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CASE REPORT

Lymphomatoid Papulosis Type E With T-Cell Receptor Gamma Positivity

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Abstract: Lymphomatoid papulosis (LyP) is currently categorized as a primary lymphoproliferative disorder that follows a chronic, recurrent clinical course. The diagnosis of LyP is mainly based on clinical presentation and histopathological correlation. Six subtypes of LyP have been described and recognized, each with different histological features and sometimes distinct clinical presentations. LyP type E is a subtype that histologically shows angioinvasion and angiodestruction by CD8 and CD30-positive pleomorphic T cells. Clinically, it usually presents with a few large necrotic nodules or ulcers on the trunk or extremities, unlike other subtypes of LyP. Despite an indolent clinical course, long-term follow-up is necessary due to the risk of developing concurrent or secondary lymphoma. In this report, we demonstrate a case of lymphomatoid papulosis type E presented with widespread small papulonecrotic eruptions, an atypical clinical manifestation, and an unusual immunohistochemical profile. The biopsy revealed CD8, CD30, CD56, and TCR-γ-positive atypical lymphocytic infiltration with angioinvasion and angiodestruction. The patient was successfully treated with low-dose methotrexate.

Keywords: CD30, CD56, cutaneous T-cell lymphoma, lymphoproliferative disorder, papulonecrotic skin disease

Introduction

Pityriasis lichenoides et varioliformis acuta (PLEVA) is an inflammatory dermatosis that usually presents with an abrupt eruption of 2–3 mm erythematous macules and papulovesicular lesions rapidly developing into necrotic crusts.[1,2] Lymphomatoid papulosis (LyP), on the other hand, has six subtypes that differ mainly by their histopathological and immunohistochemical profiles.[3] Akin to PLEVA, most LyPs manifest as recurrent crops of widespread papulonecrotic eruptions follow by spontaneous regression within several weeks.[4] Due to the resemblance of the clinical presentations of both diseases, histopathology and immunohistochemistry are crucial for a definite diagnosis. LyP type E, however, was typically reported as oligolesional, large eschar-like papules or nodules, which were confirmed by the presence of angioinvasion and destruction by CD8 and CD30-positive lymphocytes on histopathology. In this report, we present a case of LyP type E presented with clinical mimics of PLEVA and demonstrated unusual immunohistochemical staining, namely CD56 and TCR-γ positivity.

Case Report

A 17-year-old female presented with generalized papulonecrotic eruptions on her trunk and extremities for 3 weeks (Figure 1A – C). On further examination, the patient was afebrile with no other systemic signs or symptoms. There was no lymphadenopathy or hepatosplenomegaly. The patient denied any underlying disease or family history of malignancy. The differential diagnosis included PLEVA, LyP, and disseminated herpes simplex or zoster infection. A complete blood count showed only slight leukocytosis (12,300/cumm). The liver function test and the lactate dehydrogenase level were unremarkable. The skin biopsy was taken from a lesion on her right arm. Histopathology showed marked epidermal

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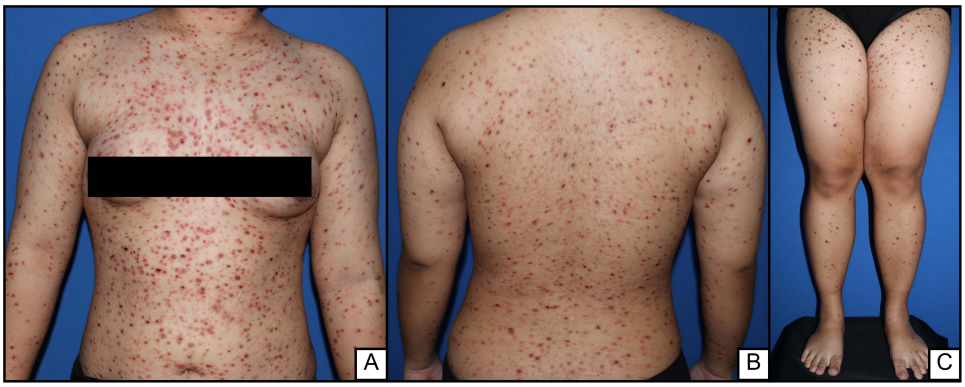

Figure 1 Multiple erythematous papules with central necrotic crusts on the trunk (**A** and **B**) and extremities (**C**).

necrosis with dense, superficial and deep perivascular and perifollicular cell infiltration. The infiltrating cells were composed mainly of atypical small-to-medium-sized lymphocytes with mitotic activity admixed with some neutrophils and extravasated erythrocytes (Figure 2A and B). The angioinvasion, with atypical cells infiltrated into the lumen of the vessels, and the angiodestruction, represented by fibrinoid necrosis, nuclear dusts, and intraluminal thrombi, were noted (Figure 2C and D). The immunohistochemistry demonstrated atypical lymphocytes stained positive for CD3 but negative for CD20, indicating T-cell origin. The cells were positive for CD8 and positive for CD30 but negative for CD4 in perivascular areas. Additionally, Ki-67 was positive at 80%, categorized as CD8+CD30+ T-cell lymphoma. The atypical cells were also positive for CD56, TIA-1, and granzyme B but negative for Epstein-Barr virus (EBV)-encoded RNA (EBER) in situ hybridization. The TCR-γ was positive, while the beta-F1 (βF1) was negative. The immunohistochemistry pictures are depicted in Figure 3A – F. The CD30 was positive at 40% of CD3-positive-cells showed in Figure 4A and B. In this case, TCR gene rearrangement demonstrated the monoclonality of both TCR-γ and TCR-β. Based on the clinical presentation of eruptive eschar-like lesions and histopathological findings of atypical CD8 and CD30-positive T-cell

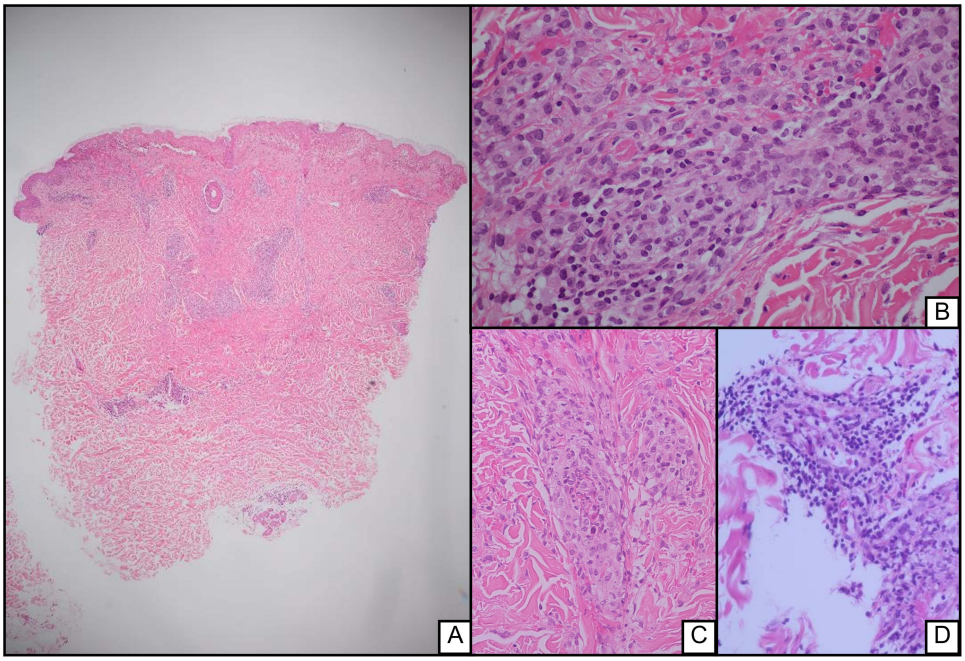

Figure 2 Dense superficial and deep perivascular cell infiltration with epidermal necrosis (H&E; original magnification x40) (**A**). Atypical small to medium sized lymphoid cells with mitotic activity admixed with some neutrophils and extravasated erythrocytes (H&E; original magnification x400) (**B**). Atypical cells infiltrated into vascular lumen (H&E; original magnification x400) (**C**). Angiodestruction of blood vessel (H&E, x400) (**D**).

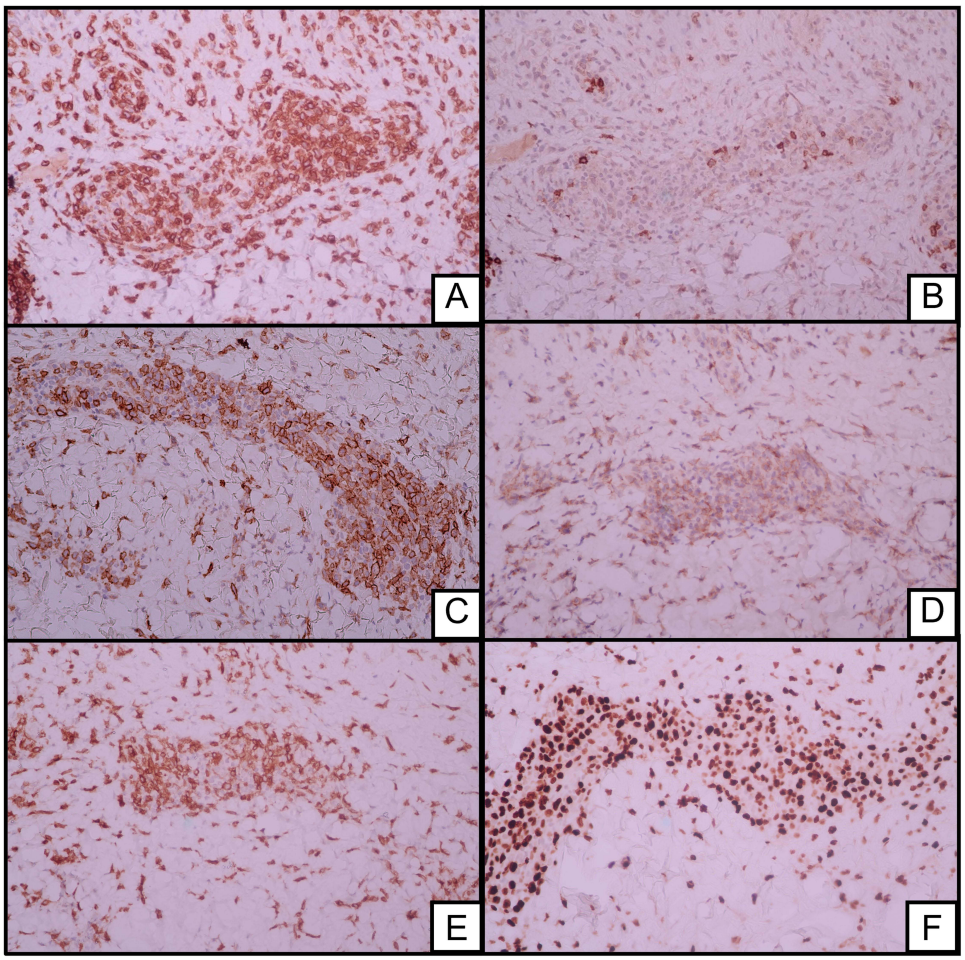

Figure 3 The atypical small-to-medium lymphoid cells infiltrating the vessels are positive for CD3 (**A**), CD8 (**B**), CD30 (**C**), CD56 (**D**), TCR-γ (**E**), and 80% positive for Ki-67 (**F**) (original magnification x400).

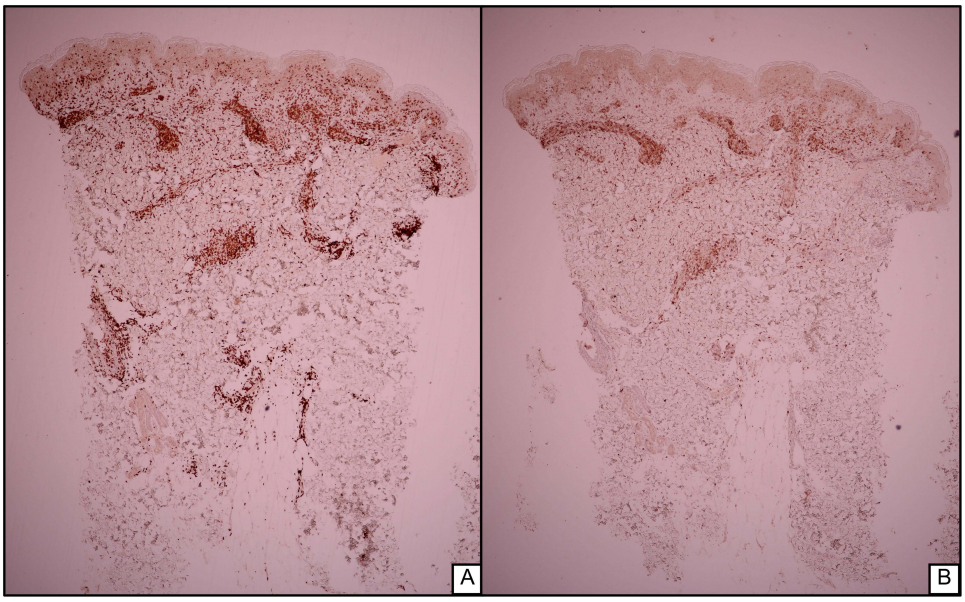

Figure 4 CD3-positive cells (**A**) compared to CD30-positive cells (40%) (**B**) (original magnification x40).

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infiltration with angioinvasion and angiodestruction, LyP type E was diagnosed in this patient. The patient was treated with 7.5 mg of methotrexate weekly, together with a daily dose of a 5-mg folate supplement and a twice-daily application of betamethasone valerate cream. The patient's skin lesions showed marked improvement after 2 months of follow-up. We decided to taper the dosage of methotrexate to 5 mg per week. No new eruptions were noted during the tapering.

Discussion

LyP is one of the CD30-positive cutaneous lymphoproliferative disorders. Its diagnosis portends a chronic and relapsing clinical course. LyP commonly presents with crops of few to numerous papulonecrotic lesions scattered on the trunk and extremities, which, after some time, spontaneously involute, leaving post-inflammatory hypopigmentation or hyperpigmentation, or atrophic varioliform scars.[4–6] According to the 2018 WHO-EORTC classification for primary cutaneous lymphomas, LyP is considered to have six histopathological variants (A to E and DUSP22-IRF4 rearrangement).[3] LyP type E accounts for approximately 4–5% of all LyPs.[7] Kempf et al had described this variant of LyP in 2013 as angioinvasive LyP, with their entire case series of 16 patients demonstrating a similar clinical presentation of oligolesioinal papulonodules that developed ulceration that expanded beyond the border of the original lesions.[8] Since then, several case reports have emerged highlighting the clinical and immunological variation of LyP type E. The reported clinical variation of LyP type E is listed in Table 1. Oligolesional nodules and papules were the most common clinical presentation of LyP type E (55.17%), with other clinical presentations being equally sparse. Our patient's clinical presentation, namely generalized papules and/or vesicles with scarring, was found only in 1 previously reported patient (3.45%).[9]

The CD30+ T-cell lymphocytic infiltration should be differentiated from other lymphomas, including extranodal NK/T-cell lymphoma nasal type (ENKL), cutaneous γ/δ T-cell lymphoma (CGD-TCL), primary cutaneous and systemic anaplastic large cell lymphoma (pcALCL and sALCL), and non-neoplastic conditions, namely pseudolymphomatous drug eruption, arthropod bite reaction, and PLEVA.[5,9] In our patient, non-neoplastic processes, especially PLEVA, were ruled out due to marked cytological atypia and the presence of mitotic activity in the cell infiltrates. The cell infiltrate in our case was positive for CD3 and CD8 and negative for CD4. This agrees with previous reports of LyP type E having mainly CD8+ T-cells.[14] Histologically, angiodestruction and angioinvasion demonstrated in our case are also found in ENKL and CGD-TCL. Negative expression of EBER in situ hybridization helped exclude ENKL in our case.[14] Lastly, correlating with the clinical presentation of waxing and waning generalized papular eruptions, the diagnosis of LyP was favored over CGD-TCL, pcALCL, and sALCL. Interestingly, the cell infiltrate in our patient also showed CD56 expression, which is rather uncommon in LyP type E.[10] CD56 expression in T-cell lymphoproliferative disorders is usually associated with aggressive diseases, namely ENKL, CGD-TCL, pcALCL, sALCL, and adult T-cell leukemia/lymphoma.[15,16] In contrast to the aggressive lymphomas, there were six cases of CD56 expression in LyP type E. Furthermore, in some of these reports, CD56 expression contrastingly suggests a better clinical prognosis for LyP.[8,10–12,17] Most T-cell neoplasms express αβ-TCR, with few showing γδ-TCR. Nevertheless, there is still no significant benefit, apart from aiding in the diagnosis of certain lymphomas, in discriminating T-cell lymphomas between

Table 1 Various Clinical Presentations of Lymphomatoid Papulosis Type E

Reported Clinical Presentations of LyP Type E[6,8,10–13]	N=29
Oligolesional ulceronecrotic papules or nodules	16 (55.17%)
Vasculitis-like or purpura-like lesions	3 (10.34%)
Pyogenic granuloma-like ulcers	2 (6.90%)
Generalized papules and/or vesicles with scarring	1 (3.45%)
Generalized papules and/or vesicles without scarring	3 (10.34%)
Oral ulcers	3 (10.34%)
Localized papules	1 (3.45%)

αβ and γδ subtypes.[15] Reported cases of LyP usually have βF1 expression, but negative TCR-γ suggests it to be an αβ T-cell neoplasm.[8] There were a few reports of LyP showing γδ TCR expression.[13,18–20] Amongst these, the recent case series, reporting 26 LyP patients with TCR-γδ expression, contained a case of LyP type E. The clinical presentation of this case was noted to be papules on the limbs, unlike our case. Looking at immunohistochemistry, both this case and our case expressed CD3, CD8, and CD30 positivity. The γδ-T-cells, having originated from the precursors that were molecularly similar to NK cells, typically express some NK-associated surface molecule such as CD56 (in our case), TIA-1, and granzyme B (in the case of LyP type E with TCR-γδ expression from the case series and our case).[13] Kempf et al also found monoclonal TCR-γ gene arrangements in 60% of LyP type E, but all cases were either negative for TCR-γ or the immunohistochemistry was not done.[8] To the best of our knowledge, our case is the first case report of LyP type E with TCR-γ positivity via immunohistochemistry but demonstrated monoclonality of both TCR-γ and TCR-β via TCR gene rearrangement study.

Having a worrisome clinical presentation, LyP type E usually has a benign clinical prognosis.[8] Our patient was readily responsive to low-dose methotrexate and topical corticosteroids. No associated secondary lymphomas were yet detected during the follow-up period. However, at the time of this case report, the follow-up duration for this patient is relatively short. Having an established tendency to develop secondary lymphoma, this LyP patient will be continuously and vigilantly monitored.[11]

Conclusion

In summary, this is a case report of LyP type E presenting with generalized eruptions of necrotic papules with unusual CD56 and TCR-γ expression. The indolent nature of the disease is affirmed by the readily resolution of the lesions following low dose systemic methotrexate and topical corticosteroids and no recurrence in the 1-year follow-up period. However, a longer follow-up period is required to establish this indolent behavior.

Ethics Approval and Informed Consent

The patient's parents provided written informed consent for case details and accompanying images to be published. Institutional approval was not required to publish the case details.

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Disclosure

The authors declare no conflicts of interest in this work.

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