Abstract: P2114

Title: CLINICAL FEATURES AND PROGNOSTIC FACTORS OF ADULT SYSTEMIC CHRONIC ACTIVE EPSTEIN-BARR VIRUS DISEASE: A RETROSPECTIVE ANALYSIS USING JAPANESE REGISTRY DATA

Abstract Type: e-Poster Presentation

Topic: Lymphoma biology & translational research

Background:

Systemic chronic active Epstein-Barr virus disease (sCAEBV) is an intractable disease in which EBV persistently infects T and NK cells, resulting in systemic chronic inflammation and their clonal proliferation. The patients of sCAEBV have been reported mainly from East Asia, particularly Japan. However, reports from Europe and the United States have increased since CAEBV was listed in the WHO classification of hematopoietic tumors revised in 2017.

Initially, sCAEBV was considered as a pediatric disease, but the report of the nationwide survey of Japan have revealed that more than half of patients with sCAEBV are adults (Blood adv. 2020, 4, p2918). According to the report, allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only curative treatment currently available. Furthermore, the prognosis of adult patients is worse than that of pediatric patients.

Aims:

The purpose of this study was to elucidate the pathophysiology of adult sCAEBV and to identify the factors contributing to its poor prognosis.

Methods:

Using the registry data of the Japanese Ministry of Health, Labour and Welfare research group, we analyzed the patients of our institutes, St. Marianna Medical University Hospital and Tokyo Medical and Dental University Hospital, which are the top two high volume institutions of sCAEBV in Japan. Patients were diagnosed as sCAEBV when they fulfilled all four of the following criteria: (1) systemic inflammatory symptoms lasting for more than 3 months, (2) Elevated EBV-DNA load in PB (> 102.5 copies/mg DNA), (3) EB virus infection in T cells or NK cells, and (4) different from other known disease. The diagnostic criteria meet the definition of sCAEBV in the WHO classification.

Results:

Fifty-eight patients were analyzed. Ages at diagnosis were between 18 and 64 (median 34), and the male/female ratio was 30/28. EBV-infected cells were CD4-positive in 25 patients, CD8-positive in eight patients, and CD56-positive in 19 patients. Two patients were of CD56-negative NK cells. Three patients were infected in both T and NK cells. One patient was identified with CD4 and CD8 co-positive cells. No patient had a history of infectious mononucleosis. Four patients developed from hydroa vacciniforme lymphoproliferative disorder, and CD4 positive cells were infected in all the four patients. Six patients developed from severe mosquito bite allergy. Among the six patients, the infected cells were CD4-positive cells in three patients and CD56-positive cells in the other three patients. The 3-year survival rate (3y-OS) from the time of diagnosis was 45.9%. Forty-eight patients underwent allo-HSCT resulting in the 3y-OS of 53.9%. The 3y-OS after allo-HSCT was significantly lower in patients with following records at diagnosis: ALT > twice the institutional standard value ($p < 0.001$), platelet count < 50,000 /μL ($p < 0.05$), and sIL-2R > 2500 U/mL ($p < 0.005$). The 3y-OS of patients with EBV-DNA detected in the plasma tended to be lower. In multivariate analysis, high ALT level was associated with poor prognosis ($p < 0.005$).

Summary/Conclusion:

Our study highlights the significance of liver dysfunction in the poor prognosis of adult sCAEBV patients.

Keywords: Hemophagocytic Lymphohistiocytosis (HLH), Lymphoma, EBV