






Pityriasis Lichenoides Et Varioliformis Acuta and Lymphomatoid Papulosis Type F: A Case Report of Two Entities in One Patient

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Abstract: Pityriasis lichenoides et varioliformis acuta (PLEVA) and lymphomatoid papulosis (LyP) are uncommon inflammatory skin disorders that occasionally share clinicopathological features. Differentiating between the two entities remains problematic, and a definitive diagnosis usually requires multi-step investigations, which is an enormous challenge to physicians. We hereby report a rare case of a 22-year-old female patient diagnosed with PLEVA who later developed LyP type F, a new histological variant of LyP. Our report highlights that long-term follow-up is essential to determine associated hematologic malignancies, particularly in cases with recalcitrant or progressive cutaneous lesions of PLEVA and/or LyP.

Keywords: chronic inflammatory skin disease, CD30 positive lymphoproliferative disorders, immunohistochemistry, mycosis fungoides, pityriasis lichenoides, cutaneous lymphoma

Introduction

Pityriasis lichenoides et varioliformis acuta (PLEVA) and lymphomatoid papulosis (LyP) are uncommon skin disorders categorized as different entities. The former is considered a chronic recurrent inflammatory skin disease while the latter refers to a primary CD30+ cutaneous lymphoproliferative disorder. Clinically, PLEVA presents with acute to subacute cutaneous eruption of multiple erythematous papules that rapidly progress into polymorphic lesions at various stages of evolution, whereas LyP is characterized by recurrent crops of papulonecrotic lesions. Both disorders predominantly appear on the trunk and extremities and sometimes share similar clinical manifestations, leading to delayed or misdiagnosis.¹⁻³ Therefore, the correlation between clinical features, histopathology, and immunohistochemistry is essential to distinguish these two conditions. Herein, we report a rare co-occurrence of PLEVA and LyP type F developing in the same patient.

Case Report

A 22-year-old female presented with a recurrent pruritic rash on the trunk and all extremities for two months. She had no systemic symptoms and denied family history of the same condition. Dermatological examination revealed multiple discrete erythematous papules with crusted lesions on the trunk and extremities, and some healed with varioliform scars (Figure 1). Other systems were unremarkable. Skin biopsy taken from a lesion on the left hand demonstrated dense superficial and deep perivascular and interface dermatitis of lymphocytes admixed with some extravasated erythrocytes. Scatter and confluent necrotic keratinocytes, parakeratosis, and exocytosis of lymphocytes into the epidermis were noted (Figure 2). Lymphocytes were stained positive for CD3, but negative for CD 20, demonstrating that they were T cells. Further immunohistochemistry revealed predominate CD8-positive cytotoxic T cells over CD4-positive T cells and negative for CD 30 staining. (Figure 3). The clinicopathological findings were consistent with PLEVA. She had been



Figure 1 Clinical characteristics of pityriasis lichenoides et varioliformis acuta. Multiple discrete erythematous papules with crusted lesions on the (A) trunk and (B and C) extremities, some healed with varioliform scar.

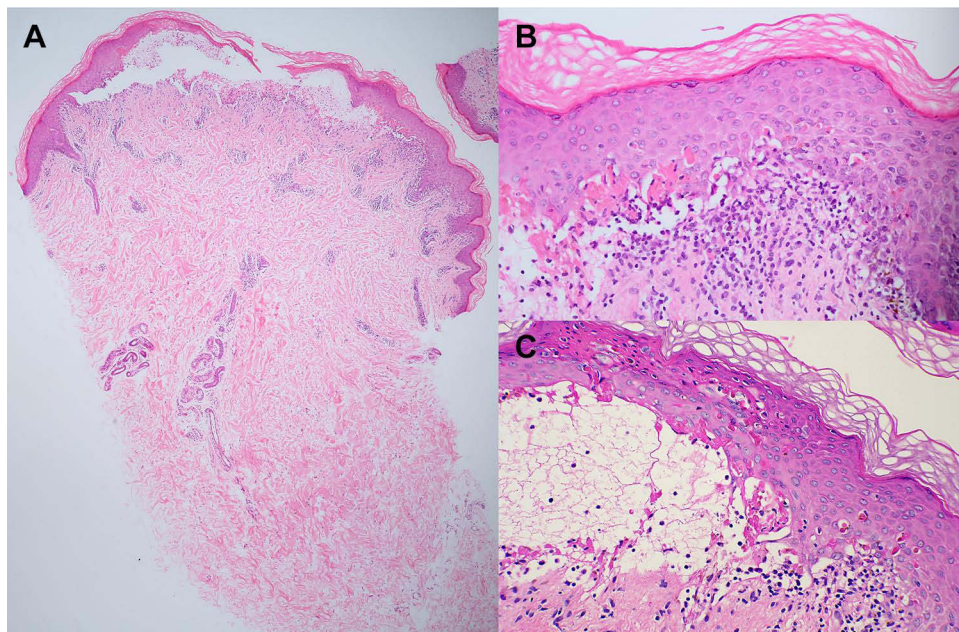


Figure 2 Histopathology of pityriasis lichenoides et varioliformis acuta. (A) Dense superficial and deep perivascular infiltrate and interface dermatitis (H&E 40X), (B) consisting of lymphocytes admixed with extravasated erythrocytes (H&E 100X). (C) Scatter and confluent necrotic keratinocytes, parakeratosis, and exocytosis of lymphocytes into the epidermis (H&E 400X).

Abbreviation: H&E, hematoxylin and eosin.

treated with topical corticosteroids, doxycycline 200 mg daily, and narrow-band ultraviolet B (NB-UVB) phototherapy two times/week. After 30 sessions of NB-UVB, the treatment was stopped during the Coronavirus disease pandemic with partially clinical improvement. Methotrexate 10 mg/week had been prescribed for 1 month; however, the treatment was switched to cyclosporine 2.5 mg/kg/day due to leukopenia. After 4 months of treatment, cyclosporine was discontinued because of gastrointestinal discomfort. However, skin lesions gradually improved and were totally cleared within 1 year.

Three months following the remission, the patient developed a new waxing and waning rash with no systemic symptoms. Dermatological examination revealed multiple discrete erythematous-to-brownish papules with some central necrotic crusts on the trunk and extremities (Figure 4). There was no lymphadenopathy and hepatosplenomegaly. Laboratory investigations, including complete blood count, lactate dehydrogenase level, liver and renal function tests were within normal limits. Skin biopsy obtained from the right arm revealed perifollicular infiltrate of large atypical mononuclear cells with abundant cytoplasm and prominent nuclei admixed with lymphocytes, few neutrophils, and

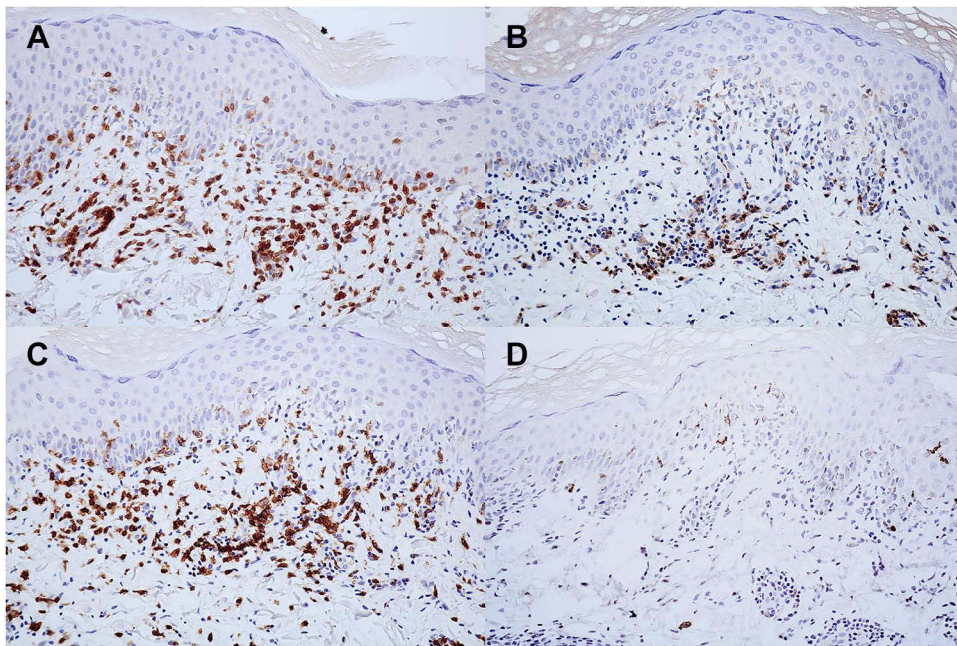


Figure 3 Immunohistochemistry of pityriasis lichenoides et varioliformis acuta. Positive (A) CD3, (B) CD4, and (C) CD8 but negative (D) CD30 staining of lymphocytes. (x40 original magnification).



Figure 4 Clinical characteristics of lymphomatoid papulosis. Multiple discrete erythematous-to-brownish papules with some central necrotic crusts on the (A) trunk and (B) extremities.

eosinophils with folliculotropism (Figure 5). Immunohistochemistry demonstrated large atypical CD30+ cell infiltrate within the hair follicle and CD3+, CD4+, and CD8+ small lymphocytes in perivascular areas. (Figure 6). Regarding clinicopathological correlation, the definitive diagnosis was LyP type F. Acitretin 20 mg/day and NB-UVB 2–3 times/week were given, and partial remission was observed after nine consecutive months of treatments.

Discussion

PLEVA, one of pityriasis lichenoides variants, is an uncommon inflammatory skin disease, which may potentially be malignant. It generally presents with an acute-to-subacute eruption of multiple erythematous papules with hemorrhagic

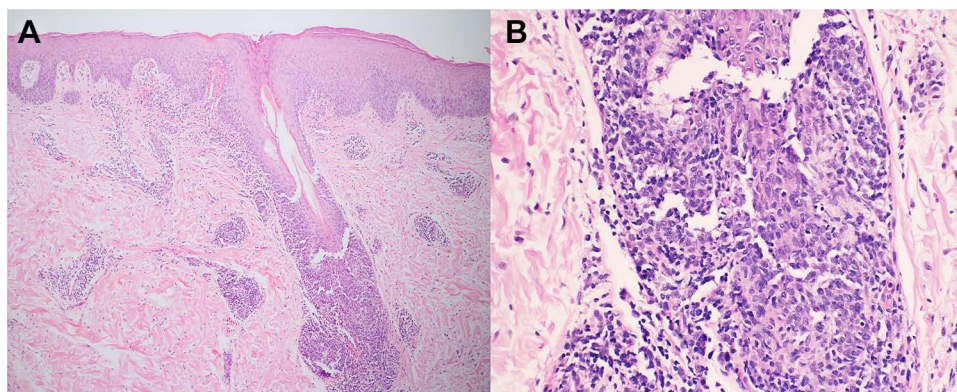


Figure 5 Histopathology of lymphomatoid papulosis type F. **(A)** Superficial and deep perivascular and perifollicular infiltrate with epidermal hyperplasia and focal hyperkeratosis (H&E 100X). **(B)** Perifollicular infiltrate of atypical large mononuclear cells with folliculotropism (H&E 400X).

Abbreviation: H&E, hematoxylin and eosin.

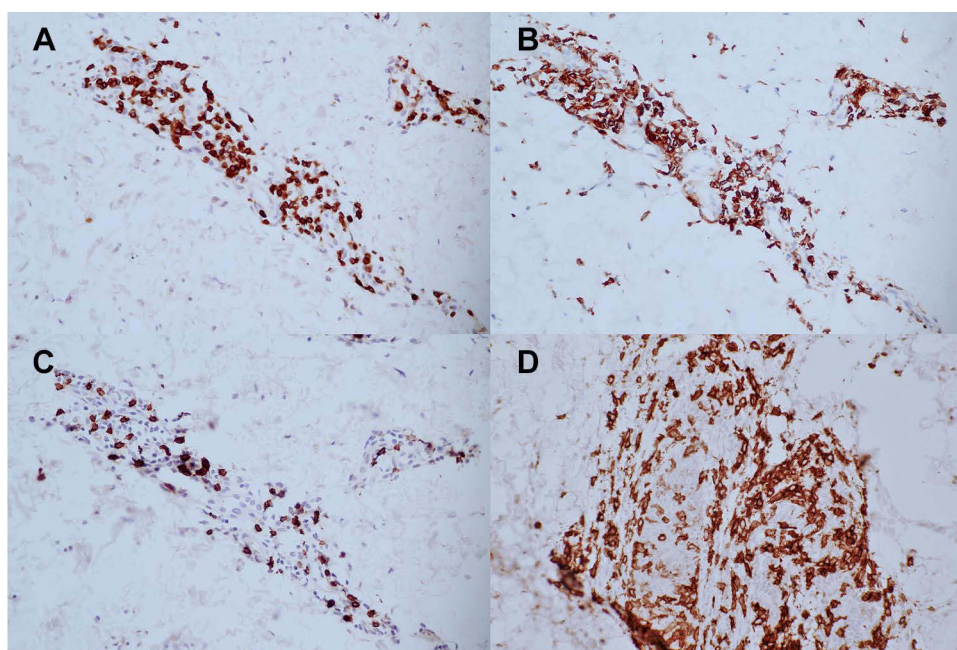


Figure 6 Immunohistochemistry of lymphomatoid papulosis type F. Positive **(A)** CD3, **(B)** CD4, and **(C)** CD8 staining of small lymphocytes in perivascular area. **(D)** Perifollicular and follicular infiltrate of positive CD30 large atypical mononuclear cells (x40 original magnification).

necrosis and crusting and often heals with atrophic varioliform scars. The lesions are frequently self-healing; however, recalcitrance may occur.¹ To confirm the diagnosis, histopathologic examination is required. PLEVA is characterized by interface dermatitis with prominent lymphocytic infiltration and epidermal involvement.⁴ The exact pathogenesis remains unclear; however, immune dysregulation against medications/infectious agents or an evolution to cutaneous T-cell dyscrasia is an accepted hypothesis.^{1,4} Despite lacking standard treatment, topical corticosteroids are commonly prescribed as the first-line therapy. Phototherapy, especially NB-UVB, and antibiotics including tetracyclines and erythromycin are also recommended. Low-dose methotrexate and other systemic immunosuppressants are indicated for severe or recalcitrant PLEVA.⁵

LyP is a rare dermatological condition and classified in primary CD30+ cutaneous lymphoproliferative disorders.⁶ LyP typically presents with recurrent crops of disseminated papulonodular eruptions, which spontaneously regress within weeks to months.^{7,8} Healing lesions appear as transient post-inflammatory hyperpigmented/hypopigmented macules and

occasionally form atrophic varioliform scars. LyP is categorized into five subtypes (A to E) according to histologic characteristics, with type A being the classic and most common type (>75%).²

LyP type F or follicular LyP is another rare histologic subtype, although not officially classified in WHO classification. It was firstly introduced by Pierard et al in 1980 and mainly manifests with follicular involvement.⁹ The prevalence of LyP type F is approximately 5.8–10% of all LyP cases.¹⁰ Histologically, it is characterized by perifollicular infiltrate with variable degrees of folliculotropism of CD30+ medium to large atypical lymphocytes. The less common features are follicular epithelial hyperplasia, ruptured hair follicle, follicular mucinosis, and intrafollicular pustules.¹⁰ The overlapping clinicopathological features between PLEVA, LyP type F, and mycosis fungoides (MF) may exist.^{11,12} Therefore, clinicopathological correlations and further immunohistochemistry are crucial to distinguish among the three conditions (Table 1).^{4,10,13–15}

Since LyP is a recurring condition, and its curative therapy is not available, methotrexate and/or phototherapy, including NB-UVB and psoralen ultraviolet-A are the first-line option for cases with disseminated or recurrent scarring lesions on cosmetically sensitive areas. Methotrexate usually reaches disease control after 3–4 weeks, but a relapse rate of up to 40% may occur after its discontinuation.² Recently, a novel targeted therapy, brentuximab (anti-CD30), demonstrated benefit for severe or recalcitrant LyP.¹⁶ Although various therapeutic managements are established, relapse still occurs. Whether LyP has a 10-year disease-specific survival rate of almost 100%, secondary hematologic malignancies including MF, anaplastic large cell lymphoma, and Hodgkin's lymphoma have been reported in up to 20%. The malignancies may be preceded by, associated with, or followed by LyP.¹⁷

Table 1 The Clinicopathological Features and Immunohistochemistry Between Pityriasis Lichenoides Et Varioliformis Acuta, Lymphomatoid Papulosis, and Mycosis Fungoides

Distinctive Features	PLEVA	LyP (Type F)	Papular MF	Folliculotropic MF
Clinical manifestations	- Crusted erythematous papules and vesicles - Heal with varioliform scar	- Papulonodular or papulonecrotic lesions	Monomorphous scaly erythematous papules	Papules, patches or plaques with follicular accentuation, alopecia, milia
Distribution	Trunk and extremities	Trunk and extremities	Trunk and extremities	Trunk, extremities, head and neck
Clinical course	- Chronic, last indefinitely from weeks to months to years - Spontaneous resolution	- Chronic relapsing, last weeks to months - Spontaneous resolution	Persistent	Persistent
Histopathological findings	- Parakeratosis - Exocytosis of lymphocytes - Confluent necrotic keratinocytes - Interface change - Wedge-shaped superficial and deep infiltrate of CD8+ cytotoxic lymphocytes - Extravasated erythrocytes	- Perifollicular infiltrates with variable degree of folliculotropism of medium to large atypical CD30+ cells - Eosinophils and/or neutrophils	- Band-like infiltrate of atypical small to medium CD4+ lymphocytes - Epidermotropism	- Perifollicular lymphocytic infiltrate - Folliculotropism of predominately atypical CD4+lymphocytes - Spare interfollicular epithelium - Eosinophils and/or plasma cells
Immunohistochemistry^a				
CD4	±	+	+	+
CD8	+	±	±	±
CD30	+ (Rare)	+	-	+ (Occasional)

Notes: ^aImmunohistochemistry results: + indicates positive staining; – indicates negative staining; ± indicates positive or negative staining.

Abbreviations: LyP, lymphomatoid papulosis; MF, mycosis fungoides; PLEVA, pityriasis lichenoides et varioliformis acuta.

We presented a unique case of recalcitrant PLEVA for one year, and developed LyP after 3 months of remission, demonstrating two diseases in one patient. The association between PLEVA and LyP has been proposed but remains debatable.^{11,18} However, clinicopathological and immunohistochemical evidence in the past decade has suggested PLEVA and LyP as distinct disorders.^{4,19,20} Currently, there are limited reports of PLEVA and LyP arising in the same patient.^{21,22} Sidiropoulou et al reported the coexistence of LyP type A, PLEVA, and MF over a 15-year period in one case. Different alterations in host immunity leading to discrete clinical expressions were remarked for these three separate entities.²¹ Another case presented with prolonged LyP type B for 11 years followed by PLEVA, reflecting the difference in host immune response to antigenic stimulus.²²

In conclusion, we reported a patient with PLEVA followed by LyP type F, a rare co-existence. This case underlined the importance of diagnostic confirmation with the clinicopathological and immunohistochemical distinction between these two entities. It is also essential to recognize histologic characteristics of LyP type F to halt misdiagnosis. Additionally, long-term follow-up and re-biopsy should be considered in progressive or recalcitrant cases in order to give a precise diagnosis, provide proper management, and evaluate for associated secondary hematologic malignancies.

Abbreviations

LyP, lymphomatoid papulosis; MF, mycosis fungoides; NB-UVB, narrow-band ultraviolet B; PLEVA, pityriasis lichenoides et varioliformis acuta.

Ethics Approval and Informed Consent

The patient provided written informed consent for the 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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