

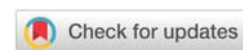


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## Case Report

# Fulminant Hemophagocytic Lymphohistiocytosis Secondary to Miliary Tuberculosis: A Fatal Case Report

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## Abstract

Hemophagocytic lymphohistiocytosis (HLH) is a hyper-inflammatory syndrome driven by uncontrolled immune activation. Although Epstein-Barr virus is the prototypical infectious trigger, disseminated tuberculosis (TB) is an increasingly recognised cause, especially in endemic regions. We describe a 49-year-old woman who presented with miliary TB complicated by secondary HLH and rapidly progressive multiorgan dysfunction. Despite prompt anti-tubercular therapy (ATT) and HLH-directed immunosuppression, she died within 48 hours of intensive-care admission. The case underlines the need for early marrow evaluation and simultaneous initiation of ATT and HLH-specific therapy when TB-HLH is suspected.

## Introduction

Secondary HLH is characterised by fever, cytopenias, organomegaly, hyper-ferritinaemia and a cytokine storm that can culminate in fatal multiorgan failure if untreated [1]. TB-associated HLH is a rare but serious complication of disseminated tuberculosis [2,3]. Distinguishing HLH from severe disseminated TB is challenging because the two entities share systemic inflammatory features [2,4]. Early recognition and concurrent management of both conditions offer the best probability of survival [2,4].

## Case presentation

A 49-year-old pre-menopausal woman with no past medical history presented with a six-month history of progressive weight loss, generalized weakness and anasarca, followed by two months of low-grade intermittent fever. She denied cough, hemoptysis, jaundice, TB contact or high-risk behaviour.

On arrival she was cachectic, afebrile, hypotensive (100/60 mmHg) and tachycardic (112 beats/min). Examination revealed severe pallor, mild icterus, bilateral pedal oedema, massive

ascites, moderate splenomegaly and diminished breath sounds bilaterally; there was no lymphadenopathy or focal neurological deficit. Oxygen saturation was 90% on room air.

Initial laboratory tests showed pancytopenia (haemoglobin 5 g/dL, leukocytes  $4 \times 10^9/L$ , platelets  $6 \times 10^9/L$ ), coagulopathy (INR 2.5), hyper-ferritinaemia (8,700 ng/mL), hyper-triglyceridaemia (389 mg/dL) and elevated C-reactive protein (127 mg/L). Liver function tests demonstrated direct hyperbilirubinaemia (4.5 mg/dL) with cholestatic enzymes markedly raised. Chest radiography revealed bilateral miliary nodules with minimal pleural effusion, while abdominal ultrasonography confirmed gross ascites and splenomegaly. F-18 FDG-PET/CT showed no hyper-metabolic lymphadenopathy or focal lesions.

Bone-marrow aspiration performed on day 1 demonstrated florid hemophagocytosis with markedly increased histiocytes; mycobacterial cultures and Ziehl-Neelsen staining were negative at that time. Ascitic fluid analysis was exudative but sterile. Based on HLH-2004 criteria, she fulfilled five diagnostic parameters, establishing secondary HLH likely precipitated by disseminated TB.

## Management and clinical course

The patient was transferred to the intensive-care unit where a modified ATT regimen—ethambutol, pyrazinamide, levofloxacin and streptomycin—was initiated; isoniazid and rifampicin were deferred because of hepatobiliary dysfunction. Concurrently, HLH-94 therapy with high-dose intravenous dexamethasone, etoposide (150 mg/m<sup>2</sup> twice weekly) and intravenous immunoglobulin was commenced. Broad-spectrum antibiotics and an echinocandin were added empirically.

Despite aggressive supportive care—including blood-component transfusion, invasive mechanical ventilation, continuous renal-replacement therapy and escalating vasopressors—her condition deteriorated rapidly. Serum ferritin rose to 83,000 ng/mL, and refractory shock ensued. The patient died 48 hours after admission from multiorgan failure.

## Discussion

This case exemplifies the lethal synergy between disseminated TB and HLH, even in an immunocompetent adult [5]. The overlapping clinical and laboratory features often delay recognition; however, a ferritin level >10,000 ng/mL, profound cytopenias and hemophagocytosis on marrow aspirate are strong clues to HLH even when microbiological confirmation of TB is pending [2].

Timely ATT is pivotal: survival falls precipitously when therapy is delayed [2,4]. Immunomodulation with dexamethasone and etoposide is recommended when organ failure or persistent hyper-inflammation is present [1]. Nonetheless, prognosis remains poor in patients who present late with advanced multiorgan dysfunction. Extreme hyper-ferritinaemia (>50,000 ng/mL) and early requirement for

mechanical ventilation portend virtually uniform fatality, underscoring the urgency of earlier diagnosis in resource-limited settings [3].

## Conclusion

HLH should be considered in any patient from TB-endemic areas who presents with unexplained pancytopenia, organomegaly, soaring ferritin and a sepsis-like picture. Simultaneous initiation of ATT and HLH-directed therapy, coupled with aggressive organ support, offers the only realistic chance of survival.

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