Hemophagocytic Lymphohistiocytosis Unmasked by Mononucleosis: A Case Report with Atypical Presentation

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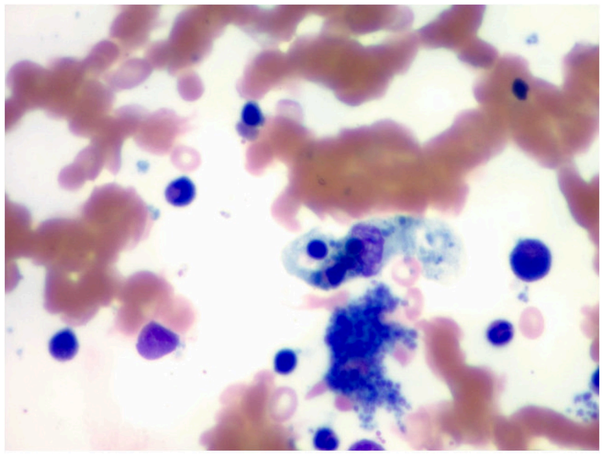
Introduction

Hemophagocytic Lymphohistiocytosis (HLH) is a rare, potentially fatal hyperinflammatory syndrome characterized by excessive immune cell activation and proliferation. While HLH can arise spontaneously (primary HLH) due to genetic mutations, it can also be secondary to infections, autoimmune diseases, or malignancies. Traditionally, HLH diagnosis relies on a constellation of clinical, laboratory, and histopathological criteria including fever, hepatosplenomegaly, cytopenias, hyperferritinemia, and elevated soluble interleukin-2 receptor levels. We present a case of a patient with atypical presentation leading to delayed diagnosis.

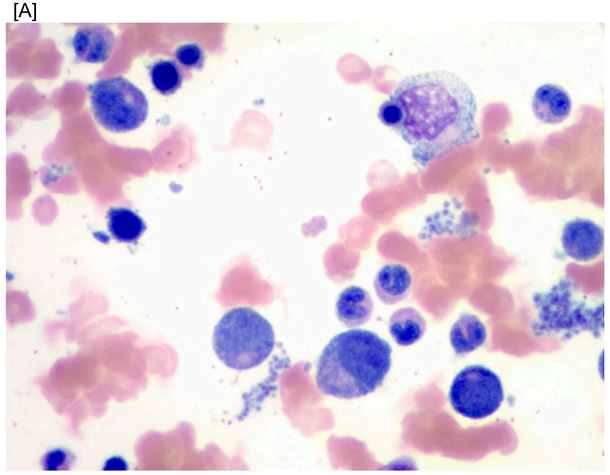
Patient Summary

Our patient, a 25-year-old male, presented with several weeks of fever, malaise, and weight loss. Clinical presentation suggested infectious mononucleosis. However, the patient continued to have progression of symptoms despite supportive care. While mononucleosis often presents with lymphocytosis and atypical lymphocytes, our patient displayed delayed pancytopenia and unresolved fevers. An early bone marrow biopsy revealed hemophagocytosis, and later, laboratory tests indicated hyperferritinemia, and elevated levels of soluble interleukin-2 receptor (sIL-2R), which are typically associated with HLH. Notably, the patient did not exhibit the thrombocytopenia and neutropenia often observed in typical HLH cases.

Imaging



[A]



[B]

Figure 1 [A&B]: *Hematopathology slide of bone biopsy*

Hospital Course

- 5/11- 20yo pt presents to ED for body aches, dizziness, low-grade fevers and anemia for 4 weeks. Elevated LFTs--> +Monospot; DCed home
- 5/12- Returned to ED, continued to have fevers, myalgias, hypotension. Labwork concerning for anemia. Admitted for supportive treatment and workup.
- ID consulted- Broadened workup to r/o viral and bacterial infection, pan cx
- Heme/Onc consulted- found that pt had lost 12lbs in 1 month. Labs included elevated CRP and a 1:320 positive ANA
- 5/14- Continuing to have high fevers despite broad spectrum abx and antipyretics. Antibiotics broadened, testing for uncommon bacteria & viruses.
- 5/15- Bone biopsy obtained. Transaminitis and fevers worsening, pt now has vision changes. Blood cx negative.
- 5/16- Imaging, Echo, viral panel negative. Worsening cytopenia. Considerations made LP, indium scan, and PET scan. Completed empiric abx. Hyperferritinemia noted. Blood cultures sent for mycobacteria.
- 5/19- Bone Marrow biopsy shows hemophagocytosis
- 5/20- Labwork reveals hypertriglyceridemia, hypofibrinogenemia. Soluble CD25 lab sent out. Rheumatology consulted, trial of pulse-dosed prednisone started.
- 5/21- Patient's myalgias improve. Heme/Onc determines autoimmune etiology. Rheumatology consulted, HLH is diagnosed.
- 5/24- Remaining viral and bacterial labwork results negative. Pt strength improved, 48 hours fever free, discharged with scheduled follow-ups with Heme/Onc and Radiology
- 5/27 CD25 findings results elevated

Conclusion

Timely recognition and treatment of HLH are crucial, as the syndrome carries a high mortality rate if left untreated. Clinicians should maintain a high index of suspicion for HLH and consider further diagnostic evaluations in patients with persistent or worsening symptoms despite appropriate management for the underlying infection.

References

1. Henter JI, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S, Ladisch S, McClain K, Webb D, Winiarski J, Janka G. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer. 2007 Feb;48(2):124-31. doi: 10.1002/pbc.21039. PMID: 16937360.