Fulminant Hepatitis Becomes the Initial Presentation of X-Linked Lymphoproliferative Disease

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Introduction

- Fulminant hepatic failure is a rapidly progressing multisystem disorder causing severe hepatocellular dysfunction, with or without encephalopathy in association with hepatocellular necrosis in patients with no recognized underlying chronic liver disease [1].
- Despite its rarity, acute liver failure in the pediatric population has remained an evolving topic for many years due to its high impact on morbidity and mortality.
- Although numerous etiologies for fulminant hepatitis have been proposed, more than 45% of cases remain cryptogenic [2].
- Here we present a case of a child who presented in fulminant hepatic failure secondary to Epstein Barr virus infection in the presence of an unknown underlying rare genetic immunological phenomenon, X-Linked Lymphoproliferative Syndrome (XLP).

Case Report

- A 17-year-old male with prior history of High-Grade B Cell Lymphoma diagnosed at 3 years of age with metastasis to the colon requiring hemicolectomy, now in remission, presented with a 2 week history of fever, diaphoresis, emesis, right upper quadrant abdominal pain, and jaundice.
- Pertinent positive labs: albumin: 2.9 g/dL, T.bili: 5.7 mg/dL, Alk phos: 806 U/L, AST: 675U/L, ALT: 417 U/L, GGT: 381 U/L, INR: 1.58, Triglycerides: 334 mg/dL, Ferritin 26,000 ng/mL, Fibrinogen: 97 mg/dL. Epstein-Barr Virus PCR: 17,600 IU/mL with both Epstein-Barr VCA IgM and Epstein-Barr Heterophile Antibodies IgM positive. Flow cytometry was obtained, and results were consistent with EBV infection.
- CT abdomen/pelvis revealed hepatomegaly, proctocolitis, and perihepatic, mesenteric, external iliac and inguinal lymphadenopathy. Liver US revealed hepatosplenomegaly with collapsed gallbladder with sludge, no biliary dilation seen.
- His clinical condition rapidly deteriorated. Within days, he developed pancytopenia, hepatic encephalopathy, hyperammonemia requiring continuous renal replacement therapy, coagulopathy, lactic acidemia, hypoglycemia, and fulminant hepatic failure which raised concern for Hemophagocytic Lymphohistiocytosis (HLH). Bone marrow biopsy was obtained and revealed numerous hemophagocytes, thus confirming the diagnosis.
- He was treated with broad spectrum antibiotics, antifungals, steroids, IVIG,, Rituximab, and Alemtuzumab. He was transferred to a higher level of care facility where the possibility of organ transplantation would be readily available, however he unfortunately died on hospital day 10.
- Post-mortem genetic panel was positive for mutation in the SH2D1A gene, which is characteristically seen in XLP.

Data

Figure 1

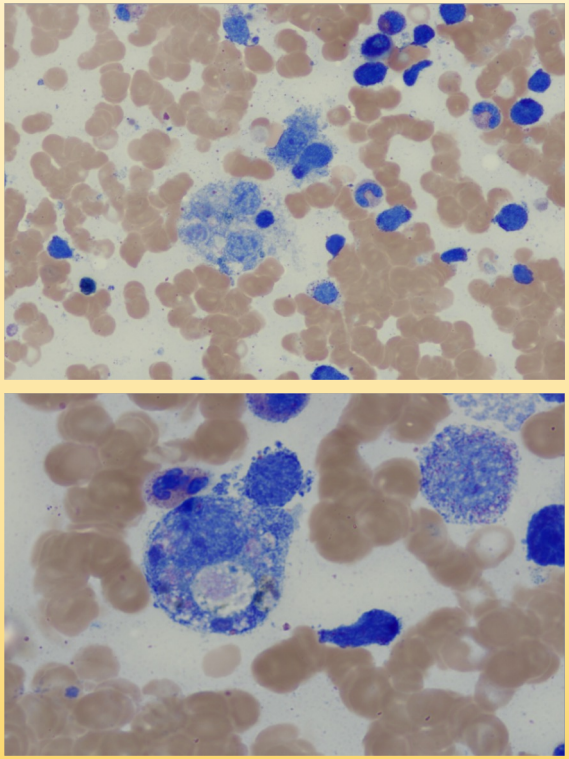

Figure 1: Bone Marrow Biopsy Results showed numerous hemophagocytes supported diagnosis of Hemophagocytic Lymphohystiocytosis

Discussion

- Acute Epstein-Barr Virus, one of the most common viruses affecting adolescents nationwide, Acute infection often leads to infectious mononucleosis which is characterized by fever, fatigue, malaise, sore throat, lymphadenopathy, and infectious hepatitis.
- EBV infections are usually self limiting, lasting only a few weeks. However, in some rare instances, immune dysregulation can occur leading to acquired HLH which can cause fulminant end organ damage.
- Although bone marrow biopsy was suggestive of HLH in our patient, post-mortem genetic panel revealed deficiency in the signaling lymphocyte activation molecule (SLAM)–associated protein (SAP) associated with a mutation in the SH2D1A gene distinctive to a rare genetic primary immunodeficiency, X-Linked Lymphoproliferative Syndrome (XLP) Type 1. Therefore, his diagnosis fit more closely with XLP, which is more rarely seen.
- Studies suggest that approximately one third of male patients with XLP Type 1 develop malignant transformation of proliferating B Cells involving the intestinal tract [3]. Non-coincidentally, our patient's history encompasses some similarities

Conclusion

XLP should be consider in the differential diagnosis for any child that presents with severe liver injury characterized by hepatocellular injury, cholestasis and impaired synthetic function in the setting of an acute EBV infection.

References

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