Case Report: Diagnosis and Acute Treatment of Hemophagocytic Lymphohistiocytosis[1]

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Introduction

Hemophagocytic lymphohistiocytosis (HLH) is a very rare disease in adults that can present primarily or secondarily. It is characterized by immune system deregulation, resulting in overactivity of the cell-mediated immune system that can ultimately lead to infection, sepsis, end organ damage, and death. The pathophysiology of secondary HLH is not well understood but is most likely multifactorial and has been associated with infection, autoimmunity, immune suppression, organ transplant, and malignancy. In order to be diagnosed with HLH, 5 of 9 diagnostic criteria must be met: fever > 38.5 C, splenomegaly, pancytopenia, hypertriglyceridemia/hypofibrogenemia, hemophagocytosis on biopsy, absent NK cell activity, ferritin > 500 ng/mL, elevated soluble CD25 (IL-2 receptor alpha), and elevated CXCL-9. Treatment includes dexamethasone and etoposide, with some cases requiring methotrexate or hematopoietic cell transplant. The prognosis is poor, with a 5-year survival rate of 54%.

Case Description

A 53-year-old woman presented to the ED with weakness, fatigue, fever/chills, nausea, vomiting, and poor appetite for 2 months. She had been admitted to other hospitals in the months prior for similar presentations. Vital signs were notable for fever, tachycardia, and hypotension. On physical exam, she was ill-appearing with purpura and pitting edema of her bilateral lower extremities and scattered ecchymoses. She was admitted to the MICU and started on antibiotics and pressors. Infectious disease, GI, rheumatology, endocrinology, and hematology/oncology were consulted. Extensive infectious workup revealed no source of infection, and antibiotics were subsequently discontinued. Hematologic workup included H/H of 8.9/26, WBC of 6.8, platelets too clumped to estimate, reticulocyte 6.3%, ferritin 4331, fibrinogen 674, IL-2 receptor 1148, and triglycerides 544. A right iliac crest bone marrow biopsy was largely unremarkable. (Her CXCL9 test was pending at discharge but eventually returned as elevated.) Additionally, her hepatologic workup revealed hepatosplenomegaly but no signs of acute infection. Unfortunately, over the following days, her condition worsened. Given her hematologic workup, the decision to start etoposide and dexamethasone was made on day 7 of admission. Her condition improved, and she was discharged on day 14 with an oral steroid taper, home health, and outpatient etoposide infusions. Unfortunately, she was readmitted multiple times in the subsequent months. Her course has since been complicated by sepsis, neutropenic fever, and invasive Aspergillosis.

Discussion

HLH is a rare, complex, life-threatening immune system proinflammatory disorder. Our patient fulfilled 7 of the 9 diagnostic criteria upon diagnosis. The exact cause of HLH in this patient is not yet understood. Although a diagnosis was reached and a treatment plan initiated, her condition has resulted in multiple extended hospital admissions. The etiology of HLH is not fully understood, especially secondary HLH. Further research is necessary for this disease so that improved therapy regimens can be developed.

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[1] References:
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