Hemophagocytic Lymphohistiocytosis

Image ID: 63563

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Category: Macrophage/Histiocytic and dendritic cell Neoplasms and disorders (2015) > H group > HLH of unknown/uncertain origin

Description:

The bone marrow aspirate stained with Wright-Giemsa from a 55-year-old female presenting with pancytopenia displays extensive hemophagocytosis.

Hemophagocytic lymphohistiocytosis (HLH) primarily involves histiocytes which engulf and destroy red blood cells, a process known as erythrophagocytosis and depicted in the images. Hematologic analysis will also likely reveal increased histiocytes, hypercellular bone marrow, and pancytopenia. Cellular damage in HLH results in stimulation of inflammatory cytokines including TNF- and IFN-, which suppress hematopoiesis, induce apoptosis in hematopoietic cells, and further activate histiocytes.1 If HLH is suspected, it is critical to evaluate serum ferritin, triglyceride, and fibrinogen levels.

- Elevated ferritin is expected because destruction of red blood cells results in the release of iron into the serum. Additionally, histiocytes increase ferritin production secondary to increased levels of heme-oxygenase due to the inflammatory cytokines.1
- Hypertriglyceridemia is expected in HLH, because TNF- and IFN- also inhibit lipoprotein lipase activity, which decreases the breakdown of triglycerides for uptake and storage by tissues.1
- Plasmin will also be elevated due to histiocyte secretion of plasminogen activator, leading to fibrin breakdown, which decreases fibrinogen1 and increases D-dimer.2
- In addition to elevated ferritin and triglycerides with lowered fibrinogen as key laboratory findings for HLH, elevated CD25 marks activated lymphocytes, and is the alpha subunit of the interleukin 2 receptor (IL-2R).1

With laboratory results corroborating HLH, it is important to distinguish between disease associated with Epstein-Barr Virus (EBV), malignancy, and immunosuppression.1 Work-up revealed positive EBV virology in this case, without morphologic or immunophenotypic evidence of lymphoma or leukemia involvement. Secondary HLH in adults is typically caused by virus or lymphoma, more commonly T Cell lymphoma. Therefore, monitoring and further testing for an occult secondary lymphoma could be beneficial.

Finally, the HLH treatment recommended by the Histiocyte Society is an 8-week induction therapy with corticosteroids, etoposide, and cyclosporine.1

Sources

1. Rosado FG, Kim AS. Hemophagocytic lymphohistiocytosis: an update on diagnosis and pathogenesis. *Am J Clin Pathol*. 2013;139(6):713-727. doi:10.1309/AJCP4ZDKJ4ICOUAT

2. Grzybowski B, Vishwanath VA. Hemophagocytic Lymphohistiocytosis: A Diagnostic Conundrum. *J Pediatr Neurosci*. 2017;12(1):55-60. doi:10.4103/jpn.JPN_140_16