Hydora Vacciniforme-like Lymphoproliferative Disorder in a Young Asian Female: From self-limited lesions to Hemophagocytic Syndrome, a Five-year Follow-up

Introduction: Hydora vacciniforme-like lymphoproliferative disorder (HV-LPD) is a rare Epstein-Barr virus (EBV)-related disease that primarily affects East Asians and Latin Americans. The clinical course and standardized management remained controversial. We reported a case presented with a progressive clinical course that harbored an immunodeficiency background detected by targeted sequencing.

Case report: A 21-year-old Chinese female presented with recurrent necrotic papulovesicular lesions distributed on the sun-exposed area without systemic symptoms for 1 year on her first visit in 2018. Skin biopsy revealed dense dermal perivascular and periadnexal lymphocytic infiltration with a few atypical lymphoid cells positive for CD3, CD8, TIA-1, and EBER. The EBV DNA level in her serum was 4 x 10^7 copies/ml (reference value <200 copies/ mL). T-cell receptor gene rearrangement studies by PCR demonstrated clonal rearrangements of the γ and β chains. A diagnosis of Hydroa vacciniforme-like lymphoproliferative disorder (HV-LPD) was made. In the following two years, the patient was successively treated by interferon subcutaneous injection, oral corticosteroids, and methotrexate and her skin lesions ran a waxing and waning course. In 2021, she visited our center for the second time due to the aggravated papulovesicles and ulcers expanding to sun-protected areas, this time accompanied by recurrent fever, anemia, and liver dysfunction. A repeated skin biopsy found deep and dense lymphoid infiltrates affecting subcutaneous adipose tissue with a similar immunophenotype and TCR rearrangement results but significantly higher cytological atypia and mitotic counts. The EBV DNA level in her serum was 9 x 10^5 copies/ml this time and EBV sorting PCR identified that EBV mainly infected T and NK cells. Targeted sequencing for hemophagocytic syndrome (HPS)-associated genes revealed a somatic mutation of RAG2 (exon2: c.577_580dup resulting in p.Ser194TyrfsTer22), indicating a potential immunodeficiency background. The patient was diagnosed with chronic active EBV infection (CAEBV) and underwent 3 cycles of PD-1 blockade immunotherapy (Nivolumab 200mg). The skin lesions and systemic symptoms were significantly alleviated in the first six months but dramatically exacerbated due to acute cholecystitis and infection-triggered hemophagocytic syndrome. After her recovery, allogeneic hematopoietic stem cell transplantation (HSCT) was suggested and matching started. Unfortunately, she died of acute liver failure during the HSCT preparation process in 2022.

Discussion: HV-LPD might run an aggressive clinical course in the Asia population, especially in individuals with high viral load. A standardized risk stratification system including targeted sequencing for HPS tendency and EBV sorting PCR might contribute to decision-making of HSCT.