Brief Report Annals of Dermatology 2022;34(5) • https://doi.org/10.5021/ad.20.199

A Case of Hydroa Vacciniforme-Like Lymphoproliferative Disorder Presenting As Orogenital Ulcerations

Yingyi Li[1,2,3], Yang Wang[1,2,3]

[1]Department of Dermatology and Venerology, Peking University First Hospital, [2]Beijing Key Laboratory of Molecular Diagnosis on Dermatoses, [3]National Clinical Research Center for Skin and Immune Diseases, Beijing, China

Dear Editor:

Hydroa vacciniforme (HV)-like lymphoproliferative disease (LPD) is associated with chronic active Epstein-Barr virus (CAEBV) infection. It ranges from classic and severe/systemic HV to HV-like lymphoma (HVLL)[1]. Cutaneous manifestations include vesiculopapules, bullae, ulcers, and facial swelling[1]. HVLL usually has a long clinical course with spontaneous resolution[1] but may progress to more severe and life-threatening conditions[2]. We report a rare case of HV-like LPD that evolved from classic HV to orogenital ulcerations.

A 17-year-old Chinese boy presented with a 2-month history of painful orogenital swelling and ulcerative lesions without constitutional symptoms. He was diagnosed with classic HV at age 2 years, based on the typical papulovesicular eruptions on his face and photosensitivity. The symptoms spontaneously resolved 2 years before without recurrence, leaving facial varioliform scars (Fig. 1A). Physical examination revealed marked swelling on the lower lip and massive erosions with ulcerations on the scrotum (Fig. 1A, B). No lymphadenopathy was observed. A skin biopsy from the lower lip showed diffuse infiltrates of atypical lymphoid cells throughout the dermis, with remarkable epidermotropism (Fig. 2A). Immunohistochemical analysis revealed CD3+++, CD4+++, Granzyme B++, and TIA1+++ infiltrating lymphocytes, consistent with

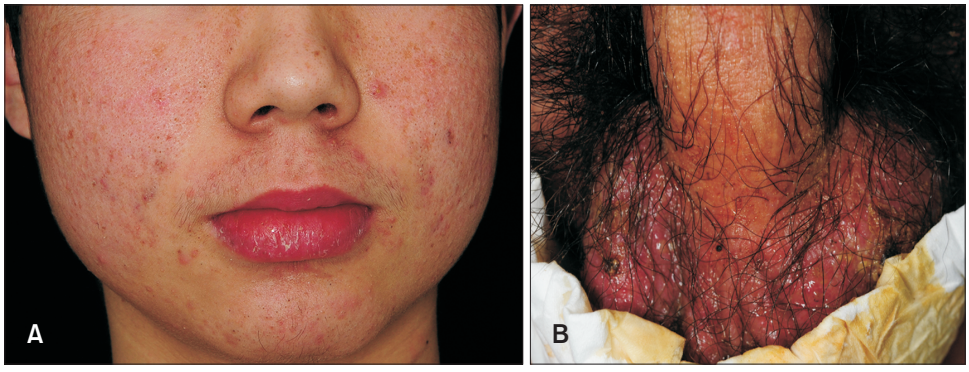

Fig. 1. We received the patient's consent form about publishing all photographic materials. (A) Lower lip swelling with scales and varioliform scars on the face. (B) Remarkable erosions and ulcerations on the scrotum.

Received July 21, 2020 **Revised** December 14, 2020 **Accepted** January 19, 2021

Corresponding Author
Yang Wang
Department of Dermatology and Venerology, Peking University First Hospital, No.8 Xishiku Street, Xicheng District, Beijing 100034, China
Tel: +86-10-83572350, Fax: +86-10-66551216, E-mail: yangwang_dr@bjmu.edu.cn
https://orcid.org/0000-0001-7805-2861

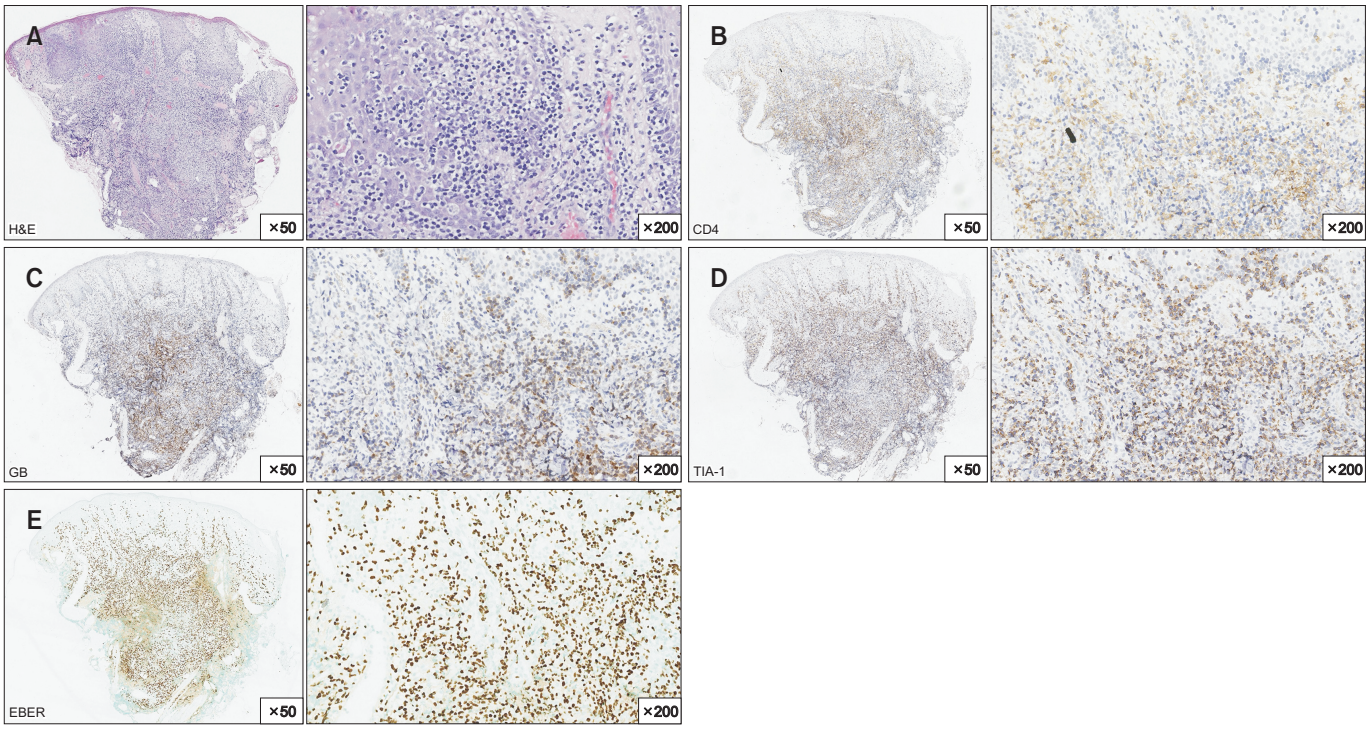

Fig. 2. (A) Histopathology shows diffuse infiltrate of atypical lymphoid cells in the dermis, with marked epidermotropism (H&E, left: magnification ×50, right: magnification ×200). (B~D) Immunostaining reveals that the infiltrating lymphocytes were positive for CD4, Granzyme B, and TIA-1 (left: magnification ×50; right: magnification ×200). (E) *In situ* hybridization showed strong EBV-encoded small RNA (EBER) positivity throughout the infiltrating lymphocytes (left: magnification ×50; right: magnification ×200).

an activated cytotoxic T-cell phenotype (Fig. 2B~D). *In situ* hybridization for EBV-encoded small RNA (EBER) revealed diffuse positivity (Fig. 2E). T-cell receptor gene gamma rearrangement indicated clonality. Peripheral blood flow cytometry demonstrated normal amounts of CD3+/CD4+ T cells and CD3+CD8+ T cells. The EBV DNA viral load in peripheral lymphocytes was elevated (1.69×10^6 copies/ml; normal range, 0~5,000 copies/ml). Titers of IgG antibodies to the EBV capsid antigen and EBV nuclear antigen-1 were high. These findings confirmed the diagnosis of HV-like LPD. The patient was then treated with interferon alpha-2b 300 IU 3 times per week based on previous reports but showed no significant improvement[2]. As his orogenital swelling and ulcerations worsened, human leukocyte antigen-haploidentical donor lymphocyte infusion was administered[3]. A total of 4.8×10^9 peripheral blood mononuclear cells (about 1×10^8/kg) was infused. The lesions gradually resolved and remained stable thereafter.

HV-like LPD is a chronic EBV-positive lymphoproliferative disorder with a broad spectrum of clinical aggressive[1,2]. Classic HV is a benign photodermatosis characterized by cursted papulovesicles and varicelliform scars after healing[1], as in our patient in childhood. As the disease progresses, more extensive skin lesions develop[1], such as blisters, ulcers, exaggerated arthropod bite reactions, and edema[4]. Oculomucosal and gastrointestinal involvement are sometimes complicated[5]. Overt systemic lymphoma may occur and lead to poor prognosis[1,4]. No standard treatment has been established. A conservative approach is recommended for indolent cases, whereas hematopoietic stem cell transplantation might benefit patients with advanced cases[1,2].

Our patient presented with ulcerative lesions solely on the orogenital area after 2 years of HV remission, which has not been described in previous cases of HV-like LPD. The presence of clonal T cells indicated the possibility of progression to lymphoma[2]. Conservative treatment was ineffective for disease control. This case highlights the importance of recognizing the uncommon clinical features of CAEBV. It shows that classic HV may progress even after years of remission of the initial manifestations.

ACKNOWLEDGMENT

The authors thank the staff of Department of Hematology at Peking University First Hospital for providing treatment information.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

FUNDING SOURCE

None.

ORCID

Yingyi Li, https://orcid.org/0000-0003-1097-0230
Yang Wang, https://orcid.org/0000-0001-7805-2861

REFERENCES

1. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, et al. WHO classification of tumours of haematopoietic and lymphoid tissues. 4th revised ed. Lyon: International Agency for Research on Cancer, 2017:355-362.
2. Quintanilla-Martinez L, Ridaura C, Nagl F, Sáez-de-Ocariz M, Durán-McKinster C, Ruiz-Maldonado R, et al. Hydroa vacciniforme-like lymphoma: a chronic EBV+ lymphoproliferative disorder with risk to develop a systemic lymphoma. Blood 2013;122:3101-3110.
3. Wang Q, Liu H, Zhang X, Liu Q, Xing Y, Zhou X, et al. High doses of mother's lymphocyte infusion to treat EBV-positive T-cell lymphoproliferative disorders in childhood. Blood 2010;116:5941-5947.
4. Sangueza M, Plaza JA. Hydroa vacciniforme-like cutaneous T-cell lymphoma: clinicopathologic and immunohistochemical study of 12 cases. J Am Acad Dermatol 2013;69:112-119.
5. Yamamoto T, Hirai Y, Miyake T, Yamasaki O, Morizane S, Iwatsuki K. Oculomucosal and gastrointestinal involvement in Epstein-Barr virus-associated hydroa vacciniforme. Eur J Dermatol 2012;22:380-383.