A Rare Case of EBV Positive T Cell Lymphoproliferative Disorder with Hemophagocytic Lymphohistiocytosis Receiving Nivolumab

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Supplemental Video

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Introduction: Epstein-Barr Virus (EBV) can range from asymptomatic to infectious mononucleosis to multi-organ failure (3). Some individuals are unable to control EBV infection due to infiltration of tissue by EBV positive T, NK, and B cells, termed chronic active EBV (CAEBV). Diagnosis includes increased EBV level with no known underlying immunodeficiency (4). CAEBV is quite rare in the U.S. (1). Hemophagocytic lymphohistiocytosis (HLH) can occur as a devastating complication in patients with CAEBV and involves dysregulation of NK cells, CD8+ cytotoxic T cells and macrophages (5). EBV-associated HLH is rare, with an approximate annual incidence of 0.4 cases per million persons (2).

Case Presentation:
A 20-year-old male with no medical problems presented with two days of diffuse abdominal pain, vomiting, and fevers. Vitals were BP of 93/49, HR 105, RR 20, and 100% O2sat on RA. Labs were significant for platelet count of 37, AST 331, ALT 166, ALK 319, BUN 60, Cr 2.9, and lactate of 6.2. HIV, HSV, CMV, COVID-19 were negative. A chest x-ray was unrevealing. A RUQ ultrasound showed pericholecystic fluid and mild extrahepatic biliary ductal dilatation. An initial diagnosis of septic shock with unknown etiology was made. He received 30 cc/kg of IV crystalloid and broad-spectrum empiric antibiotics. He later developed DIC requiring resuscitation with numerous blood products.

Final/Working Diagnosis: EBV DNA by PCR returned positive with 9.98 million copies/mL, suggesting a diagnosis of CAEBV. Ferritin was 21,2155.7 ng/ml. Bone marrow biopsy confirmed EBV positive T cell lymphoproliferative disorder with HLH. Atypical proliferation was positive for CD3, CD5, CD8, CD20 and granzyme B and negative for CD4, perforin, TCRD and CD56. EBER ISH showed focal positive cells. Flow cytometry identified 64% abnormal mature NK- cell population.

Management, Outcome and Follow Up:

He was treated with etoposide, rituximab, and dexamethasone and emapalumab-lzsg. He remained stable and was discharged with close outpatient follow-up. CHOP protocol was initiated along with nivolumab with improvement of EBV viral load to 2.76 million copies/ml. He is currently awaiting HSCT.

Learning Objectives
Discuss the importance of recognizing HLH related disease processes
Diagnose and treating chronic active EBV

References and Resources
1. Cohen JI. Optimal treatment for chronic active Epstein-Barr virus disease. Pediatr Transplant.

2009;13(4):393-396. doi:10.1111/j.1399-3046.2008.01095.

2. George MR. Hemophagocytic lymphohistiocytosis: review of etiologies and management. J Blood Med.
2014;5:69-86. Published 2014 Jun 12. doi:10.2147/JBM.S46255

3. Hoover K, Higginbotham K. Epstein Barr Virus. [Updated 2020 Nov 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan

4. Kimura H, Cohen JI. Chronic Active Epstein-Barr Virus Disease. Front Immunol. 2017;8:1867. Published
2017 Dec 22. doi:10.3389/fimmu.2017.01867

5. Konkol S, Rai M. Lymphohistiocytosis. [Updated 2021 Mar 27]. In: StatPearls [Internet]. Treasure Island
(FL): StatPearls Publishing; 2021 Jan