Acta Dermatovenerol APA

Acta Dermatovenerologica
Alpina, Pannonica et Adriatica

2025;34:151-154
doi: 10.15570/actaapa.2025.2

A case report of lymphomatoid papulosis: uncovering a rare diagnosis from a common finger ulcer

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Abstract

Lymphomatoid papulosis (LyP) is a rare, chronic CD30+ cutaneous lymphoproliferative disorder characterized by recurrent, self-healing papulonodular lesions. Despite its benign clinical course, LyP histologically resembles malignant lymphomas, necessitating careful differentiation. A 42-year-old woman presented with a 3-year history of recurring ulcerated papulonodular lesions on her index finger. Histopathological examination revealed atypical CD30+ lymphoid proliferation, confirming LyP type A. Immunohistochemical analysis was positive for CD2, CD4, CD30, and multiple myeloma oncogene 1, while systemic malignancy was excluded. The patient was treated with low-dose methotrexate (15 mg/week), leading to symptom improvement. LyP is classified into five histological subtypes (A–E) and is often misdiagnosed due to its overlap with inflammatory and neoplastic conditions. While the condition typically resolves spontaneously, it is associated with an increased risk of secondary lymphomas, including mycosis fungoides and primary cutaneous anaplastic large cell lymphoma. Accurate diagnosis relies on clinical presentation, histopathological evaluation, and immunophenotyping. Awareness of LyP's clinical and pathological features is essential for appropriate management and surveillance.

Keywords: lymphomatoid papulosis, CD30+, lymphoproliferative disorders, cutaneous T-cell lymphoma, dermatopathology

Received: 17 November 2024 | **Returned for modification:** 20 December 2024 | **Accepted:** 27 December 2024

Introduction

Lymphomatoid papulosis (LyP) is a rare, chronic, and recurrent papulonodular skin condition classified under the category of cutaneous CD30+ lymphoproliferative disorders (1). Its incidence ranges from 1.2 to 1.9 cases per million people each year (1–3). The etiopathogenesis remains incompletely understood, with ongoing research exploring the potential contributions of viruses (such as Epstein-Barr virus and human T-cell leukemia virus type 1), allergic responses, genetic factors, and immune dysfunction (2, 4).

LyP typically presents as recurrent episodes of pruritic papules or nodules, most commonly found on the trunk and extremities. However, atypical presentations have been documented, including isolated lesions on the scalp, face, or mucous membranes, with rare cases involving the eyelids (1, 5). These lesions usually undergo necrosis and resolve spontaneously within a few weeks, often leaving behind atrophic or hypopigmented scars. The chronic, recurrent nature of the disease serves as a critical clinical feature that helps distinguish it from other skin conditions, such as chronic dermatitis, viral infections, scabies, insect bites, lichen planus, pityriasis lichenoides, drug reactions, or cutaneous malignancies (2, 3).

LyP presents a paradox with its benign appearance and aggressive histopathological features that closely mimic lymphoma, necessitating careful follow-up to monitor potential association with malignancy. Herein we report the case of a 42-year-old woman an with a recurrent ulcerated papulonodular lesion on her index finger, ultimately diagnosed as LyP through histopathological and immunohistochemical examination.

Case report

A 42-year-old woman with an unremarkable medical history presented to the dermatology outpatient clinic with a 3-year history of recurring multiple papules and ulcerated papulonodular lesions on her index finger. These lesions typically resolved spontaneously within 1 month, with post-inflammatory pigmentation and minimal scarring. However, some of the papules increased in size and developed into ulcers. The patient denied any history of fever, infections, insect bites, or changes in medication, and she reported that the lesions were neither itchy nor painful.

On dermatological examination, an asymptomatic erythematous, enlarged papule with an irregular, sharp-edged ulcer at its center was noted on the dorsum of her right index finger (Fig. 1a, b). Physical examination revealed no signs of organomegaly or lymphadenopathy. Routine laboratory tests did not indicate evidence of systemic malignancy or other systemic diseases. A peripheral blood smear showed no atypical cells.

A skin punch biopsy was performed, and histopathological examination with hematoxylin and eosin staining revealed ulceration of the epidermis and a background of small-sized mature lymphocytes, neutrophils, and eosinophils (Fig. 2a). Atypical lymphoid proliferation was observed, primarily along the dermal vessels (Fig. 2b, c). This proliferation exhibited pleomorphic features, including large cells with eosinophilic cytoplasm, mononuclear vesicular nuclei, and a prominent single nucleolus (Fig. 2d). Immunohistochemical staining showed positivity for CD2, CD4, CD30, and multiple myeloma oncogene 1 (MUM-1) (Fig. 3a–d), whereas CD1a, CD3, CD5, CD7, CD8, CD20, epithelial membrane antigen (EMA), anaplastic lymphoma kinase (ALK), CD15, T-cell intracellular antigen 1, and granzyme B were negative. Epstein–Barr virus in situ hybridization was negative.

A diagnosis of LyP-type A was made based on the clinical, histopathological, and immunohistochemical findings. The patient was referred to the hematology–oncology department for further evaluation to rule out other CD30+ lymphoproliferative disorders.

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Flow cytometric analysis of peripheral blood revealed no neoplastic cells, and computed tomography imaging of the chest, abdomen, and pelvis showed no signs of occult malignancy.

Given the refractory nature of the disease, treatment with low-dose methotrexate (15 mg/week) was initiated. At the 12-week follow-up, the patient showed a positive response to the treatment, with a decrease in lesion frequency and severity.

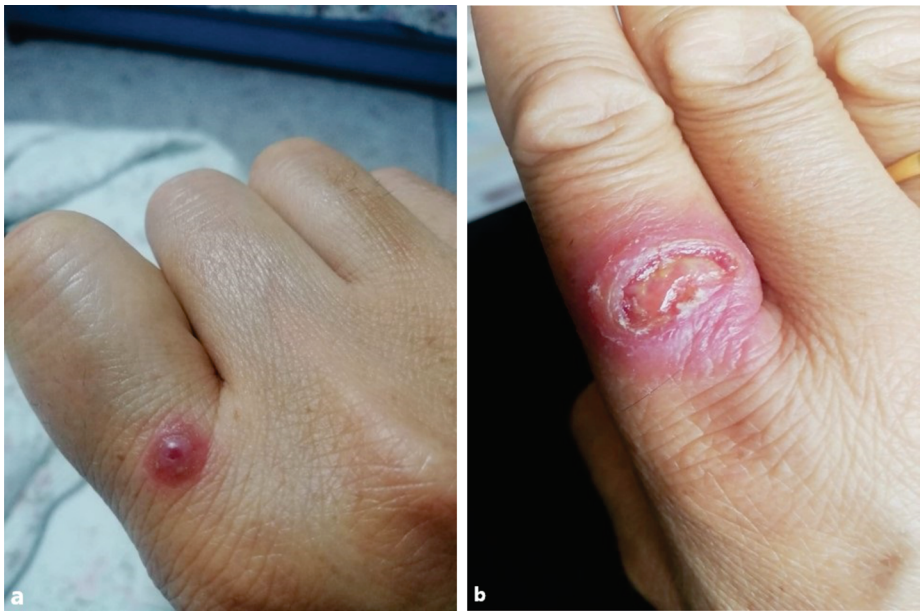

Figure 1 | a) Asymptomatic, dome-shaped, erythematous papule on the dorsum of the right index finger; b) asymptomatic erythematous, enlarged papulonodular lesion with an irregularly sharp-edged ulcer at its center on the dorsum of the right index finger.

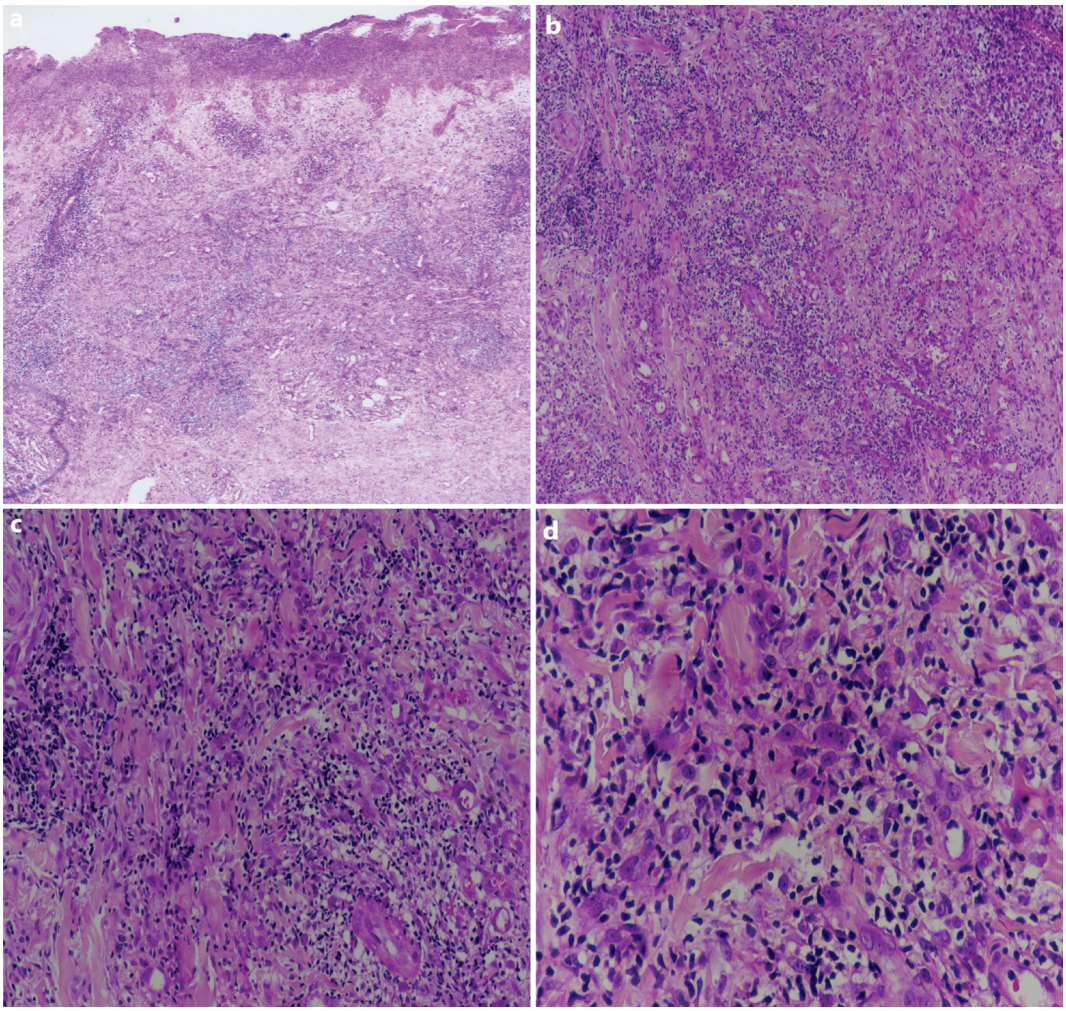

Figure 2 | a) Epidermis showing ulceration, with many small mature lymphocytes, neutrophils, and eosinophils in the background (hematoxylin and eosin, ×40); b) an atypical lymphoid proliferation primarily localized along the dermal vessels (hematoxylin and eosin, ×100); c) an atypical lymphoid proliferation primarily localized along the dermal vessels (hematoxylin and eosin, ×200); d) atypical lymphoid proliferation with large cells, eosinophilic cytoplasm, vesicular nuclei, and usually a single prominent nucleolus (hematoxylin and eosin, ×400).

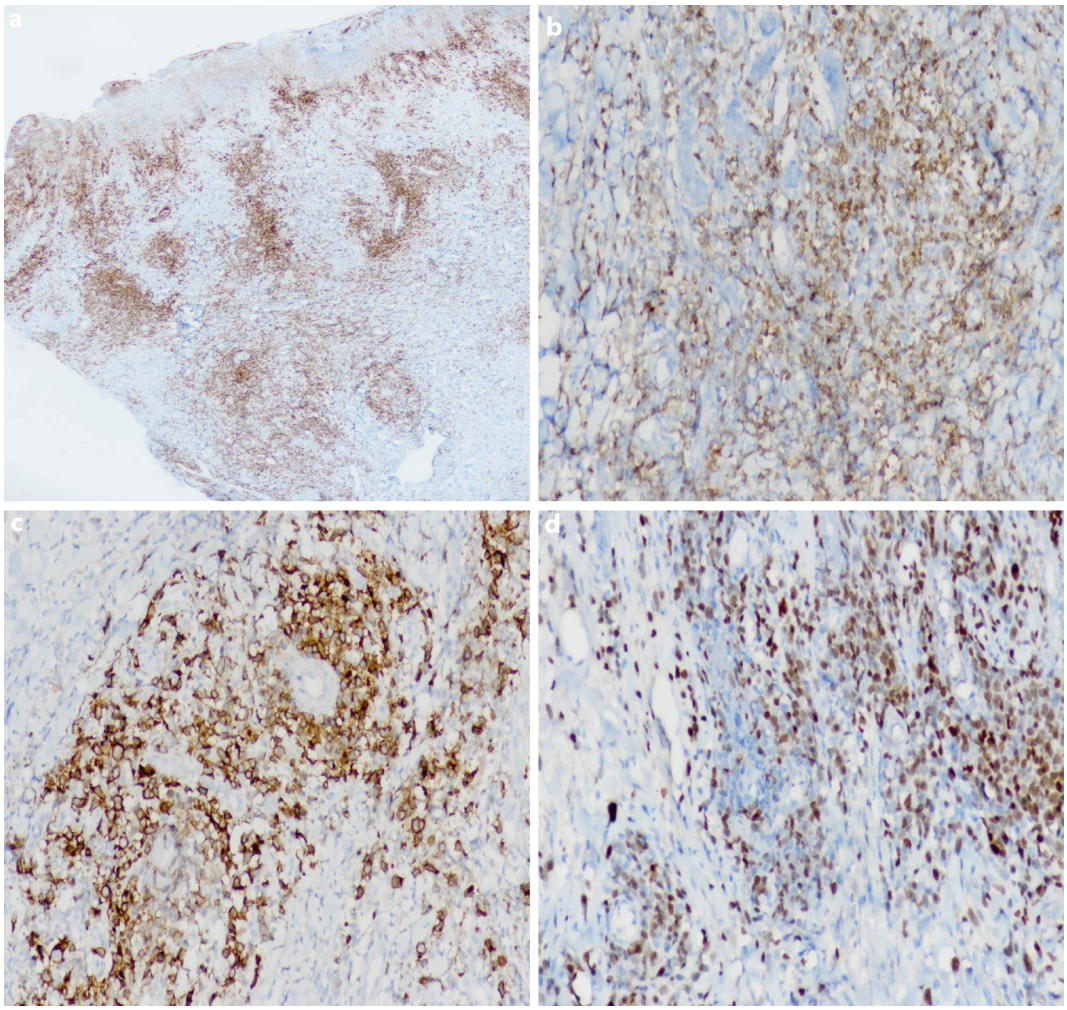

Figure 3 | a) Atypical lymphoid cells stained CD2+ (hematoxylin and eosin, ×40); b) atypical lymphoid cells stained CD4+ (hematoxylin and eosin, ×200); c) atypical lymphoid cells stained CD30+ (hematoxylin and eosin, ×200); d) atypical lymphoid cells stained MUM-1 positive (hematoxylin and eosin, ×200).

Discussion

LyP was first described by Macaulay in 1968 as a "self-healing, rhythmic and paradoxical eruption, histologically malignant but clinically benign" (6). However, it is now widely recognized that LyP is a recurrent, slow-progressing skin disorder that can histopathologically resemble more aggressive cutaneous lymphoid proliferations (1, 2).

LyP is histologically categorized into five distinct types: A, B, C, D, and E (1, 3–5). In our case, LyP-type A is characterized by large pleomorphic CD30+ lymphocytes within a mixed inflammatory infiltrate. These histopathological subtypes, which can coexist or present at different times in the same patient, are crucial for diagnosis (5). Histopathological overlap within a single specimen or patient is observed in up to 10% of skin biopsies, most commonly involving types A and C, which are the predominant forms of LyP (7).

All types of LyP present with several small red or brown bumps that evolve into larger papulonodular lesions. These lesions quickly progress to larger ulcerative cutaneous lesions, which typically undergo spontaneous resolution within a few weeks, sometimes leaving residual scarring and post-inflammatory pigmentation. The typical clinical criteria for diagnosing LyP include the presence of multiple papules or nodules, complete regression of lesions, no increase in size beyond 3 cm over a 3-month observation period without treatment, and the absence of lymphadenopathy (1, 2). Although there is some clinical similarity, significant morphological heterogeneity can occur both within biopsies from the same patient and between different biopsies. A diagnosis of LyP requires combining clinical findings with histopathological and immunophenotypic evidence to distinguish it from other lymphoproliferative disorders (1).

LyP presents with a diverse clinical and histopathological profile. Although the exact rate of misdiagnosis is difficult to determine, it is estimated to be around 30%, including both clinical and histopathological misdiagnoses. This high rate of misdiagnosis often results in inappropriate treatments, such as unnecessary antibiotic therapy, chemotherapy, or radiotherapy (2). It is generally accepted that LyP can sometimes be associated with the later development of lymphoma, either before, during, or after the appearance of LyP (1, 3). Studies suggest that approximately 19.4% to 52% of patients with LyP develop secondary lymphomas, with some individuals experiencing multiple malignancies (8).

The most frequently associated secondary malignancies include mycosis fungoides (MF), which accounts for 61% of cases, and primary cutaneous anaplastic large cell lymphoma (cALCL), observed in 26% of cases (8). Other malignancies, such as Hodgkin lymphoma, acute and chronic leukemias, and Waldenström's macroglobulinemia, have also been reported (8–10). Importantly, these malignancies are not direct transformations of LyP lesions but are associated secondary lymphatic neoplasms (8).

The likelihood of developing lymphoma associated with LyP is two to 7.5 times higher in patients that exhibit a monoclonal rearrangement of the T-cell receptor (TCR) gene chain in their

skin lesions (2). As our case illustrates, LyP type A is the most frequently diagnosed subtype, with an incidence rate ranging from 47.2% to 82.0% compared to other variants. Although LyP type A has a 5-year survival rate of 100%, the prognosis can be negatively impacted by an increased risk of association with lymphoma, estimated to be between 10% and 20% in cases of adult-onset LyP (1–4).

Diagnosis of LyP depends on a combination of clinical, histopathological, and immunohistochemical evidence. Skin lesions in LyP typically exhibit a specific cytotoxic phenotype, most often CD30+/CD4+/CD8– cells (1–3). However, diagnosis can be complicated by histological similarities to other CD30+ lymphoproliferative disorders. Immunophenotyping using flow cytometry or immunohistochemistry is increasingly employed for precise identification. Given that CD30 is overexpressed and LyP can resemble inflammatory conditions, it is crucial to accurately diagnose and differentiate it from diseases such as Hodgkin lymphoma, lichen planus, primary cutaneous ALCL, MF, cutaneous T-cell lymphoma, and other less severe conditions such as mycobacterial infections, viral infections, scabies, and drug reactions (1–3, 7).

For limited or asymptomatic LyP, a "wait and see" approach is generally recommended (11). In cases of severe or refractory disease, or when aesthetically sensitive areas are involved, low-dose methotrexate (10 to 25 mg weekly) is often the preferred treatment (1, 2). Other available treatment options include topical steroids, topical mechlorethamine, targeted phototherapy, photodynamic therapy, radiotherapy, oral or topical retinoids, interferon, and the anti-CD30 monoclonal antibody-drug brentuximab vedotin (1, 3). Although these treatments may accelerate lesion healing and prevent new lesions, they do not alter the disease's natural course or reduce the risk of developing associated lymphoma.

Conclusions

The case presented underscores the critical importance of accurate diagnosis for both dermatology and hematology. Recognizing LyP, especially in atypical presentations, is essential for ensuring appropriate management and monitoring for potential associations with lymphomas such as MF and ALCL.

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