Clinical Features and Prognostic Factors of Children with Chronic Active Epstein-Barr Virus Infection: A Retrospective Analysis of a Single-center

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Background: CAEBV is considered rare and geographically limited to China, Japan, and the East Asia; however, is drawing international attention because of the increasing case number reported worldwide. In 2016 WHO classification, CAEBV was identified as the EBV-positive T- or NK-neoplasms. Patients with CAEBV present EBV infected T-lymphocytes or NK cells clonally proliferation, causing elevated levels of EBV-DNA in the blood and infiltration of multiple organs by EBV-positive lymphocytes. The clinical symptoms of patients with CAEBV include fever, lymphadenopathy, hepatomegaly, splenomegaly or pancytopenia, and some children would suffer from hemophagocytic lymphohistiocytosis (HLH) or develop chemotherapy resistant lymphoma with dismal prognosis. Unfortunately, the mechanisms of EBV infecting T-lymphocytes or NK cells in patients with CAEBV are still unclear, and there was no safe and effective treatment for CAEBV now. In this study, we collected the clinical data of 96 children with CAEBV in our center to analyze the clinical characteristics and the prognostic factors of this disease.

Materials and Method: Observational analysis of baseline data and follow-up evaluation data of children with CAEBV in our center between Jan 1st, 2016 and Dec 31st, 2019, and were followed up to Jun 30th, 2020.

Results: There were 96 children with CAEBV, including 50 males and 46 females, with the median age was 6.7 years (range from 0.6-17.6 years). The median follow-up time was 16.5 months. The three most common clinical manifestations were fever, lymph node enlargement, and hepatomegaly or splenomegaly. Thirty-three patients (36.3%) also had a diagnosis of hemophagocytic lymphohistiocytosis (HLH). EBV infected only T-lymphocytes, NK cells, or both T- and NK-cell types in 15 (33.3%), 17 (37.8%), and 13 (28.9%) respectively. At the end of follow-up, 26 children died and 60 survived, 10 were lost to follow-up. Generally, progression-free survival was 69.8 ± 2.4%. The level of "IL-6 and IL-10" and the combination of 'younger age and lower pathologic grade' were independent prognostic factors by Cox regression analysis (P=0.009 and 0.018 respectively).

Conclusion: Children with lower IL-6 and IL-10, or with younger age and lower pathological grades, generally had favorable outcomes at the terminal point of following-up, indicated better prognostic signs.

Keywords: Chronic active Epstein-Barr virus, Children, Clinical characteristics, Prognostic factors