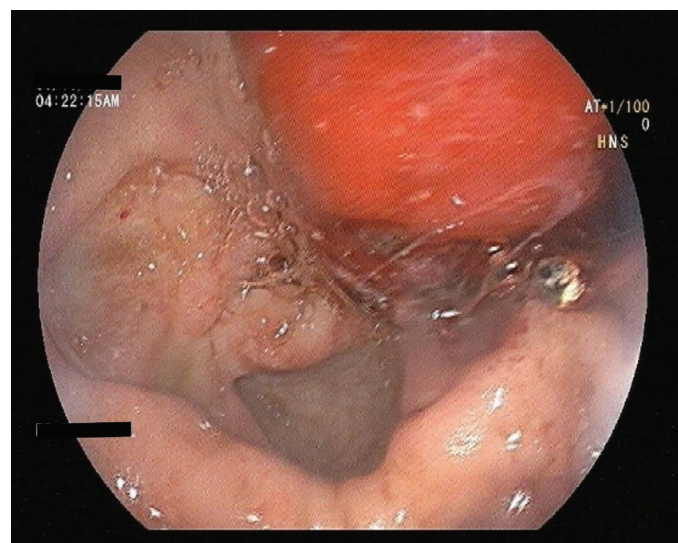


Figure 5. Upper gastrointestinal endoscopy showing gastric ulcers.

After completion of therapy, the patient was discharged on ART and advised to receive monthly amphotericin B deoxycholate at a dose of 1 mg/kg as secondary prophylaxis.

At the 6-month follow-up, there was no evidence of recurrent leishmaniasis, and the CD4 count had improved to 366 cells/ μ L. Subsequently, the patient was lost to follow-up.

Discussion

VL, or “kala-azar,” is the most severe form of leishmaniasis and remains a major public health problem in endemic regions such as India. It is caused by intracellular protozoa

of the *Leishmania* genus, which survive and replicate within macrophages and other mononuclear phagocytic cells. More than 20 *Leishmania* species cause human disease, with *Leishmania donovani* being the predominant cause of VL in the Indian subcontinent. Globally, the incidence of leishmaniasis is estimated at 700,000-1 million new cases annually, with nearly 90% of VL cases reported from a limited number of countries, including India, Bangladesh, Brazil, Ethiopia, South Sudan, and Sudan^[1,2,11].

In India, VL is primarily an anthroponotic disease transmitted by *Phlebotomus argentipes* and disproportionately affects socioeconomically disadvantaged populations, particularly migrant workers residing in or originating from endemic areas, including Bihar, Jharkhand, West Bengal, and eastern Uttar Pradesh^[1,2]. In addition to vector-borne transmission, leishmaniasis may rarely be acquired through needle sharing among people who inject drugs, transfusion of infected blood, or vertical transmission from mother to child^[3].

Most *Leishmania* infections in immunocompetent hosts remain asymptomatic, with parasites persisting in a latent state for prolonged periods. However, progression to active disease may occur months to years later when host cell-mediated immunity is compromised^[12].

Classical VL manifests with prolonged fever, weight loss, hepatosplenomegaly, hypoalbuminemia, and pancytopenia due to infiltration of the reticuloendothelial system, bone marrow suppression, and chronic immune activation. Without timely treatment, VL is almost uniformly fatal, with death resulting from complications such as secondary infections, severe cytopenias, hepatic dysfunction, or immune-mediated syndromes such as HLH^[2,9].

HIV and VL are mutually reinforcing infections with synergistic pathogenic effects. Since the first reports of HIV-VL coinfection in the late 1980s, cases have been documented in more than 45 countries worldwide^[3,13]. Although the incidence declined substantially in high-income countries following the introduction of combination ART, HIV-VL coinfection remains a significant concern in parts of Asia, Africa, and Latin America^[3,13,14].

In India, the burden of VL-HIV coinfection has increased over time, with recent estimates suggesting that 5%-7% of patients with VL are coinfecting with HIV, particularly in endemic states such as Bihar^[15-17].

HIV infection increases the risk of developing clinical VL by more than 100-fold, while VL accelerates HIV disease progression by enhancing viral replication and worsening CD4⁺ T-cell depletion^[5]. Both pathogens target macrophages and

dendritic cells, resulting in profound immune dysregulation, increased parasite loads, and impaired immune recovery despite virologic suppression^[18,19].

Clinically, the most common presentation of leishmaniasis in people living with HIV (PLHIV) is severe systemic visceral disease, characterized by prolonged fever, weight loss, hepatosplenomegaly, and pancytopenia.^[4,20,21] However, splenomegaly may be less prominent than in immunocompetent individuals, and atypical manifestations are frequent in patients with advanced immunosuppression (CD4⁺ T-cell count <200 cells/mm³)^[20]. These manifestations include gastrointestinal, mucosal, pulmonary, serosal, and cutaneous involvement^[22]. Gastrointestinal leishmaniasis may manifest as abdominal pain, diarrhea, malabsorption, gastrointestinal bleeding, dysphagia, or ulcerative lesions^[6,22]. High parasite burdens, poor serological responses, and relapses are also frequent in immunosuppressed hosts^[19,23].

In the present case, the patient exhibited classical features of VL along with atypical manifestations—notably melena, dysphagia, and gastric ulcers—which were subsequently confirmed to result from gastrointestinal involvement by *Leishmania donovani*. Our patient had poor ART adherence for nearly a year, resulting in virologic failure and significant immunosuppression (CD4 count, 157 cells/μL), which most likely predisposed him to severe disseminated leishmaniasis.

The diagnosis of VL relies on a combination of clinical suspicion, serological testing, and parasitological confirmation. Serological tests such as the rK39 immunochromatographic assay detect host antibodies directed against a recombinant kinesin-related antigen of *Leishmania* species and are widely used as rapid diagnostic tests for VL in endemic areas because of their ease of use and high sensitivity in immunocompetent individuals, with a reported sensitivity of 97% in the Indian subcontinent. However, in advanced HIV infection, rK39 sensitivity is significantly reduced because of an impaired humoral immune response, leading to false-negative results. Consequently, a negative rK39 test should not exclude the diagnosis when clinical suspicion remains high, and a tissue-based diagnosis may be required for confirmation^[24,25].

Parasitological confirmation through the demonstration of *Leishmania donovani* bodies remains the diagnostic gold standard. Bone marrow aspiration, splenic aspiration, lymph node biopsy, and tissue biopsies from involved organs can demonstrate intracellular amastigotes, with splenic aspiration having the highest sensitivity but also an increased procedural risk^[16,13]. Bone marrow examination, although less sensitive than splenic aspiration, is safer and particularly valuable in patients with pancytopenia and suspected HLH because it

allows simultaneous evaluation for hemophagocytosis and opportunistic infections^[13,10].

Molecular methods such as PCR offer high sensitivity but are not universally available in many resource-limited endemic regions^[5].

In our patient, the initial evaluation for common opportunistic infections was negative. The rK39 serological test for leishmaniasis was also negative, consistent with the reported reduced sensitivity of this test in individuals with HIV infection. Persistent fever, worsening cytopenias, hepatosplenomegaly, and biochemical evidence of hyperinflammation prompted further evaluation.

Bone marrow aspiration and biopsy revealed hemophagocytosis along with intracellular *Leishmania donovani* bodies, establishing the diagnosis of VL with secondary HLH. Additionally, upper gastrointestinal endoscopy with biopsy of the gastric ulcers demonstrated intracellular and extracellular *Leishmania donovani* bodies, confirming disseminated VL with gastrointestinal involvement—an uncommon but well-documented manifestation in VL-HIV coinfection. It is also noteworthy that *Leishmania* amastigotes were identified on routine histopathological examination of the gastric biopsy specimens rather than through targeted testing for leishmaniasis. This finding highlights the importance of meticulous pathological evaluation in immunocompromised patients presenting with atypical gastrointestinal lesions, as careful examination of routinely processed biopsy specimens may provide the first clue to an otherwise unsuspected diagnosis.

HLH is a rare but life-threatening hyperinflammatory syndrome driven by uncontrolled activation of cytotoxic T lymphocytes and macrophages, resulting in excessive cytokine release and multiorgan dysfunction. HLH may be primary (genetic) or secondary, with infections being the most common triggers in adults^[7,9,26].

HLH is diagnosed using the HLH-2004 criteria proposed by the Histiocyte Society, which require either a pathogenic HLH-associated genetic mutation or fulfillment of at least five of eight criteria: fever, splenomegaly, cytopenias involving ≥2 blood cell lineages, hypertriglyceridemia and/or hypofibrinogenemia, hemophagocytosis in tissue samples, low or absent natural killer cell activity, hyperferritinemia, and elevated sCD25 levels^[7].

Clinically, HLH presents with persistent high-grade fever, hepatosplenomegaly, lymphadenopathy, and rapid systemic deterioration, while laboratory abnormalities typically include pancytopenia, markedly elevated serum ferritin

levels, hypertriglyceridemia, coagulopathy, transaminitis, and cholestatic liver dysfunction with rising bilirubin levels. Cholestasis in HLH is attributed to cytokine-mediated hepatocellular injury, sinusoidal infiltration by activated macrophages, and hepatic hemophagocytosis and may be a marker of severe disease^[8]. In PLHIV, HLH often follows a more fulminant course because of immune dysregulation and delayed pathogen clearance^[27].

VL is a recognized but uncommon infectious trigger of secondary HLH in adults.

Diagnosis is particularly challenging in VL–HIV coinfection because of overlapping clinical and laboratory features with HLH. This overlap may lead to delayed recognition of VL and the inappropriate initiation of aggressive immunosuppressive therapy without antiparasitic treatment, potentially resulting in fatal outcomes^[9].

In our patient, the diagnosis of secondary HLH was established based on the fulfillment of six HLH-2004 criteria: persistent fever, splenomegaly, pancytopenia, hypertriglyceridemia, marked hyperferritinemia, and hemophagocytosis on bone marrow examination. The precipitating trigger was VL in the setting of advanced HIV infection. The patient also developed progressive conjugated hyperbilirubinemia with a cholestatic pattern, consistent with hepatic involvement in HLH.

Management of VL in PLHIV requires a combined approach addressing both infections. International guidelines recommend initiating or optimizing ART as soon as patients can tolerate therapy, as immune reconstitution improves survival and reduces relapse rates^[16,13].

Reinitiation of ART in patients with VL–HIV coinfection may occasionally be associated with immune reconstitution inflammatory syndrome (IRIS), manifesting as paradoxical worsening of previously diagnosed leishmaniasis or unmasking of subclinical disease. Although IRIS was not observed in our patient, awareness of this phenomenon is important when restarting ART in severely immunosuppressed individuals with VL^[4,13].

Among antileishmanial agents, liposomal amphotericin B is preferred because of its superior efficacy and lower nephrotoxicity compared with amphotericin B deoxycholate. In accordance with current guidelines, amphotericin B deoxycholate remains an acceptable alternative when liposomal formulations are unaffordable, provided that close monitoring is ensured. Other alternatives include miltefosine and pentavalent antimonial agents such as meglumine antimoniate^[13].

In cases of VL-associated HLH, prompt initiation of targeted antileishmanial therapy is the cornerstone of management.

Adjunctive low-dose corticosteroids may be beneficial in controlling the cytokine storm and preventing organ failure in severe cases^[28].

More aggressive HLH-directed regimens are generally reserved for refractory disease because of concerns that they may worsen the underlying infection^[28].

Secondary prophylaxis is recommended for all patients with CD4 counts <200 cells/ μ L because of the high risk of relapse. Discontinuation should be considered only after sustained immune recovery, as evidenced by a CD4 count exceeding 350 cells/ μ L or an undetectable viral load for at least 6 months^[3,13].

Our patient was successfully treated with amphotericin B deoxycholate (1 mg/kg/day for 30 days), along with continuation of ART and a short course of low-dose corticosteroids for HLH. Despite electrolyte disturbances, notably hypokalemia, treatment was completed successfully with careful monitoring. The patient demonstrated rapid clinical and laboratory improvement, with resolution of fever, cytopenias, hepatosplenomegaly, and liver dysfunction, supporting previous reports that successful treatment of VL may lead to the resolution of secondary HLH without the need for intensive HLH-directed immunochemotherapy in many cases^[9,10].

Secondary prophylaxis with monthly amphotericin B deoxycholate (1 mg/kg) was instituted as recommended by the World Health Organization and National Institutes of Health guidelines^[16,13].

This case highlights the complex diagnostic and therapeutic challenges posed by the coexistence of advanced HIV infection, disseminated VL, and secondary HLH. In endemic settings, VL and HLH should be considered in PLHIV who present with prolonged fever, pancytopenia, and organomegaly, even when serological tests such as rK39 are negative. Atypical manifestations, including gastrointestinal involvement, and the substantial clinical overlap among HIV infection, VL, and HLH can delay diagnosis, underscoring the importance of maintaining a high index of suspicion and pursuing early tissue-based diagnostic confirmation when indicated. Prompt initiation of antileishmanial therapy is critical and can be lifesaving. This case also illustrates the challenges associated with limited access to liposomal amphotericin B, which may necessitate the use of amphotericin B deoxycholate and increase the risk of treatment-related adverse effects, such as persistent hypokalemia. Furthermore, poor adherence to ART because of migration and socioeconomic barriers can exacerbate immunosuppression, increase disease severity, and predispose patients to relapse. Strengthening access to diagnostic facilities, affordable treatment options, and uninterrupted HIV care is essential to improving outcomes in this vulnerable population.

Ethics

Informed Consent: Written informed consent for publication was obtained from the patient and his son.

Footnotes

Authorship Contributions

Concept: G.S.S., U.S., Design: U.S., S.K., Data Collection or Processing: U.S., Analysis or Interpretation: G.S.S., S.K., Literature Search: U.S., N.O., Writing: U.S., N.O.

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