Chronic Activation of Epstein-Barr virus mimicking toxic hepatitis

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Introduction: In rare cases, Epstein-Barr virus(EBV) develops into a chronic disease, in which its symptoms are similar to those of infectious mononucleosis. This disease is called chronic activation of EBV(CAEBV) and the only curative treatment is hematopoietic stem cell transplantation(HSCT). We report a rare case of this disease which was similar to toxic hepatitis.

Case: 2 years ago, A 24-year-old female who was previously healthy incidentally found her liver enzyme was elevated. Her only symptom was intermittent mild fever, which was refractory to antipyretics. Despite taking hepatotonic, her liver enzyme didn't normalize. Her ANA and ASMA markers were positive so a liver biopsy was performed to diagnose autoimmune hepatitis. We found the liver specimen to be EBV positive, but further pathology found it more likely to be mild toxic hepatitis. After having hepatotonics for 4months her liver enzyme was normalized temporarily, but after 10months it was elevated again. At that point we detected 1% of atypical lymphocyte in blood. We biopsied her liver again and EBV was still positive, and atypical lymphocyte in blood was increased to 66%. Her serology showed EBV-VCA IgG positive, VAC IgM negative, EBV-NA positive but EBV-EA positive. EBV IgG and DNA were positive too, so bone marrow biopsy was done to find out the possibility of hematologic disorder including malignancy. With the second biopsy and lab results, CAEBV was diagnosed. In bone marrow, NK cells and EBV positive lymphoid cell were found. We used etoposide but EBV DNA and atypical lymphocyte were still high, so rituximab was used together. But her EBV DNA was still positive and atypical lymphocyte was 41%. We decided rituximab had failed so HSCT was planned. After HSCT her EBV DNA was converted to negative and atypical lymphocyte was not found.

Conclusion: In this case chemotherapy and rituximab weren't helpful so early HSCT was used as a curative approach. If diagnosis was delayed, the patient may have had more severe course such as multiorgan failure or EBV-related malignancy. CAEBV can be mistaken as hepatitis, so it's important to consider CAEBV if patient with hepatitis and EBV marker is positive.

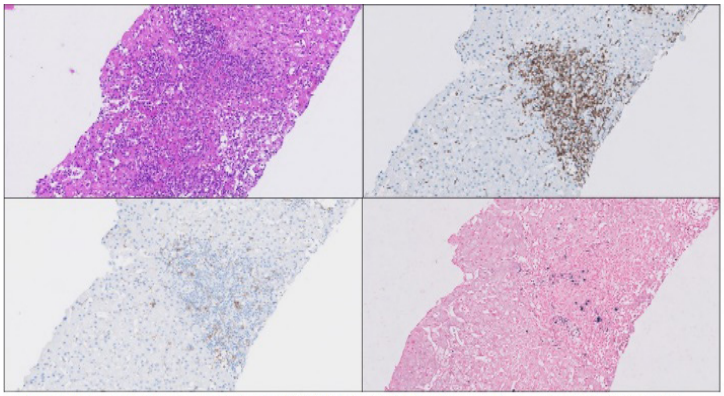

Figure 1. (A) The liver was involved by sinusoidal infiltration of lymphocytes which are small and without atypia. These lymphocytes are positive for (B) CD3, (C) CD56, and (D) EBV in situ hybridization, which support the both T and NK cell lineage feature with EBV infection.

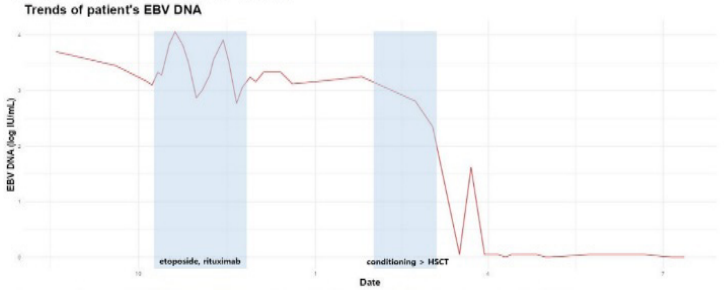

Figure 2. Patient's EBV DNA was decreased after HSCT and did not elevated again after discharge.

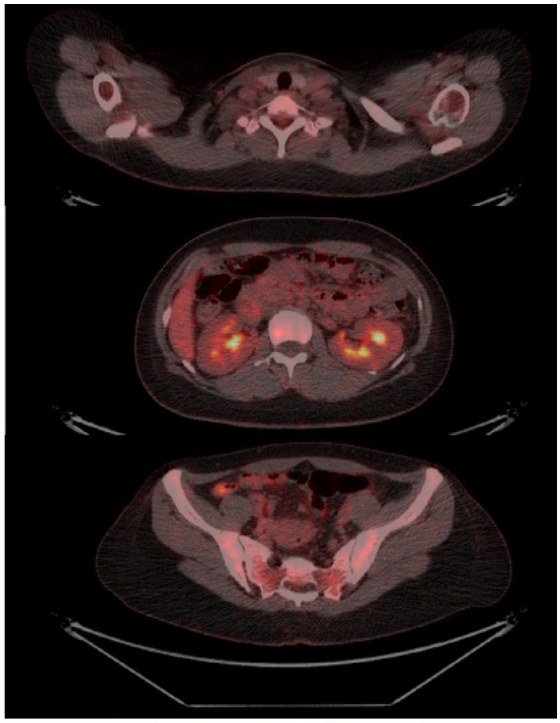

Figure 3. On patient's PET-CT, there was no lymph node enlargement, suggesting that she do not have malignant disease.