A rare case of EBV-associated HLH with spontaneous resolution

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BACKGROUND

- Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening syndrome of excessive immune activation.
- It often manifests as a persistent fever, splenomegaly, pancytopenia, and hemophagocytosis in the bone marrow.
- HLH can be familial or acquired, both of which are triggered by an event that disrupts immune homeostasis.
- Acquired HLH is mostly caused by infection, malignancy, and autoimmune disease.
- Epstein-Barr virus-associated HLH is the most common type of infection-associated HLH.

CASE PRESENTATION

- History:

34-year-old female with a prior history of EBV-associated HLH who presented to the hospital with a fall preceded by a week of generalized body aches, fever, and fatigue. Pancytopenia developed during the hospitalization.

- PE:

Temperature 39.5C, spleen palpable 1 cm below costal margin

- Labs:

White blood cell count 1.5E3/uL, absolute neutrophil count 830, hemoglobin 8.2 g/dL, platelet count 58E3/uL, soluble IL-2 receptor 4,611 U/mL, EBV blood PCR 672,000 cpy/mL, fibrinogen 89 mg/dL, ferritin 2133 ng/mL, LDH 1,139 IU/L, AST 290 IU/L, alkaline phosphatase 354 IU/L

- Imaging:

CT chest/abd/pelvis: enlarged liver and enlarged spleen 14.7 cm.

- Pathology

Bone marrow biopsy: hemophagocytic lymphohistiocytosis is present and prominent. The is hypercellularity and trilineage hematopoiesis.

DIAGNOSIS AND TREATMENT

- A clinical diagnosis is consistent with HLH if 5/8 of the following are met: fever > 38.5C, splenomegaly, cytopenias, hypertriglyceridemia and/or hypofibinogenemia, hemophagocytosis, low or absent NK cell activity, ferritin > 500 ng/mL, and elevated soluble IL-2 receptor >2,400 U/mL.
- Prompt treatment is typically required for this highly fatal condition.
- Our patient's pancytopenia, inflammatory markers, and EBV blood PCR slowly returned to normal without treatment.

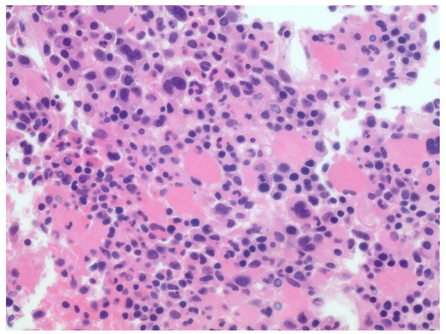

Figure 1: bone marrow biopsy at 40x magnification with prominent hemophagocytosis.

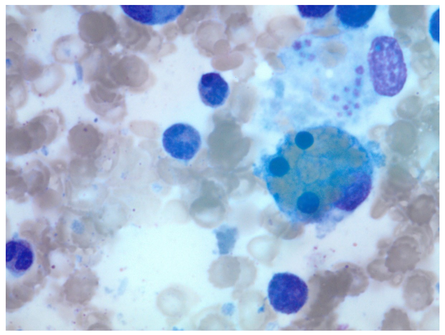

Figure 2: bone marrow aspirate at 100x magnification with reactive histiocytes and phagocytosis of nucleated red blood cells.

DISCUSSION

- Our patient met 7/8 criteria for HLH with hemophagocytosis in bone marrow, fever, cytopenias, splenomegaly, hypofibrinogenemia, elevated ferritin, and elevated soluble IL-2R.
- To distinguish between familial and acquired HLH, an HLH genetic panel was performed and was negative.
- A regimen of dexamethasone and etoposide has been the mainstay of treatment based on the HLH-1994 and HLH-2004 studies.
- In patients with EBV-associated HLH, the addition of rituximab can be useful to deplete the reservoir of EBV in B cells.
- The distinction between HLH and primary EBV infection can be very difficult, as patients with primary EBV may develop some of the hallmark signs of HLH as part of natural infection.
- During the patient's hospitalization, her pancytopenia, inflammatory markers, fever, transaminitis, and EBV PCR all slowly resolved.
- A literature review was performed. Our cause is the first case published of a patient with EBV-associated HLH with spontaneous resolution.

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