Hemophagocytic Lymphohistiocytosis, An Overlooked Culprit Of Disseminated Intravascular Coagulation

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Hemophagocytic Lymphohistiocytosis, An Overlooked Culprit of Disseminated Intravascular Coagulation

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Introduction

- Hemophagocytic lymphohistiocytosis (HLH) is an immune system disorder with aberrant activation of T cells and macrophages resulting in vast tissue destruction. There are two forms of HLH: inherited HLH (autosomal recessive) and secondary HLH, occurring after strong immunologic activation.
- Primary HLH results from defective proteins involved in the cytolytic secretory pathway. These defective proteins prevent cytotoxic T lymphocytes and Natural Killer (NK) cells from maintaining immune homeostasis.
- In contrast, secondary HLH results from upregulation of proinflammatory cytokines which results in overactivation of T lymphocytes and NK cells. However, the end result of both primary and secondary HLH is the same; cellular death and organ failure.

Case Presentation

Vitals	
Temperature	100.7°F
Pusle	105 BPM
Respiratory Rate	20 RPM
Blood Pressure	162/79 mmHg
Pulse Oxygenation	98% on room air

Laboratory Values	
Lab	Value
Hemoglobin	9.5 g/dL (L)
Hematocrit	27.9% (L)
WBC	10.5 (H)
RBC	3.40 mill/cmm (L)
Platelet count	12,000/cmm (LL)
RDW	21.2% (H)
Immature Cells	23% (H)
Nucleated RBC	2 per 100 WBC (H)
PT	16.5 seconds
PT INR	1.4
Fibrinogen	110 mg/dL (L)
Immature Cells	23% (H)

- A 56 y.o. female with a history of Essential thrombocytosis (ET) s/p hydroxyurea treatment presented to the ED with an episode of gross hematuria. She was hypertensive and febrile. Physical exam was significant for petechiae on all extremities, tachycardia, diffuse abdominal tenderness, and splenomegaly.
- Considering patient's history of ET, which has a predisposition to progress to Acute Myeloid Leukemia, and long term exposure to hydroxyurea (a leukemogenic agent) suspicion for leukemia was very high.
- However, a low fibrinogen level indicated DIC. It wasn't clear as to whether the DIC resulted from bacteremia or acute promyelocytic leukemia (APL), a variant of AML known to precipitate DIC. As such, a bone marrow biopsy was conducted for further analysis.
- However, cytogentic testing failed to reveal (15; 17) translocation; which, as a result, ruled out APL.
- With findings of hypercellularity and increased levels of myeloblasts in the bone marrow, a diagnosis of AML was made.
- A closer re-examination of bone marrow biopsy revealed histiophagocytic behavior (Figure D). Such morphological presentation raised the suspicion for HLH. As such, ferritin and triglyceride levels were ordered which revealed a level of >12,000 and 226, respectively.
- A diagnosis of HLH was made considering negative blood cultures, biopsy findings, hyper-ferritinemia and hypofibrinoginemia.
- Pt was started on HLH-94 Protocol along with idarubicin and cytarabine for AML induction therapy.

Hallmarks of HLH
Fever
Hepatosplenomegaly
Cytopenia
Hypertriglyceridemia
Hemophagycytosis
Elevated ferritin
Low Fibrinogen

Hallmarks of HLH	Patient
Fever	100.7°F
Hepatosplenomegaly	Yes
Cytopenia	Yes
Hypertriglyceridemia	226 mg/dL
Hemophagocytosis	Yes, see Figure D
Elevated Ferritin	>12,000 (H)
Low Fibrinogen	110 mg/dL (L)

Bone Marrow Biopsy

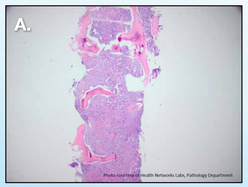

Figure A. The bone marrow biopsy is noted to be hypercellular. With progression of age, bone marrow is gradually replaced with adipose tissue. Considering patient's age, approximately 20-30% of her bone marrow should be adipose. Presentation is suggestive of leukemia.

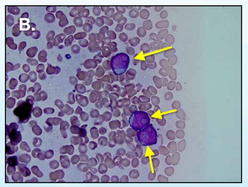

Figure B. Under magnification. Arrows point to myeloblasts. Suggestive of acute myeloblastic leukemia (AML).

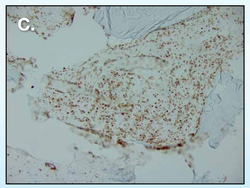

Figure C. Anti-CD34 Stain. This stain tests for CD34, a cell surface protein found on myeloblasts.

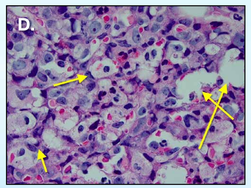

Figure D. Arrows point to macrophages phagocytosing neutrophils; note the large vacuoles. Though not pathognomonic, such activity is suggestive of hemophagocytic lymphohistiocytosis.

Discussion & Follow-up

DISCUSSION:

- This presentation illustrates a transformation of ET into AML with concurrent HLH; highlighting the importance of considering HLH in AML patients presenting with DIC, as early detection could be essential in managing both patients' malignancy and hemodynamic status.

FOLLOW-UP:

- Patient was started on HLH-94 Protocol (etoposide and tapering steroids) along with idarubicin and cytarabine; subsequently platelets increased to 37,000 and both ferritin and fibrinogen normalized.
- Upon stabilization, pt was discharged and scheduled for follow up by Hematology Oncology at Penn State University for bone marrow transplant.

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