Diagnosing Disseminated Tuberculosis with HLH in the Context of Lymphoma-Like Presentation

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INTRODUCTION

Hemophagocytic lymphohistiocytosis (HLH) is a severe condition marked by uncontrolled activation of macrophages and immune cells, leading to a cytokine storm and damage to multiple organs.Tuberculosis, though rare(3%), is a significant cause of secondary HLH, commonly presenting with non specific symptoms. Given the overlap in symptoms and the potential for confusion with lymphoma especially in critically ill patients, it's crucial to consider tuberculosis as a cause of HLH to ensure timely diagnosis and treatment, particularly in regions with high tuberculosis prevalence

"TB-triggered HLH is a rare, deadly storm requiring rapid diagnosis and synchronized treatment.

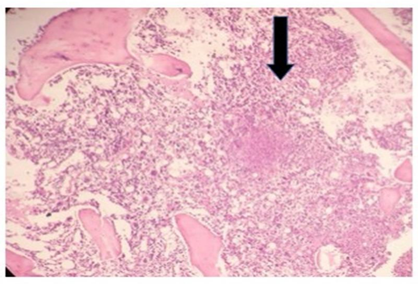
CASE PRESENTATION

A 14yr/ Male with history of old treated cervical lymph node tuberculosis presented with c/o:

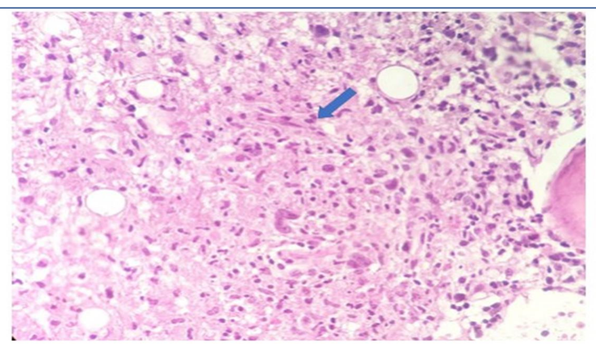
1. Fever, generalised weakness for 1 month
2. Progressive yellowish discolouration of skin and sclera with abdominal distension associated with vomiting for 20 days
3. Blackish discolouration of stools with blood urine for 2 days.

His vitals on presentation were Bp=80/50, PR= 112, RR=22/min with saturation of 86% on room air.

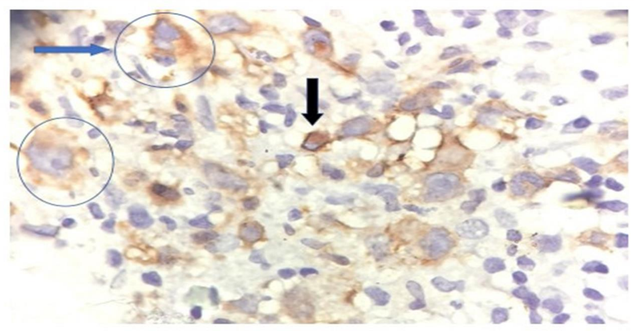
On Examination he was febrile with significant pallor and scleral icterus and had palpable lymphadenopathy in cervical region with tense ascitis with no palpable hepatosplenomegaly, bilateral Coarse crests on lung ascultation.



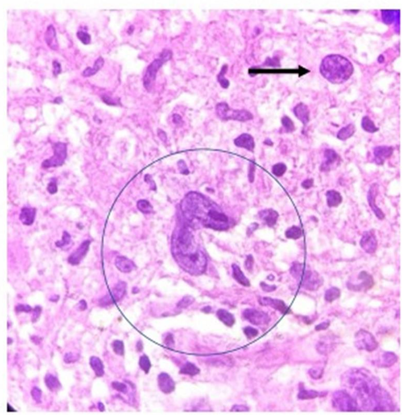
Bone marrow biopsy revealing epithelioid cell granuloma (arrow)



RS cells in a Necrotic Background with Histiocytes and Scattered Epitheloid cells



IHC : RS cells revealing CD 30 Positivity , DOT like pattern (ARROWS) , Membranous Pattern– Circle



Reed Sternberg cells(binucleated) with prominent eosinophilic nucleolus – circle Mononuclear RS cells also seen (arrow) H&E 1000X

PARAMETERS	VALUE
HB (g/dL)	4.6
TLC (x 10^3 /microL)	1100
PLATELET (x 10^3 /microL)	53000
ESR (mm at the end of 1hr)	275
TBIL (mg/dL)	1.8
DBIL (mg/dL)	1.5
AST (IU/L)	256
ALT (IU/L)	277
ALP (IU/L)	364
LDH (IU/L)	696
TRIGLYCERIDES (mg/dL)	541
TOTAL CHOLESTEROL (mg/dL)	150
S.Ferritin (microgram/L)	>5000
TIBC	233
S.IRON (microgram/dL)	16
HSV, CMV, EBV	Negative by PCR

Ultrasound whole abdomen/PanCT/PetCt : generalised lymphadenopathy and hepatosplenomegly with multiple hypodense lesions in liver and spleen, modular opacities in bilateral lung fields likely tuberculosis but possibility of lymphoma cannot be ruled out.

Bone marrow biopsy : possibility of granulomatous inflammation with biochemical correlation for HLH. **Pretracheal Lymph node biopsy** done under endoscopic ultrasound : necrotising granulomatous lymphadenitis. AFB/ CBNAAT were negative on all biopsies and sputum.

MANAGEMENT

Patient was managed symptomatically with blood product and Inotropes. Steroid pulse was given I/v/o HLH along with Att was initially hepatic modified later discharged on full dose of ATT.

Patient improved symptomatically with biochemical parameters improved to baseline and reduction in size of palpable lymph nodes.

DISSCUSION:

HLH is a characterized by a faulty immune response against an intracellular pathogen.The dysfunction of cytotoxic T cells and NK cells contribute to the ineffective clearance of antigens resulting the prolonged inflammatory response. This eventually leads to hemophagocytosis, hypercytokinemia, and macrophage hyperactivity, which cause organomegaly and fever. In HLH, cytokine levels of IFN-γ, TNF-α, GM-CSF, and IL-18 increases resulting in bi/pancytopenia due to the suppression of hematopoiesis and the increased apoptosis of cells. TNF-α and IFN-γ inhibit lipoprotein lipase, leading to hypertriglyceridemia. MTB is an intracellular pathogen that can exacerbate the faults in the immune response mechanism leading to HLH in susceptible individuals. The increased levels of IFN-γ, M-CSF, and TNF-α in patients with tuberculosis support this hypothesis.

Conclusion:

TB might rarely be complicated by HLH, and the diagnosis is often challenging to the clinician. The clinician should consider HLH as an important differential diagnosis of TB patients with pancytopenia, organomegaly, and coagulopathy. Hscore and HLH-2004 are the main diagnostic scoring systems for HLH. Any delay in the definitive therapy will lead to increase morbidity and mortality. Corticosteroids and IVIG have shown to be effective in the treatment of severe TB-HLH.

Reference:
1.Padhi S, Ravichandran K, Sahoo J, Varghese RG, Basheer A. Hemophagocytic lymphohistiocytosis: An unusual complication in disseminated Mycobacterium tuberculosis. Lung India. 2015 Nov-Dec;32(6):593-601. doi: 10.4103/0970-2113.168100. PMID: 26664166; PMCID: PMC4663863.
2. Abdulrahman F., Al-Mashdali, Musaed, S. Al Samawi. Disseminated tuberculosis complicated by hemophagocytic lymphohistiocytosis in an immunocompetent adult with favorable outcomes: A case report. Volume 22