**Autoimmune Hepatitis: A Possible Harbinger of Hemophagocytic Lymphohistiocytosis**

Nick Coombs DO, Kaamya Bhandari MD, Sanket Patel DO, Murali Dharan MD MRCP FASGE

University of Connecticut Health Center, Department of Internal Medicine

### Introduction

- Autoimmune hepatitis (AIH) is a rare condition with a growing panel of testing for etiologies.
- Presented is a clinical course of AIH and a possible association with hemophagocytic lymphohistiocytosis (HLH).

### Case Report

58-year-old male with no past medical history presented to the hospital with painless jaundice, dark urine, pale stools and one week of nausea and vomiting.

- Physical exam was positive for jaundice and scleral icterus, but otherwise unremarkable.
- Initial blood work revealed elevated transaminases >1000 u/L, an alkaline phosphatase of 215 u/L, a bilirubin of 52.7 mg/dL, a BUN/Cr 48/2.5 mg/dL, and a ferritin level > 11,000 units.
- MRCP showed no intra or extrahepatic biliary ductal dilatation.
- Endoscopic ultrasound showed a hypoechoic liver and peri-portal and peri-hepatic lymph nodes (LNs).
- Fine needle aspiration of the LNs was normal.
- An extensive work-up for hepatitis was unremarkable, but a liver biopsy showed numerous plasma cells suspicious for AIH.

**Given concern for HLH, a bone marrow biopsy (BMB) was done and demonstrated occasional hemophagocytosis.**

- Patient was diagnosed with seronegative AIH and was treated with azathioprine and steroids resulting in improvement in clinical condition.

The patient had a subsequent admission with fever, altered mental status, and generalized weakness.

- Over the course of the hospital admission, he developed pancytopenia and ferritin levels were >40,000 units.
- A CT abdomen/pelvis showed splenomegaly (Figure B).
- Repeat BMB (Figures C and D) demonstrated phagocytized mature and immature hematopoietic cells which supported a diagnosis of HLH.

**Patient was started on Etoposide, but unfortunately succumbed to his illness after an extended inpatient admission.**

### Discussion

- Hepatitis is a commonly diagnosed condition – AIH is among etiologies that should be considered.
- An association between AIH and HLH has been theorized – a prior case report discussed a two-hit hypothesis.
  - Any immune system overactivation can potentially lead to HLH, especially in those predisposed.
  - HLH has almost a 70% mortality rate with a median survival of about 4 months.
  - Survival rates are higher in those with HLH secondary to autoimmunity.
- AIH should raise suspicion for development of HLH in those with clinically significant lab work.
- Early recognition and treatment of HLH may lead to a better prognosis.

### Acknowledgements

- Thiruchelvam, B. (2016). Figure A [Diagnostic criteria for HLH]. Hemophagocytic lymphohistiocytosis presentation retrieved through SlideShare.net (https://www.slideshare.net/Thiruchelvam/fig18).

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**Figure A: Diagnostic criteria of HLH**

- 1. Fever >38.5°C
- 2. Splenomegaly
- 3. Cytopenia, with at least two of the following:
  - a. Hgb <9 g/dL (for infants <4 weeks, Hgb <10 g/dL)
  - b. Platelets <100,000/microL
  - c. Absolute neutrophil count <1000/microL
- 4. Hypertriglyceridemia
  - a. Fasting triglycerides >265 mg/dL AND/OR
  - b. Hyperfibrinogenemia (fibrinogen <150 mg/dL)
- 5. Hemophagocytosis in bone marrow, spleen, lymph node, or liver
- 6. Low or absent NK cell activity
- 7. Ferritin >500 ng/mL
- 8. Elevated soluble CD25 (soluble IL-2 receptor alpha) >2400 U/mL

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**Figure B: CT abdomen/pelvis showing splenomegaly**

**Figure C: Macrophage engulfing a neutrophil**

**Figure D: Macrophage engulfing erythroid precursors**