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Epstein Barr Virus induced Hemophagocytic Lymphohistiocytosis and Autoimmune Hepatitis

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Clinical Scenario

We present the case of a previously healthy 18-year old male that presented with physical examination and laboratory findings consistent with acute liver failure (ALF) after being diagnosed with acute Ebstein-Barr virus (EBV) infection five days prior to presentation. Secondary causes of ALF, including acute viral hepatitis, acetaminophen level, and thrombus were ruled out. Bone marrow biopsy showed hemophagocytic cells. Serum soluble IL-2 receptor and ferritin levels were markedly elevated consistent with hemophagocytic lymphohistiocytosis (HLH). Liver biopsy showed panlobular hepatitis with plasma cells, mild interface activity, and positive anti-smooth muscle antibody, suggestive of autoimmune hepatitis (AIH) with concurrent HLH.

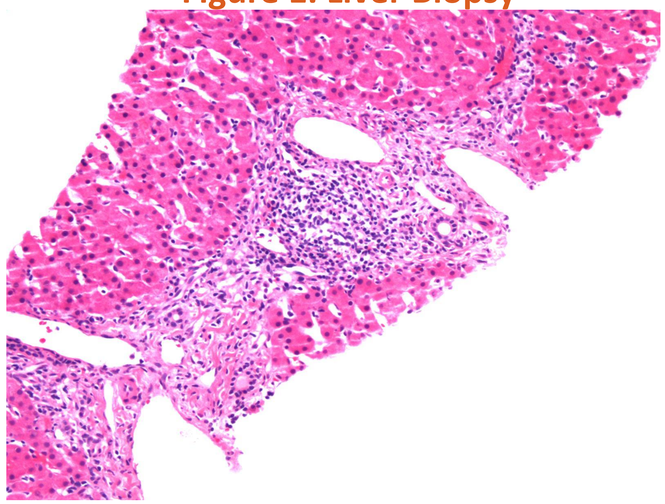
Literature Review

Previous case reports have described EBV induced HLH and AIH; however, to our knowledge, no findings of all three conditions present in one individual in an acute illness setting have been described.

Unique Aspects

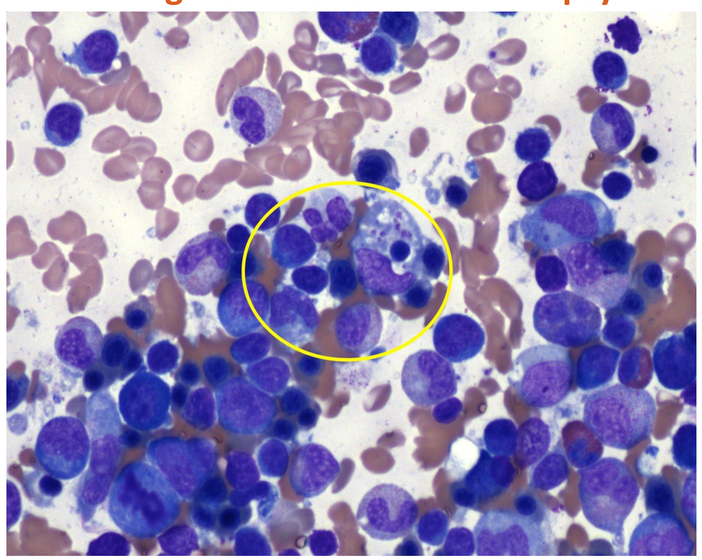
The patient was started on dexamethasone therapy with complete resolution of symptoms and laboratory abnormalities eight weeks following hospital discharge.

Figure 1. Liver Biopsy



Liver biopsy showing panlobular hepatitis with plasma cells, portal and periportal fibrosis, mild interface activity, positive smooth muscle antibody, and presence of activated macrophages, which was suggestive of autoimmune hepatitis with overlapping HLH

Figure 2. Bone Marrow Biopsy



Bone marrow biopsy showing hemophagocytic cells, normocellular marrow with hematopoiesis, adequate iron stores, and no evidence of acute leukemia or lymphoma.

Recommendations

We recommend consideration of glucocorticoid therapy in patients presenting with features of HLH or AIH causing acute liver failure in the setting of acute EBV infection.

Conclusions

In conclusion, we present the unique case of EBV induced HLH and AIH. We discussed the diagnosis and management of these pathologies in the acute setting and seek to contribute to the limited literature of these exceedingly rare diseases.

Diagnosis of HLH

HLH can be diagnosed by any combination of 5 of the 9 findings:

1. Fever ≥38.5°C
2. Splenomegaly
3. Peripheral blood cytopenia, with at least two of the following: hemoglobin <9 g/dL; platelets <100,000/microL; absolute neutrophil count <1000/microL
4. Hypertriglyceridemia (fasting triglycerides >265 mg/dL) and/or hypofibrinogenemia (fibrinogen <150 mg/dL)
5. Hemophagocytosis in bone marrow, spleen, lymph node, or liver
6. Low or absent Natural Killer cell activity
7. Ferritin >500 ng/mL (often >6,000 ng/mL)
8. Elevated soluble CD25 (soluble IL-2 receptor alpha [sIL-2R]) two standard deviations above age-adjusted laboratory-specific norms
9. Elevated CXCL9 (chemokine released by macrophages in response to IFN-gamma)