Post Covid-19 HLH masked by Acute Gastrointestinal Illness and Acute Renal Failure: A Diagnostic Challenge

Hina Bangash, MD, Sanjana Kamat, MD, Warsha Korani, MD, Asghar Marwat, MD, Mohsin Hamid, MD

Department of Internal Medicine, Conemaugh Memorial Medical Center, Johnstown, PA

INTRODUCTION

- Hemophagocytic lymphohistiocytosis (HLH) is a multi-system hyperinflammatory syndrome.
- In the post COVID-19 era, HLH continues to increase in prominence.
- The clinical presentation of HLH is usually non-specific and resembles an acute febrile illness of unknown origin.
- We present the case of secondary HLH (sHLD) presenting with gastrointestinal symptoms and acute anuric renal failure following a COVID-19 infection.

A. Molecular diagnosis consistent with HLH Or
B. 5 of the 8 criteria listed below
1. Fever ≥38.3°C
2. Splenomegaly
3. Cytopenia (affecting at least two of the three lineages in the peripheral blood) Hemoglobin <9 g/dL (infants <4 weeks: hemoglobin <10g/dL) Platelets $<100\times10^3/\mu L$ Neutrophils <1000/ μL
4. Hypertriglyceridemia (≥265 mg/dL) and/or hypofibrinogenemia (≤150 mg/dL)
5. Hemophagocytosis in bone marrow or spleen or lymph nodes or liver
6. Low or absent NK cell activity
7. Ferritin ≥500 ng/mL
8. sCD 25 (sIL2Ra) ≥ 2400 U/mL

CASE PRESENTATION

- A 53-year-old female with a history of diabetes, hypertension, and recent COVID-19 infection presented with oliguria progressing to anuria over several days.
- Patient also endorsed abdominal pain, nausea, and diarrhea.
- Lab work showed Cr 14, BUN 158, and pancytopenia characterized by Hgb 8, platelets 29, and WBC 3.6, all of which were significantly altered from her normal baseline.
- CTAP revealed splenomegaly.
- Despite initial treatment with IV fluids, her renal function did not improve, and due to concomitant worsening respiration, dialysis was initiated.
- Her clinical condition continued to decline with high-grade fevers and fluctuating mental status, prompting treatment with antibiotics and stress-dose steroids.
- Evaluation for microangiopathic disorders and an infectious workup was also negative.
- Additional laboratory tests showed hypertriglyceridemia and a ferritin level exceeding 500 ng/mL.
- Given the suspicion for HLH, she was started on dexamethasone, and a BM biopsy was performed, revealing rare hemophagocytosis. Her H Score was calculated at 234, indicating a 98-99% probability of HLH.
- Following treatment, the patient's condition improved, with resolution of acute kidney injury and pancytopenia, allowing discharge without permanent dialysis.

DISCUSSION

HLH is characterized by unrelenting immune activation and tissue inflammation that can precipitate multi-organ dysfunction. Primary HLH, usually presents during childhood and is commonly attributed to a genetic mutation causing dysregulated activation of granulocyte-mediated cytotoxicity in innate (NK cells) and adaptive (CD8+ T cells) immunity. sHLH on the other hand, is thought to present in response to acute illnesses that span infections, autoimmune disorders, or malignancy (1,2). Vague, non-localizing initial presentations can stall the path to definitive diagnosis in HLH.

A 2004 prospective study testing the efficacy of etoposide and dexamethasone in HLH reported discerning clinical findings that were combined with the recommended HLH-94 criteria – fever, splenomegaly, cytopenia, hypertriglyceridemia/hyperfibrinogenemia, biopsy-proven hemophagocytosis, ferritin >500 mcg/mL, low/absent NK activity, elevated soluble CD25, and elevated CXCL9. The presence of 5 out of 9 would equate to a conclusive diagnosis (3,4). The H Score can also be used to generate a probability to support a diagnosis of HLH (5).

CONCLUSION

Given the gravity and clinical implications of progressive HLH, timely medical intervention is of the utmost importance. However, the greatest barrier to a positive clinical outcome is a delay in time to diagnosis due to the non-specificity of clinical presentation and lack of uniformity in objective laboratory evidence. Against the backdrop of such limitations, physicians must have a low threshold of clinical suspicion for HLH, especially in the setting of acute illnesses that predispose to a multi-system inflammatory process.

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