

Lymphomatoid Papulosis Associated with Recurrent Cutaneous T-Cell Lymphoma

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Abstract

Introduction: Lymphomatoid papulosis is a chronic benign disease which may be associated with malignant lymphomas. This case illustrates the relapsing and remitting nature of both lymphomatoid papulosis and its potential of developing cutaneous T-cell lymphoma and narrow-band ultraviolet B (NB-UVB) phototherapy as a new modality of treatment of early-stage mycosis fungoides in these patients. **Clinical Picture:** A 44-year-old woman has had recurrent crops of papules and nodules of lymphomatoid papulosis on the limbs for 15 years. Histological features are consistent with the type B lesions of lymphomatoid papulosis. Eight years after the initial onset of these lesions she developed cutaneous T-cell lymphoma (mycosis fungoides). Since then, she has had recurrence of mycosis fungoides following the cessation of phototherapy, but had no evidence of systemic involvement. **Treatment:** The lesions of lymphomatoid papulosis responded to intermittent courses of oral methotrexate. Mycosis fungoides was treated with oral psoralen and ultraviolet A phototherapy with good response. Unfortunately, the lesions relapsed whenever phototherapy was discontinued. The most recent recurrence of mycosis fungoides was treated with NB-UVB therapy. **Outcome:** The papules of lymphomatoid papulosis continue to appear but she remains free of lesions of mycosis fungoides, 10 months after cessation of NB-UVB therapy. **Conclusion:** Long-term surveillance is essential in all cases of lymphomatoid papulosis as accurate predictors for the development of malignant lymphoma in these individuals are still lacking.

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Key words: CD30, Methotrexate, Mycosis fungoides, Narrow-band UVB

Introduction

Lymphomatoid papulosis is a self-healing recurrent papular eruption often exhibiting a chronic course. It is associated with malignant lymphomas in 10% to 20% of cases.

Case Report

A 44-year-old Chinese woman with lymphomatoid papulosis first presented 15 years ago in 1987 with multiple erythematous non-pruritic papules on the upper and lower limbs (Fig. 1). There were tender nodules on the lower limbs. Several of these lesions had a necrotic or crusted centre. These papules healed with scarring after 4 to 6 weeks. The histology of a papule on the arm showed a dense dermal infiltrate with large numbers of atypical mononuclear cells, with increased mitotic figures (Figs. 2 and 3). The infiltrate also showed plasma cells, eosinophils and neutrophils and extended into the subcutis. Immunohistochemical staining with monoclonal antibodies to CD30 was negative. Histological features were consistent with type B lesions of lymphomatoid papulosis. There was no evidence of lymphoma. Blood counts, chest radiograph,

computed tomography (CT) of the abdomen and bone marrow studies were unremarkable. She was treated with intermittent doses of methotrexate of 7.5 mg to 15 mg/week over the next 8 years. Recurrent crops of these papules were well controlled on this dose.

In 1995, she developed acquired ichthyosis as well as annular lesions on the thighs (Fig. 4). A biopsy of these lesions confirmed mycosis fungoides. The histology showed epidermotropism of mycosis cells from the dermal infiltrate. Clinically, there was no lymphadenopathy or hepatosplenomegaly. White cell count was $4.6 \times 10^9 \text{ L}^{-1}$, with a normal differential count. Liver function tests and a chest radiograph were normal and CT did not reveal any intrathoracic or intraabdominal lymphadenopathy. She was treated with low-dose phototherapy consisting of 30 mg of oral 8-methoxypsoralen (8MOP) and ultraviolet A (PUVA) commencing at 2 Jcm^{-2} (light source: Waldmann). However, she developed an acute flare like a sunburn, involving 50% of the body surface area only after 2 sessions of phototherapy. Treatment was discontinued and recommenced 2 months later

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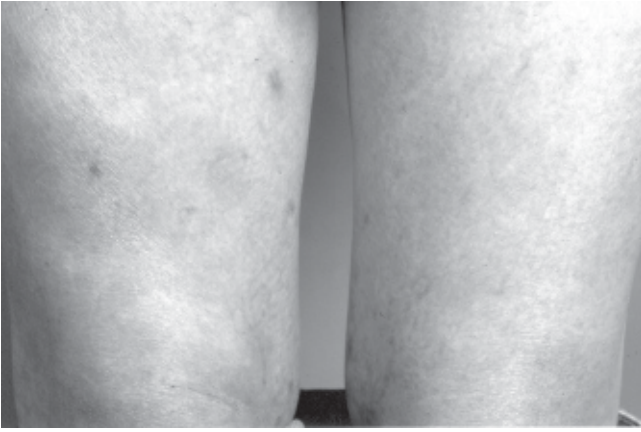


Fig. 1. Lymphomatoid papulosis: discrete erythematous papules on the thighs.

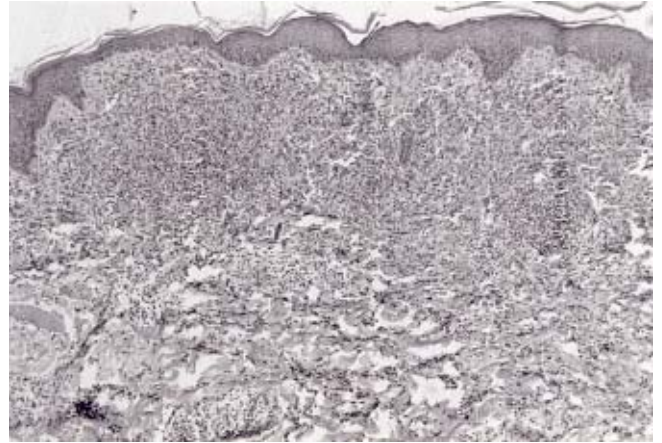


Fig. 2. Biopsy of papule on the arm: dense dermal infiltrate (haematoxylin-eosin, original magnification x40).

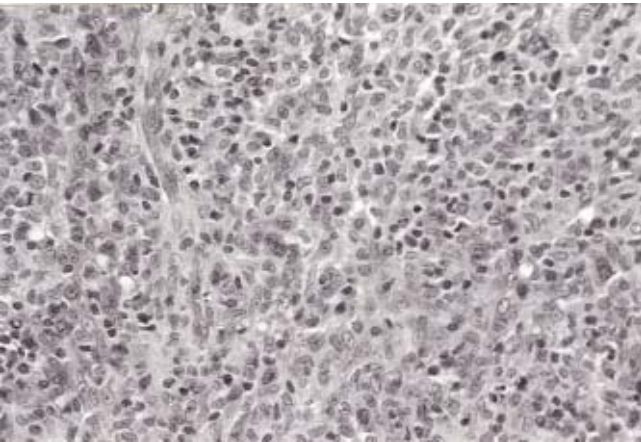


Fig. 3. Dermal infiltrate comprising large numbers of atypical mononuclear cells (haematoxylin-eosin, original magnification x200).

with no further flares.

She responded well to phototherapy and PUVA was discontinued after 6 months, achieving a total dose of 78 Jcm⁻² over 36 sessions. She developed a relapse 4 months later with an eruption of annular lesions, which resolved with another 30 sessions of PUVA, achieving a total dose of 60 Jcm⁻² over 7 months. She continued, however, to have scattered papules of lymphomatoid papulosis on the limbs. These responded to intermittent courses of oral methotrexate lasting 6 weeks to 2 months. In 2001, she relapsed for a third time and developed multiple plaques of mycosis fungoides on the buttocks and thighs. Phototherapy with narrow-band ultraviolet B (NB-UVB) was commenced instead of PUVA. After 15 sessions of NB-UVB (light source: TL01) and a total dose of 18022 mJcm⁻², lesions of mycosis fungoides had resolved, leaving several papules of lymphomatoid papulosis.

Discussion

Lymphomatoid papulosis was originally described by Macaulay in 1968 as a “self-healing rhythmical paradoxical papular eruption, histologically malignant but clinically benign”.¹ Lymphomatoid papulosis occurs most commonly in adults between the ages of 20 and 40 years and shows a predilection for the trunk and extremities. It runs a chronic

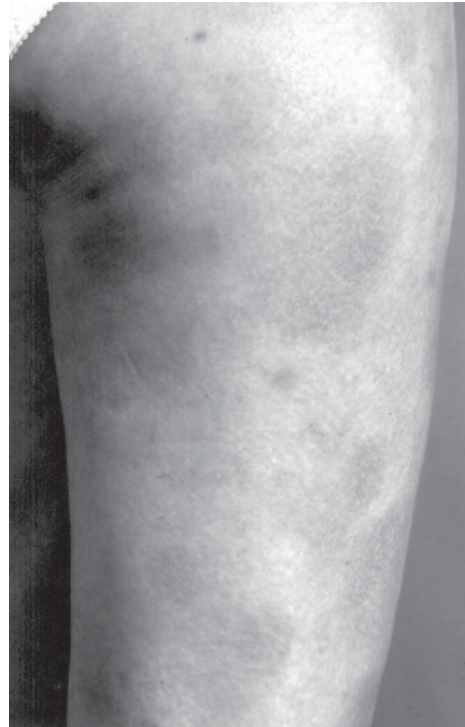


Fig. 4. Mycosis fungoides: annular plaques and patches on the thigh, with a papule of lymphomatoid papulosis on the right buttock.

course with lesions recurring in crops for up to 40 years. Lymphomatoid papulosis is characterised by erythematous papules or nodules that progress to form vesicular crusted or haemorrhagic lesions, which then undergo spontaneous healing with scarring.² Smaller papules, with a tendency to spontaneous ulceration, may be clinically indistinguishable from those seen in pityriasis lichenoides et varioliformis acuta (PLEVA/Mucha-Habermann disease). Nodules and plaques are, however, not found in PLEVA.

Histologically, a wedge-shaped dermal infiltrate composed of lymphoid cells, eosinophils, neutrophils and larger mononuclear cells is seen. Atypical large or small lymphoid cells may comprise up to 50% of the infiltrate. There may be epidermotropism of inflammatory cells. The histological features may be divided into 2 subgroups. In type A lesions,

there is a predominance of large cells with vesicular nuclei, prominent nucleoli and abundant rim of cytoplasm. Multinucleate forms are often present, some resembling Reed Sternberg cells typical of Hodgkin's disease. Unlike Hodgkin's disease, type A cells are CD30+ and CD15-.^{3,4} Type B cells are medium-sized cerebriform mononuclear cells with scant cytoplasm which resemble the atypical lymphoid cells seen in mycosis fungoides. These cells are CD3+ and CD30-, and resemble those seen in the early stages of mycosis fungoides. The histological features in our case were consistent with type B lesions and she also went on to develop mycosis fungoides. CD30 appears to be a representative marker for type A cells in lymphomatoid papulosis although CD 30-positive cells are not specific for lymphomatoid papulosis.²

Lymphomatoid papulosis is preceded by, associated with or followed by malignant lymphoma in 10% to 20% of patients.^{5,6} Mycosis fungoides, Hodgkin's disease and diffuse large cell lymphoma account for more than 90% of the associated malignancies.⁷ In the series by Basarab et al,³ lymphomatoid papulosis preceded mycosis fungoides in 4 cases, occurred after the onset of mycosis fungoides in 5 cases and occurred concurrently with mycosis fungoides in 6 cases. Data suggest that mycosis fungoides with co-existent lymphomatoid papulosis runs an indolent clinical course and that the association of mycosis fungoides with lymphomatoid papulosis carries a favourable prognosis as compared with patch or plaque stage mycosis fungoides alone.^{3,7,8} As this patient demonstrated, lesions of lymphoma and lymphomatoid papulosis may behave independently. She exhibited lesions of both conditions concurrently and lymphomatoid papulosis continued despite clearing of lesions of mycosis fungoides with phototherapy.

Various treatment modalities of lymphomatoid papulosis have been employed, including systemic corticosteroids, UV phototherapy, topical chemotherapy with carmustine and psoralen photochemotherapy. Methotrexate (MTX) at dosages of 15 mg/week appears to be effective therapy for lymphomatoid papulosis, although remission may not be maintained once treatment is discontinued.^{9,10} MTX in low weekly doses induces complete remission of lymphomatoid papulosis in our case but relapse follows soon after discontinuation of phototherapy on each occasion. MTX therapy does not appear to prevent progression into more aggressive lymphoma but long-term prospective studies are required to determine whether long-term suppressive therapy with MTX decreases the risk of developing a systemic lymphoma.⁹

Lesions of mycosis fungoides in this woman showed good clinical response to treatment with PUVA but recurred on cessation of phototherapy. Although reports have demonstrated that lymphomatoid papulosis responds to treatment with PUVA,¹¹ our patient had persistent papules after 30 sessions and a cumulative dose of 60 Jcm⁻² of PUVA. She has, however, not had any evidence of recurrence of mycosis fungoides 10 months after cessation of NB-UVB, although she continues to have new papules of lymphomatoid papulosis. In contrast to PUVA, NB-UVB does not require a photosensitiser and appears to have a lower carcinogenic potential. In a recent

study by Gathers et al,¹² of 24 patients with early-stage mycosis fungoides, 13 patients had a complete response with NB-UVB. Four of these patients subsequently relapsed upon discontinuation of treatment. The mean time to relapse was 12.5 weeks.

Clonal T-cell receptor (TCR) gene rearrangements have been detected in skin lesions from patients with lymphomatoid papulosis.¹³ Although lesions of lymphomatoid papulosis and associated lymphomas may show identical TCR gene rearrangements, there is insufficient evidence to suggest that the presence of a clonal T-cell population *per se* is associated with increased risk of developing a malignant lymphoma.⁷

Accurate parameters predicting the development of a malignant lymphoma in individuals with lymphomatoid papulosis are still lacking. Long-term surveillance is therefore essential in all cases of chronic lymphomatoid papulosis. This case has had several recurrences of cutaneous T-cell lymphoma on cessation of treatment and highlights the importance of close surveillance for such recurrences and prompt treatment. It will be interesting to assess the long-term efficacy and safety of NB-UVB as compared with PUVA in the treatment of mycosis fungoides in individuals with lymphomatoid papulosis.

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