Case of a young patient with Sickle cell SC disease complicated by severe hemolysis and HLH

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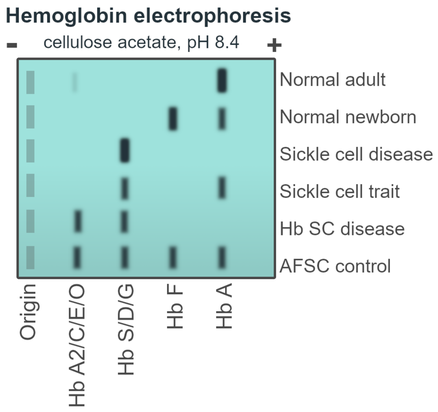
INTRODUCTION

Sickle cell disease (SCD) often leads to complex clinical scenarios, especially when compounded by additional comorbidities and acute complications. This case report details the challenges and management strategies in a young female with SCD who presented with severe complications including acute respiratory distress, severe hemolysis, and hemophagocytic lymphohistiocytosis (HLH)

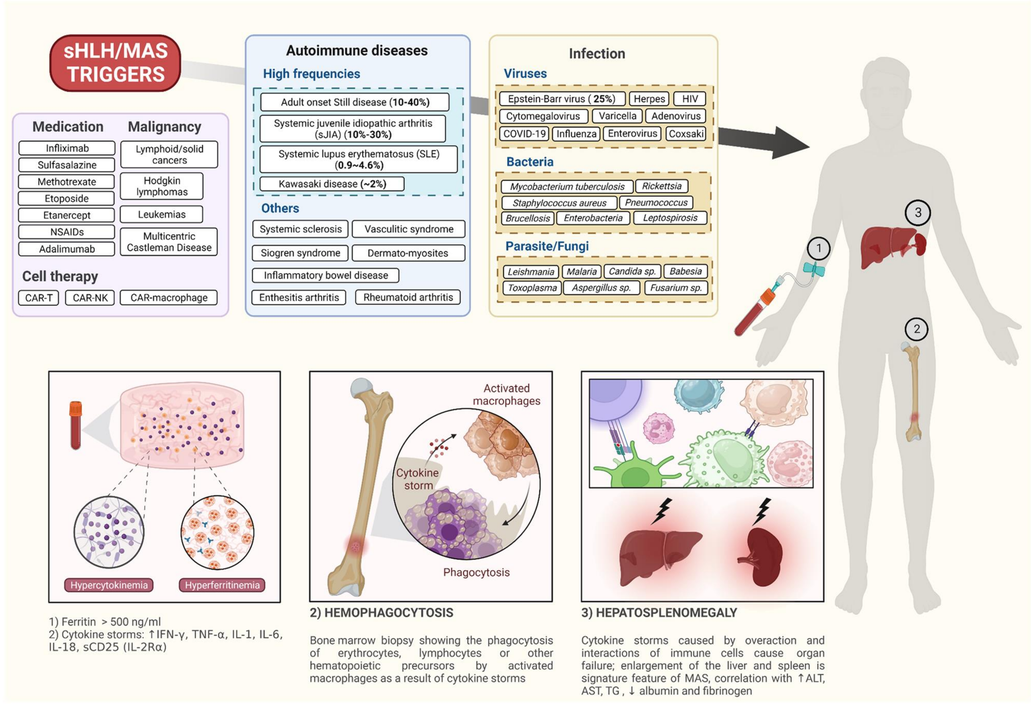


CASE PRESENTATION

A 29-year-old female with a medical history significant for SCD, asthma, rheumatoid arthritis (RA), chronic pain, and recent MRSA bacteremia presented with acute respiratory distress. At that time she was found to be in septic shock with severe hemolysis.

The diagnosis of HLH can be established if either 1 or 2 below is fulfilled:

1. A molecular diagnosis consistent with HLH
2. Diagnostic criteria for HLH are fulfilled (five out of the eight criteria below):
   - Fever
   - Splenomegaly
   - Cytopenias (affecting ≥ 2 lineages in the peripheral blood):
     - Hemoglobin <90 g/L (in infants<4 weeks: hemoglobin <100 g/L)
     - Platelets <100.000/µl
     - Neutrophils <1000/µl
   - Hypertriglyceridemia and/or hypofibrinogenemia:
     - Fasting triglycerides ≥ 265 mg/dL
     - Fibrinogen ≤ 1.5 g/L
   - Hemophagocytosis in bone marrow or spleen or lymph nodes
   - Low or absent NK-cell activity
   - Ferritin ≥ 500 µg/L
   - Soluble CD25 ≥ 2400 U/L
   - Supportive clinical criteria include neurologic symptoms and cerebrospinal fluid pleocytosis, conjugated hyperbilirubinemia, and transaminitis, hypoalbuminemia and hyponatremia



1) Ferritin > 500 ng/ml
2) Cytokine storms: ↑IFN-γ, TNF-α, IL-1, IL-6, IL-18, sCD25 (IL-2Rα)

2) HEMOPHAGOCYTOSIS

Bone marrow biopsy showing the phagocytosis of erythrocytes, lymphocytes or other hematopoietic precursors by activated macrophages as a result of cytokine storms

3) HEPATOSPLENOMEGALY

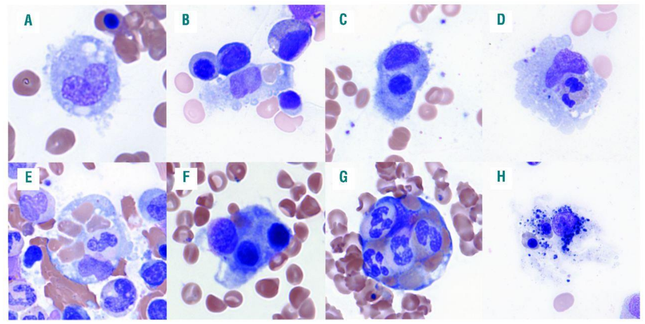
Cytokine storms caused by overaction and interactions of immune cells cause organ failure; enlargement of the liver and spleen is signature feature of MAS, correlation with ↑ALT, AST, TG , ↓ albumin and fibrinogen

HOSPITAL COURSE

- The patient experienced a severe sickle cell pain crisis and acute chest syndrome, with notable hypoxemic respiratory failure initially managed with a 72-hour course of dexamethasone and various respiratory support measures including intubation. She was extubated and transitioned to high-flow nasal cannula and intermittent BiPAP, eventually improving and being weaned to room air.
- E. coli bacteremia led to septic shock, managed with antibiotics and supportive care.
- The patient exhibited severe hemolysis, with elevated inflammatory markers and potential HLH criteria (high fevers, hypertriglyceridemia, hyperferritinemia, elevated AST, and splenomegaly).
- Anakinra was used but subsequently discontinued as HLH was not confirmed since some of the lab derangements could have been explained by her SCD and/or propofol usage while intubated.
- Inflammatory markers included elevated soluble IL-2 receptor (1335), CXCL9 (633), IL-18 (1141), and NK activity. The elevated NK activity suggested that HLH was less likely, although ferritin remained high.
- Laboratory findings included an elevated free light chain ratio (3.02long-termorderline elevations in alpha-1 and alpha-2 globulins, and an elevated gamma globulin (2.98). Immunofixation electrophoresis (IFE) indicated a possible monoclonal spike.
- These findings, in the context of acute inflammation and hypercalcemia, suggested a polygammopathy rather than a monoclonal gammopathy, though the elevated free light chain ratio raised concerns for a possible underlying monoclonal process.
- Her hospital course was prolonged and included multiple interventions, such as transfusions, plasmapheresis, and long duration of broad-spectrum antibiotics.

DISCUSSION

Given the multiple triggers and clinical scenarios associated with sHLH/MAS, establishing a biomarker-based diagnostic approach and pinpointing targeted therapies remain challenging. Artificial intelligence-based algorithms integrating etiology, cytokine profiles, and biochemical and clinical parameters could offer precise diagnostic solutions, facilitate accurate patient identification, and be used to monitor disease progression.



Examples of hemophagocytosis in patients with HLH
(A) Histiocytes in patients with HLH often display rounded contour with cytoplasmic projections.
(B-D) Hemophagocytes with a single ingested mature red blood cell (RBC), nucleated RBC progenitor, and granulocyte, respectively. Hematopoietic progenitor cells (HPCs) often contain single nucleated hematopoietic cells in addition to multiple mature RBCs (E); however, the presence of multiple nucleated cells within the cytoplasm of a single HPC (F and G) is highly predictive of the diagnosis of HLH.
(H) An example of a histiocyte with degenerating nuclear debris, indistinct cytoplasmic contour, and equivocal intracytoplasmic nucleated RBCs that we do not consider to be a definite hemophagocyte.

CONCLUSION

This case highlights the complexity of managing a young patient with SCD who experiences severe, multifaceted complications. The interplay between sickle cell crisis, acute infections, and potential HLH required a multidisciplinary approach and frequent adjustments to the treatment plan. This case also emphasizes that although rare, very little is known about HLH and there is need for further research into this topic to improve treatment outcomes for patients.

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