



CASE REPORT

Hemophagocytic Lymphohistiocytosis With Severe Infection and Gastrointestinal Bleeding

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Abstract

A 19-year-old male presented with secondary hemophagocytic lymphohistiocytosis, persistent fever, abdominal pain and melaena. His clinical course was complicated by gram-negative sepsis (*Klebsiella* NDM-positive and *E coli*), *Clostridioides difficile* infection, cytomegalovirus (CMV) pneumonia and *Elizabethkingia anophelis* infection, leading to multiorgan dysfunction syndrome and massive gastrointestinal bleeding. Diagnosis was confirmed via bone marrow biopsy and relevant imaging. Management included HLH-2004 immunochemotherapy, broad-spectrum antimicrobials, ICU support and blood transfusions. This report underscores the diagnostic difficulty, rapid deterioration and high mortality risk when HLH coexists with opportunistic infections.

Key words: Lymphohistiocytosis, hemophagocytic; *Elizabethkingia anophelis*; Pneumonia, viral; Cytomegalovirus; Gastrointestinal haemorrhage.

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Citation:

Rajendhiran R, Thomas SA, Chenthilkumar K, Sailaja BK, Kothandaramanujam RM, Harikrishnan MR. Hemophagocytic lymphohistiocytosis with severe infection and gastrointestinal bleeding. Scr Med. 2026 Jul-Aug;57(4):963-5.

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Received: 14 October 2025
Revision received: 8 December 2025
Accepted: 8 December 2025

Introduction

Hemophagocytic lymphohistiocytosis (HLH) is a severe hyperinflammatory condition characterised by uncontrolled activation of lymphocytes and macrophages, resulting in cytokine storm and multiorgan tissue injury.¹ Secondary HLH may be triggered by infections, malignancies, or autoimmune disorders.² The disease is rare, frequently presents non-specifically and is associated with high mortality if not recognised early.³ This case highlights the diagnostic and therapeutic challenges of managing HLH complicated by multiple opportunistic infections and gastrointestinal bleeding.

Case history

A 19-year-old male presented with a two-month history of fever, abdominal pain, weight loss and melaena. The patient had no known comorbidities or autoimmune diseases. He was diagnosed at an external hospital with secondary HLH based on bone marrow aspiration and biopsy findings and treatment was initiated according to the HLH-2004 protocol. Physical examination on admission showed pallor, tachycardia and hepatosplenomegaly.

Laboratory investigations revealed: haemoglobin: 6.2 g/dL; Platelet count: $120 \times 10^9 / L$; total leukocyte counts: $30 \times 10^9 / L$; ferritin: 10.154 ng/mL; triglycerides: 337 mg/dL; fibrinogen: 783 mg/dL. Positron emission tomography - computed tomography (PET-CT) ruled out malignancy.

During hospitalisation, he developed massive gastrointestinal bleeding, with haemoglobin dropping to 4.1 g/dL, requiring multiple transfusions. Upper GI endoscopy revealed severe esophagitis and gastric erosions. Patient later became hypotensive and required intensive care unit (ICU) admission with inotropic support. Blood cultures grew *Klebsiella pneumoniae* (NDM-positive) and *Escherichia coli*, prompting broad-spectrum antibiotics. Bronchoalveolar lavage (BAL) analysis revealed *Elizabethkingia anophelis* and cytomegalovirus (CMV) positivity.

The patient was treated according to the HLH-2004 protocol using dexamethasone and etoposide. He required endotracheal intubation and mechanical ventilation due to neurological decline and a Glasgow Coma Scale of 5/15. He received ganciclovir, vancomycin, minocycline, caspofungin, and voriconazole. Stool tests confirmed *Clostridioides difficile* infection, treated with vancomycin and metronidazole. Despite aggressive critical care and immunochemotherapy, his condition deteriorated due to persistent multiorgan dysfunction.

Discussion

Secondary hemophagocytic lymphohistiocytosis is a critical condition requiring prompt diagnosis and immunochemotherapy. HLH is rare, with an estimated incidence of 1–2 per 100,000 population. Adult mortality ranges from 40–70 %, especially when complicated by sepsis, organ dysfunction or gastrointestinal bleeding.

The HLH-2004 guidelines require either a compatible molecular diagnosis or fulfilment of ≥ 5 of the following 8 criteria:

1. Fever
2. Splenomegaly
3. Cytopenia in ≥ 2 lineages
4. Hypertriglyceridemia and/or hypofibrinogenemia
5. Hemophagocytosis in bone marrow or organs
6. Low/absent NK-cell activity
7. Ferritin ≥ 500 ng/mL
8. Elevated soluble CD25 ≥ 2400 U/mL

Differential diagnoses include severe sepsis, lymphoma, tuberculosis, macrophage activation syndrome and autoimmune disorders. HLH causes profound immune dysregulation, increasing susceptibility to opportunistic pathogens. Similar reports describe HLH associated with CMV reactivation, multidrug-resistant gram-negative sepsis and invasive fungal disease. Gastrointestinal bleeding further worsens prognosis due to mucosal disruption and coagulopathy.⁴

Standard HLH therapy includes corticosteroids (dexamethasone) and etoposide to control cytokine activation and eliminate hyperstimulated lymphocytes. Cyclosporine may be added in evolving disease and intravenous immunoglobulin (IVIG) is often used for immunomodulation. Refractory cases may benefit from anakinra or ruxolitinib. Hematopoietic stem cell transplantation is an option for persistent or familial HLH.⁵ Multidisciplinary management and aggressive infection control strategies are crucial, as illustrated in this case complicated by multidrug-resistant organisms, CMV and *Elizabethkingia anophelis*.

Conclusion

Secondary HLH complicated by severe opportunistic infections and gastrointestinal bleeding presents major diagnostic and therapeutic challenges. Early recognition, protocol-based immunochemotherapy and aggressive infection control are essential for improving outcomes in these critically ill patients.

Ethics

Our institution does not require ethics approval for reporting individual cases or case series. A written informed consent for anonymised patient information to be published in this article was obtained from the patient next of kin.

Acknowledgement

None.

Conflicts of interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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