A case study of refractory secondary HLH treated with splenectomy in an adult patient

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BACKGROUND

Hemophagocytic lymphohistiocytosis (HLH) in adults is a rare disease marked by inappropriate immune activation resulting in pancytopenia. This inappropriate immune activation is attributed to aberrant T-lymphocyte and macrophage activation resulting is phagocytosis of blood cells. The disease is divided into primary, familial variety seen more commonly in children, and secondary which is often from underlaying malignancy, infection, or an autoimmune disorder.[1] As it pertains to secondary causes of HLH, infections account for ~40% of cases with EBV, CMV, and HSV being the most common etiologies, and malignancy account for~ 35% of cases with T and B-cell lymphomas being the most common.[2]

Diagnostic criteria is based on the HLH-94 and the HLH-2004 protocols which look at molecular diagnosis of genetic defects or five of the following: fever, splenomegaly, cytopenia, hypertriglyceridemia or hypofibrinogenemia, hemophagocytosis in bone marrow, spleen, or lymph nodes, lower or absent NK activity, elevated ferritin, soluble CD25.[3] In 2013, the H score was developed relying on similar criteria and predicts the likelihood of a patient have a hemophagocytic syndrome.[3] Surgical splenectomy has been recommended for establishing diagnosis especially in cases in which diagnosis is not confirmed on bone marrow biopsy, but the therapeutic effect of splenectomy in HLH remains unclear.

H Score

Category	Criteria	Points
Known underlying immunosuppression	no	+0
Temperature (F)	>102.9	+49
Organomegaly	splenomegaly	+23
# of cytopenias	3 lineages	+34
Ferritin	>6,000	+50
Triglycerides	>354	+64
Fibrinogen	>250	+0
AST	<30	+0
Hemophagocytosis on bone marrow	n/a	+0
	TOTAL	**220**
	93-96% probability of hemophagocytic syndrome	

CASE REPORT

We present the case of a 60 year old female who presented with abdominal pain, recurrent fevers as high as 105F, and pancytopenia. She had recently relocated to the US after living in the Democratic Republic of Congo and Uganda. Other labs significant for ferritin 75,000 ng/ml, triglycerides 480 mg/dL, CD25 11983 pg/mL, and LFTs increased throughout her stay. H Score calculated with a 93% probability of having HLH. Initial CT showed splenomegaly measuring 14.5cm in length.

The patient underwent extensive investigation for underling etiologies including EBV, HIV, CMV, hepatitis, malaria, parvovirus, rickettsia, babesia, brucella, screening for lupus, and rheumatoid factor which were all negative. A bone marrow biopsy was obtained but was without evidence of lymphophagocytosis. She was treated with dexamethasone, IVIG, etoposide, and anakinra. Repeat imaging showed worsening splenomegaly up to 21cm in size and a spontaneous psoas hematoma.

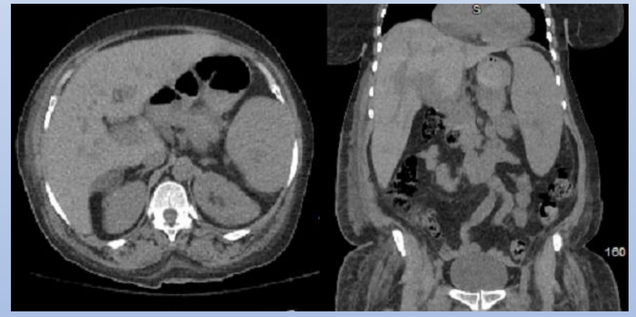

Figure: CT abdomen and pelvis without contrast showing splenomegaly with spleen measuring 21.1cm on hospital day 30 (a) axial view (b) coronal view

Given failure of improvement despite medical investigation and intervention, the patient was taken for a robotic assisted laparoscopic splenectomy. Pathology showed splenomegaly with extensive extramedullary hematopoiesis. Postoperatively, tocilizumab was started, however the patient remained without improvement and thus was transferred to a tertiary care center where she continued to decompensate and ultimately expired.

DISCUSSION

HLH is a hyperinflammatory condition that can ultimately lead to multi-organ failure and death. Treating the underlying etiology while managing the patients inflammatory state remains the hallmark of treating this disease. Unfortunately, there is a large percentage of cases in which an underlying etiology cannot be identified, making treatment more complex especial in refractory cases of secondary HLH like the patient presented here.

Splenectomy is known to play a role in diagnosis, however its therapeutic benefit is not well understood. Refractory cases of secondary HLH remain difficult to diagnose and treat. It comprises an extensive list of differential diagnosis's which need to be systematically assessed. In cases that are not responding to medical therapy alone, splenectomy can be considered for further diagnostic potential, but the therapeutic benefit is still debated.

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