Epstein-Barr Virus Positive T-Cell Lymphoproliferative Disorder: One Case and a Short Literature Review

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Abstract: This report delineates a rare case of Epstein-Barr Virus-Positive T-Cell Lymphoproliferative Disorder (EBV+T-LPD), which represents a disease spectrum encompassing entities from indolent cutaneous forms to aggressive systemic lymphomas. This case concerns an 85-year-old male who presented with a four-month history of recurrent rash, fever, and localized lymphadenopathy. Notably, this elderly male patient exhibited cutaneous-limited involvement and demonstrated a favorable prognosis-an outcome rarely documented in previous literature, and to the best of our knowledge, this represents the oldest case reported to date. Additionally, a review of published literature on adult-onset EBV^+ T-LPD presenting with cutaneous manifestations is also provided.

***Keywords*:** Epstein-Barr Virus-Positive T-Cell Lymphoproliferative Disorder; EBV; elderly; case summary

1. Introduction

Epstein-Barr virus-positive T-cell lymphoproliferative disorder(EBV+T-LPD) is a rare disease spectrum associated with EBV infection, predominantly exhibiting a T-cell phenotype and commonly affecting individuals of Asian and Latin American descent. The 2022 World Health Organization (WHO) classification recognizes several entities within this spectrum, characterized by divergent outcomes: EBV-positive nodal T- and NK-cell lymphoma, extranodal NK/T-cell lymphoma, severe mosquito bite allergy, hydroa vacciniforme lymphoproliferative disorder (HV-LPD), systemic chronic active EBV disease, and systemic EBV-positive T-cell lymphoma of childhood[1]. Herein, we present two cases, focusing primarily on their cutaneous manifestations and diagnostic approach.

2. Case Presentation

An 85-year-old man without immunodeficiency presented with a four-month history of high-grade fever, painful nodules, papules, necrosis, and deep, well-demarcated ulcers with black eschars on the trunk and limbs (Figure 1). He initially sought care at a local hospital, where a skin biopsy suggested leukocytoclastic vasculitis, leading to a diagnosis of 'vasculitis and skin infection'. Treatment with methylprednisolone (for immunosuppression) and clindamycin (for anti-infection) was ineffective. The skin biopsy revealed necrotic epidermis/dermis, extensive extravasation of red blood cells and scattered lymphocytic infiltration. Critically, immunohistochemistry was negative for CD3, CD20, CD30, and CD56, but was focally positive for EBER (EBV-encoded RNA).

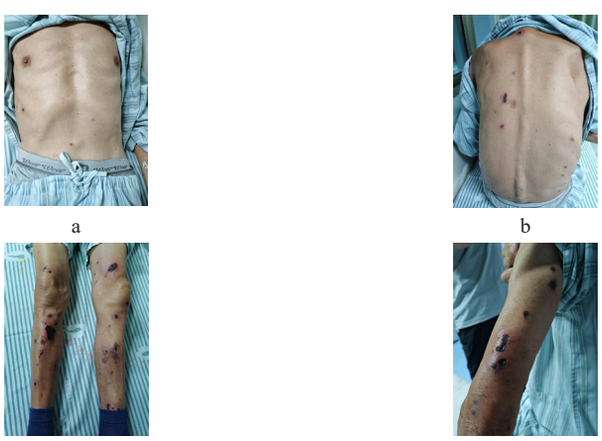

Figure 1. Clinical features. Diffuse papules, necrosis and scabs on the trunk and limbs (a,b). Deep ulcers with a diameter of 1-5 cm scattered on both lower limbs with clear boundaries, black thick scabs at the bottom, edematous redness at the periphery, and edema of the right lower limb (c,d).

Following admission, reevaluation showed elevated monocytes and basophils, mild anemia, and positive EBV serology (VCA-IgG 588.00 U/mL, EBNA-IgG 36.60 U/mL).The remaining test, including electrolytes, tumor markers, and culture of skin lesion secretions, showed no significant abnormalities. To evaluate for systemic involvement, a PET-CT scan was performed. It revealed enlarged axillary nodes and FDG-avid skin thickening in lower limbs without visceral involvement. Integrating these findings, a diagnosis of EBV+ T-LPD was made.

The patient received intravenous methylprednisolone 40 mg daily for several days, followed by a transition to oral prednisolone (30 mg/day) with a subsequent slow taper. Adjunctive therapy included ganciclovir (antiviral) and piperacillin (anti-infective). The patient's clinical symptoms showed significant improvement by the time of discharge.

3. Case Summary

Furthermore, we retrieved and summarized the relevant clinical data of adult patients with EBV T-cell lymphoproliferative disorder presenting with cutaneous manifestations, as detailed in Table 1.Among the reported cases, except for one attributed to immunosuppression from long-term methotrexate use (with rash resolving after discontinuation), all other patients were treated with chemotherapeutic agents. In contrast, our patient received only glucocorticoids and antiviral therapy, which led to rash improvement. This suggests that EBV T-LPD can follow an indolent course in older patients, and in this context, aggressive treatment may be avoided.

Table 1. Summary of the adult cases presenting with cutaneous involvement

Publication Year	Case No.	Patient Demographics	Key Clinical Manifestations	Primary Treatment	Outcome & Follow-up
2010	2	Male, 58; Male, 57	Ulcerative lesion on left forearm; Erythema, swelling, and ulceration on left upper and lower limbs	Chemotherapy (including cyclophosphamide)	Skin lesions improved
2014	1	Male, 70 years old	Multiple papules on face and back; Pulmonary involvement	11 cycles of chemotherapy with cyclophosphamide	Skin rash improved
2015	1	White female (onset in childhood)	Recurrent necrotizing skin papules; Involvement of paranasal and maxillary sinuses; Hepatosplenomegaly	Chemotherapy, prednisone, cyclophosphamide, rituximab	Recurrent skin eruptions
2022	1	Female, 32 years old	Solitary reddish-brown plaque on trunk following adalimumab therapy; Systemic lymphoma	Chemotherapy	Death at 4 weeks
2025	1	Female, 33 years old	Large ulcer on left upper limb exposing muscle and nerve tissue	Interferon, chemotherapy, phototherapy, anti-infection, nutritional support	Lesions gradually healed

4. Discussion

EBV-associated lymphoproliferative disorders constitute a broad category of diseases characterized by excessive lymphoid proliferation. This entity essentially represents a disease spectrum encompassing various stages, from benign hyperplasia to malignant lymphoma. Adult-onset cases are rare and typically exhibit rapid progression. However, the elderly patient reported herein demonstrated relatively mild clinical symptoms and a favorable prognosis, which contrasts with typical reports. The pathogenesis of EBV+ T-LPD remains incompletely elucidated,genetic polymorphisms in host immune response genes are believed to play a significant role. Through analysis of 21 patients, W et al. proposed a potential association between the disease and deletions in the EBV genome[2]. R et al. suggested that mutations in PIK3CD and TNFRSF9 cause abnormal proliferation of EBV-infected T cells by disrupting the functional balance of T cells[3].

Currently, no standardized treatment protocols exist for this disease. Conservative management strategies include antiviral agents, interferon-gamma, systemic corticosteroids, and cyclosporine A. Recently, Susan J. Keam reported on the potential approval of tabelecleucel for treating recurrent or refractory EBV+ T-LPD[4]. Based on an overview of transcriptomic abnormalities, Eel et al. proposed that immune checkpoint inhibition and JAK inhibition hold potential therapeutic value[5]. Ruan et al. first described the use of intravenous immunoglobulin (IVIG) as a treatment, reporting higher survival rates and significant reductions in both disease severity and recurrence frequency[6]. Guo et al. indicated that hematopoietic stem cell transplantation (HSCT) remains the only potentially curative treatment for HV-LPD.A recent study reported that the combination of Nivolumab and emapalumab exhibited efficacy against EBV-associated T/NK-cell lymphoproliferative disorders (EBV T/NK-LPDs), with an acceptable safety profile[7].

5. Conclusion

In summary, we reported a EBV+ T-LPD typically affects children and young adults, with most reported cases being severe and rapidly progressive. However, our case was characterized not only by distinctive cutaneous manifestations, but also by an older age at onset, absence of an immunodeficiency history, and a favorable prognosis,this is uncommon among previously described cases.

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