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HEALTH SCIENCES

Insights into EBV Infection in an Adult with X-Linked Lymphoproliferative Syndrome

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Background

- X-Linked Lymphoproliferative disease (XLP) is a rare Inborn Error of Immunity (IEI) characterized by immune dysregulation and increased susceptibility to Epstein-Barr Virus (EBV)¹.
- Hemophagocytic lymphohistiocytosis (HLH), often associated with EBV², is the leading cause of mortality in patients with XLP who forego haematopoietic stem cell transplantation (HSCT).
- Rituximab has been used in the treatment of EBV viremia in the setting of post-transplant lymphoproliferative disease³⁻⁴. In this case, it was ineffective.
- We present a patient with XLP1, and progressive EBV viremia, who responded well to one dose of nivolumab.

Mechanism of Action



Figure 1. Mechanism of action of Nivolumab in EBV infection.

Clinical Case Presentation

Initial Presentation (Age 8)

-Initially seen for recurrent otitis media and an episode of septic hip arthritis

-Diagnosed with common variable immunodeficiency (CVID) at age 8 and started on immunoglobulin replacement therapy

Adult Hospitalizations (Age 37)

-Admitted for respiratory failure to ICU

-Found to have hemolytic anemia and thrombocytopenia and started on steroids for presumed Evan's syndrome

-Admitted due to brain abscesses requiring surgical evacuation

Interval History

-Approximately 30 years on IVIG without any significant infectious or autoimmune conditions

-Diagnosed with noncirrhotic portal hypertension, presumed secondary to nodular regenerative hyperplasia (NRH)

Adult Hospitalizations (Age 37)

-Multiple admissions for progressive ascites and liver abscesses, severe COVID requiring ICU admission, and gram negative bacteremia

-Evaluated for possible liver transplant due to hepatopulmonary syndrome

-Immunology team re-involved, genetic testing sent and referral made for stem cell transplant

Genetic testing revealed a pathogenic variant in SH2D1A c.138-2A>G predicted to affect an acceptor splice site in Exon 1

XLP1 Diagnosis

-Genetic testing identified a pathogenic variant in SH2D1A c.138-2A>G consistent with XLP1

-Admitted due to EBV viremia and EBV hepatitis, started on Rituximab. Deemed ineligible for stem cell and liver transplantation

-Due to progressive EBV viremia despite rituximab, virus-specific T-cell therapy (VST) pursued but too unstable for transfer to US facility

Outcome

-Given a single dose of PD-1 inhibitor (nivolumab)

-EBV viremia decreased from approximately 201,000 IU/mL to 9,600 IU/mL

-Unfortunately succumbed to sepsis and multiorgan failure



References



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EBV DNA and Nivolumab



Figure 2. EBV DNA levels in relation to Nivolumab administration.

Outcome and Recommendations

- Our patient ultimately succumbed to sepsis and respiratory failure.
- Despite limited literature, PD-1 inhibitors may play a significant role in the treatment of certain EBVassociated conditions, particularly in patients with IEIs.
- We recommend considering PD-1 inhibition for any patient with overwhelming EBV infection.
- Severe EBV disease in a patient with a longstanding CVID diagnosis emphasizes the need to genotype for potentially pivotal molecular diagnosis.
- Treatment options for EBV susceptibility disorders need further exploration and accessibility.