ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 06 | June - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

WHEN INFECTIONS IGNITE THE IMMUNE SYSTEM: A CASE REPORT OF SEPSIS-HLH OVERLAP SYNDROME

Internal Medicine

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ABSTRACT

Hemophagocytic lymphohistiocytosis (HLH) is an immune-mediated, life-threatening condition caused by dysfunction of natural killer (NK) and cytotoxic T-cells. While predominantly recognized in pediatric populations, secondary HLH is increasingly seen in adolescents and adults. Infections can trigger a hyperinflammatory response, leading to sepsis-HLH overlap syndrome (SHLHOS). We present the case of a 53-year-old woman who developed SHLHOS, presenting with fever, loin-to-groin pain, and loose stools. Initial investigations revealed anemia, hyponatremia, leukocytosis, and elevated creatinine. Imaging confirmed left-sided hydronephrosis due to a ureteric calculus, managed with bilateral DJ stenting. Elevated ferritin, liver enzymes, and triglycerides raised suspicion for HLH, prompting corticosteroid therapy, resulting in complete recovery.

KEYWORDS

INTRODUCTION

Hemophagocytic lymphohistiocytosis (HLH) is a syndrome of excessive immune activation resulting in cytokine-mediated bone marrow suppression and hemophagocytosis in the bone marrow and liver.[1] It can be classified as primary (genetic) or secondary (acquired). Genetic HLH involves mutations in genes regulating cytotoxic function (e.g., PRF1, UNC13D, STXBP2, STX11) and others linked to pigment abnormalities or X-linked lympho-proliferative diseases.

Secondary HLH is commonly triggered by infections (especially Epstein-Barr virus), malignancies (e.g., T-cell lymphoma), or autoimmune conditions. Clinical manifestations include fever, constitutional symptoms, hepatosplenomegaly, neurological impairment, and multiorgan dysfunction.[1]

Diagnostic Criteria for HLH (HLH-2004):[2]
Diagnosis requires a molecular confirmation or fulfillment of 5 of the following 8 criteria:

- Fever
- Cytopenia affecting ≥2 cell lines
- Splenomegaly
- Hypertriglyceridemia and/or hypofibrinogenemia
- Ferritin >500 ng/mL
- Elevated soluble IL-2 receptor (sCD25)
- Hemophagocytosis in bone marrow/spleen/lymph nodes
- Low or absent NK cell activity

Sepsis is defined as life-threatening organ dysfunction due to a dysregulated host response to infection. It involves endothelial injury, increased vascular permeability, and coagulopathies, potentially progressing to multiorgan failure.

Case Presentation

A 53-year-old woman with a history of type 2 diabetes mellitus, hypertension, dyslipidemia, and diabetic nephropathy presented with a one-week history of fever and loin-to-groin pain, along with one day of loose stools and vomiting. She denied chest pain, dyspnea, dysuria, or sick contacts. Clinical examination revealed pallor, tachycardia (130 bpm), blood pressure of 160/60 mmHg, and low-grade fever (99.7°F).

Initial laboratory results showed:

- Hemoglobin: 10.8 g/dL
- WBC: 17.6 ×10³/µL
- Platelets: 456 ×10³/µL
- Sodium: 122 mmol/L
- Potassium: 5.7 mmol/L
- Creatinine: 1.3 mg/dL
- CRP: 94.3 mg/L

She was started on intravenous ceftriaxone and metronidazole. Ultrasound revealed left mild hydronephrosis due to a ureteric stone, confirmed by CT-KUB. Later, she developed central chest pain, hypotension, and electrolyte imbalance, necessitating transfer to the ICU. Echocardiography showed apical hypokinesis and mild left ventricular dysfunction. Despite fluid resuscitation, she deteriorated and required dual ionotropes. A diagnosis of septic cardiomyopathy was made, and antibiotics were escalated to intravenous meropenem.

The patient subsequently underwent bilateral DJ stenting. She developed hepatic dysfunction (shock liver), progressive metabolic acidosis, and worsening renal function. Cultures from blood and urine yielded E. coli sensitive to meropenem.

Additional investigations showed:

- Ferritin: 8836 ng/mL
- LDH: 6017 U/L
- Troponin I: >50 ng/mL
- Thrombocytopenia and anemia

These findings were supportive of a diagnosis of SHLHOS. The patient was managed with broad-spectrum antibiotics, corticosteroids, diuretics, thiamine, ursodeoxycholic acid, and supportive care. She showed gradual improvement by day five and was discharged in a stable condition on 09/02/23.

Date Inv	31/01/23	01/02/23	02/02/23	03/02/23	04/02/23	06/02/23
Hb	10.8	8.1	7.8	9.1	9.8	10.2
PCV	32.4	24.6	23.6	27.5	29.2	30.9
TLC	17.6	15.2	25.9	25.4	31	41.4
PC	456	288	52	34	69	116
S. Urea	35	33	69	102	104	68
S. Creatinine	1.3	1.8	2.5	2.4	2.0	1.3
S. Na	122	121	122	122	130	
S. K	5.7	4.3	4.4	3.9	2.9	
S. Albumin		1.9	2.1	2.3	2.4	
S. Globulin		3.2	3.6	3.9	3.9	
SGOT		48	6127	6292	2307	255
SGPT		41	2959	4554	3021	1376
TG			268		208	
S. CPK			1418			
S. LDH			6017	4721		
CRP	94.3	248.7		462	317.2	
FERRITIN			8836		3079.5	
Pro Cal		69.6				
PT/INR	16.06/1.16					

DISCUSSION

Sepsis and HLH, while distinct syndromes, may present with overlapping clinical and laboratory features, complicating diagnosis and treatment. HLH is characterized by immune overactivation and cytokine storm, which may be triggered or exacerbated by sepsis. Conversely, severe sepsis may induce HLH in susceptible individuals.

This case illustrates the diagnostic challenge and importance of early recognition of SHLHOS. Despite initial deterioration, the patient responded well to prompt, aggressive management including immunosuppressive therapy and supportive care. High ferritin levels, cytopenias, elevated liver enzymes, and multiorgan involvement were key indicators.

The prognosis for SHLHOS remains guarded, and awareness is crucial to initiate timely therapy. Steroids and supportive care remain cornerstones of treatment, while IVIG or immunosuppressants may be considered in refractory cases.[3][4]

CONCLUSION

Sepsis-HLH overlap syndrome is a critical, under-recognized condition with high mortality. Early identification through clinical suspicion and laboratory markers is vital. Multidisciplinary management, including infectious disease and critical care teams, is essential for improving patient outcomes.

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