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# Rare Case of Post-Infectitous Hemophagocytic Lymphohistiocytosis resenting as Panniculitis & Multi-Organ Dysfunction Syndrome

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ABSTRACT

Hemophagocytic lymphohistiocytosis (HLH) is a rare, life-threatening hyperinflammatory syndrome caused by excessive activation of the immune system. It often mimics severe infections or sepsis and poses a significant diagnostic challenge. We present a rare case of HLH in a 40-year-old female with an unusual presentation involving panniculitis, jaundice, and multi-organ dysfunction. Prompt recognition of persistent cytopenias and systemic inflammation led to the diagnosis through bone marrow biopsy. The patient showed significant improvement following corticosteroid therapy. This case highlights the importance of maintaining a high index of suspicion for HLH in patients with prolonged systemic inflammation and cytopenias.



## INTRODUCTION

Hemophagocytic lymphohistiocytosis (HLH) is a rare and potentially fatal syndrome characterized by excessive immune activation, cytokine storm, and hemophagocytosis. HLH may be familial (primary) or secondary to infections, autoimmune diseases, or malignancies. The secondary form can follow infections of even unknown significance, and may present as systemic inflammatory response syndrome (SIRS), sepsis, or multi-organ dysfunction syndrome (MODS). Diagnosing HLH is often delayed due to its nonspecific presentation, especially when initial symptoms mimic common infectious etiologies. We report a case of post-infectious secondary HLH that presents with systemic signs including panniculitis and septic shock.

## Case History

A 32-year-old female presented to the emergency department in a conscious and oriented state with complaints of three episodes of high-grade, intermittent fever without associated chills, which temporarily subsided with medications provided by a local practitioner. She also developed a progressively enlarging abdominal wound over the past week. Associated symptoms included yellowish discoloration of the skin and mucous membranes and markedly reduced urine output (~100 mL in 24 hours) over five days. Three weeks prior, she had experienced an episode of nausea, vomiting, and diarrhea, which resolved with symptomatic treatment.

On examination, the patient was hypotensive and tachycardic, requiring supplemental oxygen. Clinical findings included pallor, icterus, bilateral pedal edema, raised jugular venous pressure, fine basal crepitations on chest auscultation, and palpable splenomegaly.

Initial laboratory work-up revealed elevated serum creatinine, metabolic acidosis, anemia, and thrombocytopenia. A nephrology consult was obtained, and the patient was initiated on hemodialysis along with blood transfusions. Surgery consultation was also taken and was then planned for local debridement by the surgical team due to extensive panniculitis with daily dressing to be done post procedure. A provisional diagnosis of septic acute kidney injury (AKI) with multi-organ dysfunction syndrome (MODS) was made, and appropriate supportive treatment was initiated. The patient showed gradual clinical improvement with stabilization of renal function and increased urine output.

However, persistent anemia and thrombocytopenia were noted despite multiple blood transfusions and two doses of darbepoetin. Hematology consultation was then obtained, and a bone marrow biopsy was performed which revealed features suggestive of hemophagocytosis.

## Investigations

| Test | Result | Comments |
|---|---|---|
| Hemoglobin | 6.8 g/dL | Low |
| Leukocytes | 24,200 /µL | 90% Neutrophils |
| Platelets | 48,000 /µL | Thrombocytopenia |
| Blood Smear | – | Microcytic hypochromic |
| Ferritin | 469 ng/mL | Normal to elevated |
| D-Dimer | 6.9 µg/mL | Elevated |
| Serum LDH | 264 U/L | Slightly elevated |
| Reticulocyte Count | 2.10% | Mildly increased |
| DCT / IDCT | Negative | |
| Fibrinogen | 106 mg/dL | Low (hypofibrinogenemia) |
| ESR | 120 mm/hr | Markedly elevated |
| CRP (Quantitative) | 83.7 mg/L | Elevated |
| Procalcitonin | 25.3 ng/mL | Very high (suggestive of sepsis) |

| Liver Function Tests | | |
|---|---|---|
| ALT | 26 | U/L |
| AST | 21 | U/L |
| Sr. Bilirubin Total | 7.6 | mg/dL (elevated) |
| Sr. Bilirubin Direct | 4.9 | mg/dL (elevated) |
| Sr. Bilirubin Indirect | 2.7 | mg/dL (elevated) |

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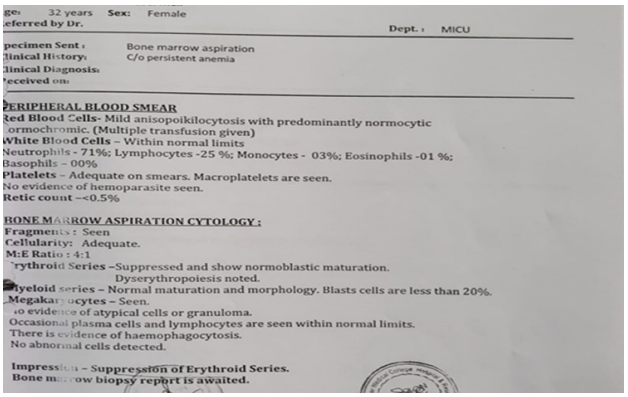
| Renal Function Tests | | |
|---|---|---|
| Blood Urea | 167 | mg/dL (elevated) |
| Serum Creatinine | 4.9 | mg/dL (elevated) |

| Other Blood Chemistry | | |
|---|---|---|
| Sr. Calcium | 7 | mg/dL (low) |
| Sr. Uric Acid | 11 | mg/dL (elevated) |

| Serum Electrolytes | | |
|---|---|---|
| Sodium / Potassium / Chloride | 126 / 4.5 / 103 | mEq/L (hyponatremia) |

| Coagulation Profile | | |
|---|---|---|
| ANA | Negative | |
| PT / INR | 31 sec / 2.2 | Prolonged |
| PTT Ratio | 2.8 | 98.0 / 35.0 sec (prolonged) |

| Infectious Panel | |
|---|---|
| HCV / HBV / HIV TriDot | Non-Reactive |
| Hepatitis A / E IgM | Negative |
| Dengue-NS1 (Rapid) | Non-Reactive |
| Dengue-IgM (Rapid) | Non-Reactive |
| Leptospirosis IgM | Negative |



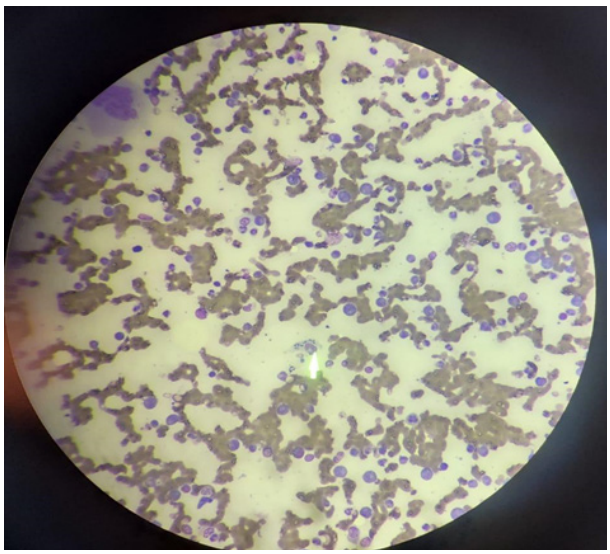
ge: 32 years Sex: Female
eferred by Dr. Dept. : MICU

pecimen Sent : Bone marrow aspiration
linical History: C/o persistent anemia
linical Diagnosis:
eceived on:

**PERIPHERAL BLOOD SMEAR**
**ed Blood Cells**- Mild anisopoikilocytosis with predominantly normocytic ormochromic. (Multiple transfusion given)
**White Blood Cells** – Within normal limits
Neutrophils - 71%; Lymphocytes -25 %; Monocytes - 03%; Eosinophils -01 %; Basophils – 00%
**Platelets** – Adequate on smears. Macroplatelets are seen.
No evidence of hemoparasite seen.
**Retic count** –<0.5%

**BONE MARROW ASPIRATION CYTOLOGY :**
Fragments : Seen
Cellularity: Adequate.
M:E Ratio : 4:1
**rythroid Series** –Suppressed and show normoblastic maturation. Dyserythropoiesis noted.
**Myeloid series** – Normal maturation and morphology. Blasts cells are less than 20%.
**Megakaryocytes** – Seen.
No evidence of atypical cells or granuloma.
Occasional plasma cells and lymphocytes are seen within normal limits.
There is evidence of haemophagocytosis.
No abnormal cells detected.

**Impression – Suppression of Erythroid Series.**
**Bone marrow biopsy report is awaited.**



**Bone Marrow Aspiration & Microscope Image: Evidence of Hemophagocytosis and Suppression of Erythroid Series.**

## Diagnostic Criteria

The diagnosis of Hemophagocytic Lymphohistiocytosis (HLH) is based on the HLH-2004 diagnostic guidelines, which require the fulfillment of **at least 5 out of the following 8 criteria**:

1. **Fever**
2. **Splenomegaly**
3. **Cytopenias** affecting at least two of the following lineages in peripheral blood:
   - Hemoglobin <9 g/dL
   - Platelets <100,000/μL
   - Neutrophils <1,000/μL
4. **Hypertriglyceridemia (fasting triglycerides ≥265 mg/dL) and/or hypofibrinogenemia (fibrinogen ≤150 mg/dL)**
5. **Hemophagocytosis in bone marrow, spleen, or lymph nodes**
6. **Low or absent NK cell activity**
7. **Hyperferritinemia (ferritin >500 μg/L)**
8. **Elevated soluble CD25 (soluble interleukin-2 receptor α) >2400 IU/mL**

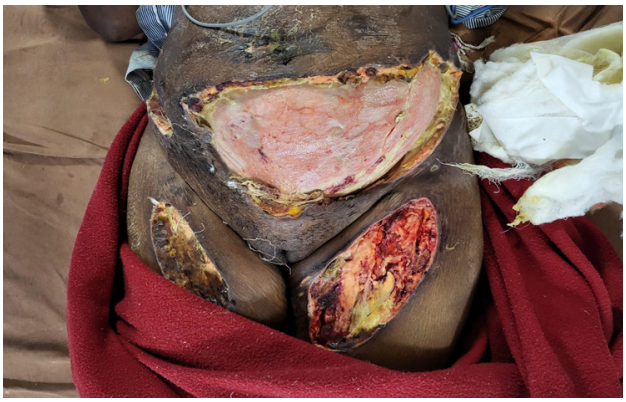


**Figure showing wound after debridement**

## Treatment

The patient was initially managed for suspected sepsis with acute kidney injury (AKI) with multi-organ dysfunction syndrome (MODS) based on clinical presentation and laboratory findings. She was started on broad-spectrum antibiotics, supportive therapy, and underwent hemodialysis on alternate days for the first week. Following one week of treatment, the patient demonstrated significant clinical improvement, with adequate urine output and a trend toward normalization of renal function tests. She underwent two surgical debridement procedures for the abdominal ulcer, during which all necrotic tissue was removed, and healthy granulation tissue was observed.

As liver and renal function tests continued to improve, the patient became hemodynamically stable and was gradually weaned off inotropic support. However, anemia and thrombocytopenia persisted despite multiple transfusions and administration of darbepoetin injections.

Due to this lack of hematologic recovery, a bone marrow biopsy was performed, which revealed evidence of hemophagocytosis. The patient fulfilled the diagnostic criteria for hemophagocytic lymphohistiocytosis (HLH) and was promptly initiated on high-dose corticosteroid therapy. Following steroid initiation, her clinical condition improved substantially. After undergoing multiple successful flap surgeries for wound coverage, the patient was discharged in stable condition.

The goal of therapy is to suppress life threatening inflammation by destroying immune cells. Induction therapy based on HLH 94 protocol consists of a series of weekly treatments with dexamethasone and etoposide. After induction, patients who are recovering are weaned off therapy, while those who are not improving are continued on therapy as a bridge to allogeneic hematopoietic cell transplantation (HCT).

## Discussion

HLH is a rare hyperinflammatory syndrome that can masquerade as other systemic illnesses. In adults, secondary HLH is more common and

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frequently associated with infections or malignancies. The condition is associated with high mortality if unrecognized or untreated.In this case, the patient presented with features typical of sepsis and MODS, including pancytopenia, liver dysfunction, renal failure, coagulopathy, and skin ulcers. The persistence of cytopenias despite clinical improvement prompted bone marrow examination, revealing classical hemophagocytosis.Though the initial trigger infection was not identified, this case represents **post-infectious HLH**. Notably, **panniculitis as a presenting feature of HLH is rare** and poses a diagnostic challenge. Prompt recognition and treatment with corticosteroids led to favorable outcomes, underlining the need for early suspicion.

## Conclusion

This case emphasizes the importance of considering HLH in patients presenting with sepsis-like features, cytopenias, and multi-organ involvement. Persistent cytopenias despite supportive therapy should prompt early bone marrow evaluation. HLH requires early and aggressive immunosuppressive therapy, and delay in diagnosis can lead to fatal outcomes. Panniculitis as a presenting symptom of HLH is extremely rare, and clinicians must remain vigilant to such atypical manifestations.

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