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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 × 10⁹/L, platelets 6 × 10⁹/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.

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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^2 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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