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Case Report

A middle-aged man with self-healing papulonecrotic lesions over the trunk and proximal limbs

一名中年男仕在其軀幹及四肢近端出現可自癒的丘疹壞死性皮損

JC Chan 陳俊彥, N Trendell-Smith, CK Yeung 楊志強

Lymphomatoid papulosis is a clinically benign, but histologically malignant form of cutaneous T-cell lymphoma. Regular surveillance is warranted to monitor development of another systemic lymphoma. We report a case of lymphomatoid papulosis, presenting as widespread papulonecrotic skin lesions. The patient developed multiple asymptomatic, self-healing lesions over the trunk and proximal limbs which resolved spontaneously within 3 months.

淋巴瘤樣丘疹病是一種臨床表現爲良性，但組織學上卻被歸納爲惡性形式的T細胞皮膚淋巴瘤。故病患必須定期跟進，以排除其發展爲另一種全身性淋巴瘤的可能。我們報告了淋巴瘤樣丘疹病一例，其表現爲廣佈的丘疹壞死性皮損。患者在其軀幹及四肢近端長出很多無症狀並可自癒的皮損，皆在三個月內自行消退。

Keywords: Cutaneous T-cell lymphoma, lymphomatoid papulosis, primary cutaneous CD30+ lymphoproliferative disorder

關鍵詞：T 細胞皮膚淋巴瘤，淋巴瘤樣丘疹病，原發性皮膚 CD30 陽性 T 細胞淋巴增生性病變

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Introduction

Lymphomatoid papulosis (LyP) is a chronic, recurrent, self-healing papulonecrotic or papulonodular skin disease with histologic features suggestive of a CD30+ malignant lymphoma. Though a benign entity, LyP may be preceded by, associated with, or followed by another type of malignant lymphoma. Regular follow-up is recommended once the diagnosis of LyP has been made.

Case report

A 45-year-old man with good past health presented with a 2-month history of erythematous papules and nodules, which first appeared on arms and later spread to the trunk and proximal thighs. Some lesions ulcerated and later healed with haemorrhagic crusts while the others regressed spontaneously with hyperpigmentation or hypopigmentation. The eruption was all along asymptomatic and the patient experienced no constitutional symptom. He worked as a salesman and there was no remarkable travel or contact history. He was not on any regular medications.

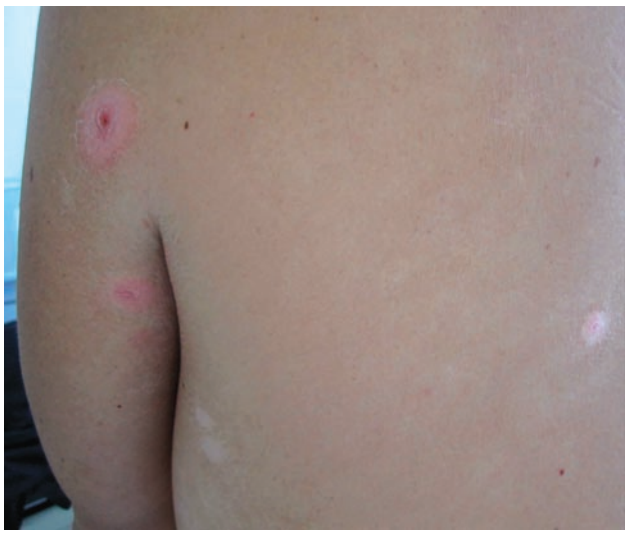

Figure 1. Multiple papulonodular lesions ranging from 1.0-4.0 cm over trunk and proximal limbs.

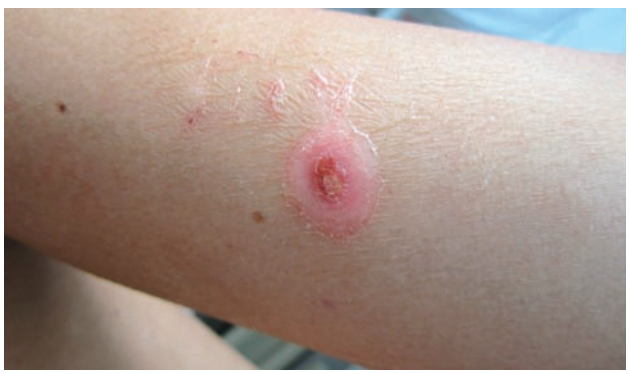

Figure 2. Some nodules ulcerated and healed with scab.

Physical examination showed widespread papulonodular lesions ranging from 1.0 to 4.0 cm located on the trunk and bilateral proximal limbs (Figures 1-3). Some lesions were eroded and covered with scabs. Hypopigmented (Figure 3a) or hyperpigmented (Figure 3b) atrophic patches were noted over areas of regressed lesions. The nails and mucosal membranes were unremarkable. The patient was afebrile and there were no lymphadenopathy and hepatosplenomegaly. Clinical differential diagnoses for the cutaneous lesions included lymphoproliferative disorders such as lymphomatoid papulosis, cutaneous anaplastic T-cell lymphoma, tumour phase of mycosis fungoides, nummular eczema, ecthyma, discoid lupus erythematosus and hypertrophic lichen

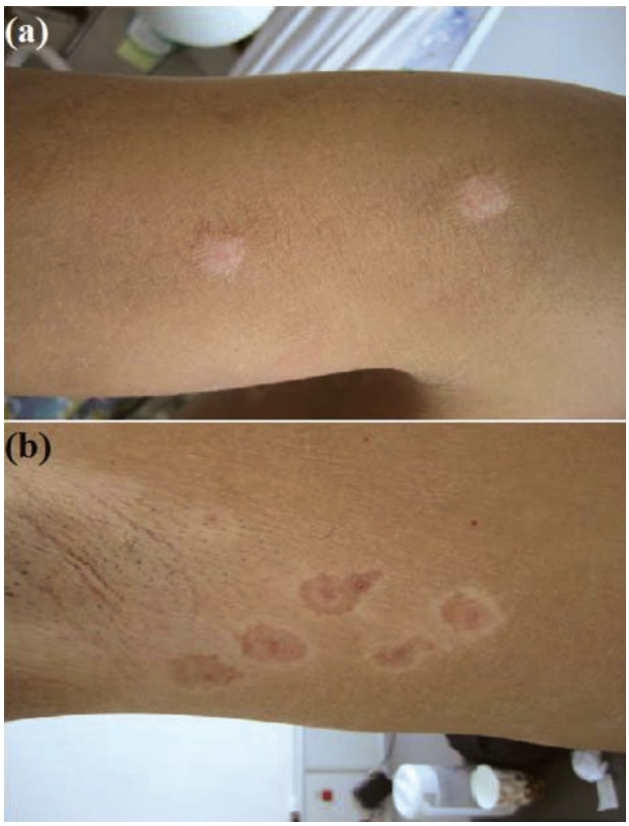

Figure 3. Spontaneous resolution was noted for individual lesions. (a) Hypopigmented and (b) hyperpigmented atrophic scars developed over areas of resolved lesions.

planus. Blood tests showed normal complete blood picture and lactate dehydrogenase (LDH) level. Peripheral blood smear was unremarkable.

An incisional biopsy of one of the papules showed a dermal wedge-shaped polymorphic mixed chronic inflammatory cell infiltrate consisting of lymphocytes, histiocytes, eosinophils and some neutrophils (Figures 4 & 5). The central epidermis was eroded but no epidermotropism was present. The subcutis was not involved. Scattered atypical cells with dense hyperchromatic nuclei resembling "chunks of coal" were present within the dermal infiltrate. Immunohistochemistry for CD30 showed strong positive staining of these atypical cells, some of the larger histiocytoid cells and other lymphoid cells (Figure 6). The histology and immunophenotype in this clinical setting confirmed the diagnosis of lymphomatoid papulosis. The patient subsequently underwent further investigations to rule out systemic lymphoma. Bone marrow aspirate and trephine biopsy were performed and there was no evidence of lymphoma infiltration of the bone marrow. A positron-emission tomography (PET) scan was done which showed no hypermetabolic signal. The patient was followed-up regularly and all papulonodular lesions resolved within 3 months, leaving similar dyspigmented atrophic scars. The patient is now on regular follow-ups to monitor development of another malignant lymphoma.

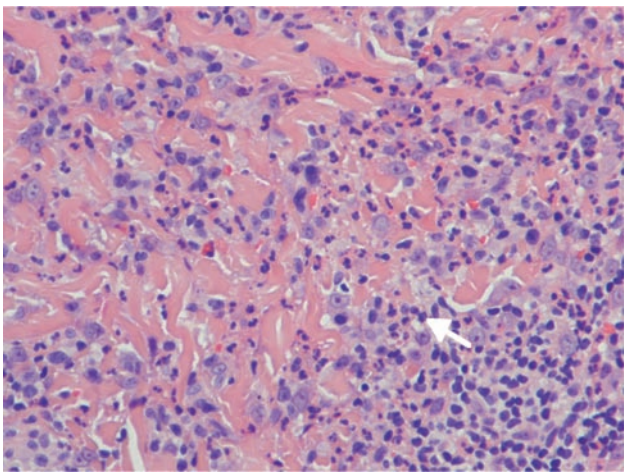

Figure 5. High power H&E (x 200) photomicrograph of the papule showing the polymorphic dermal infiltrate with many lymphocytes, histiocytoid cells, eosinophils and some neutrophils. Occasional atypical cells with densely hyperchromatic nuclei resembling "chunks of coal" (arrow) are identified.

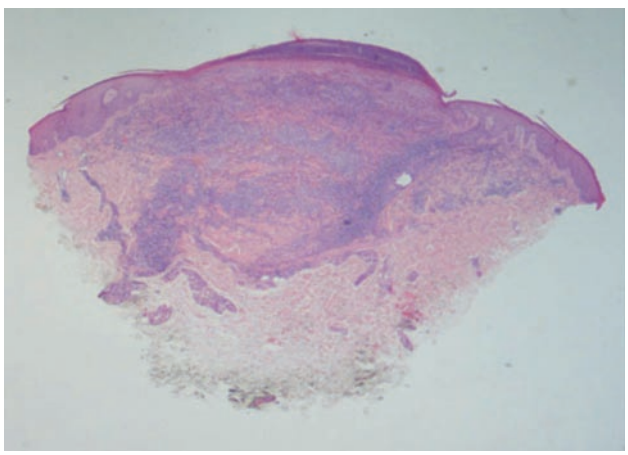

Figure 4. Low power H&E (x 10) photomicrograph of the papule with a diffuse wedge-shaped dermal infiltrate. There is central epidermal erosion but no evidence of epidermotropism or involvement of the subcutis.

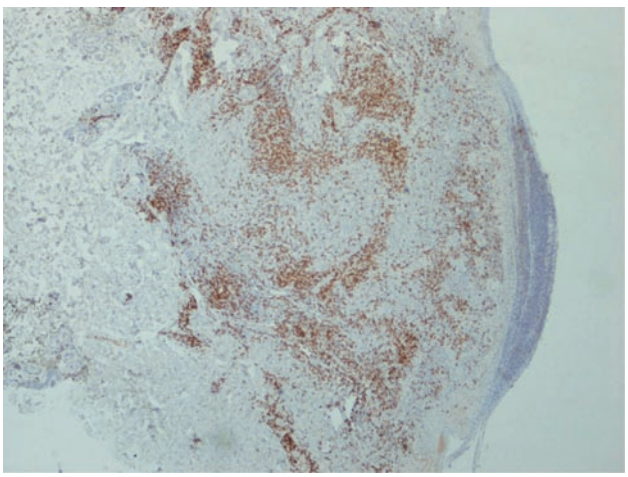

Figure 6. Photomicrograph of immunohistochemical staining for CD30 (x 15). The atypical cells, some of the histiocytoid cells and lymphoid cells are staining up strongly with CD30.

Discussion

Lymphomatoid papulosis (LyP) is a low-grade primary cutaneous T-cell lymphoma from histological point of view, though it is a benign papulonodular eruption clinically. The condition was first described by Dupont in 1956 as "histiomonocytic reticulosis". More than a decade later, Macaulay coined the term "lymphomatoid papulosis" as a chronic, recurrent, self-healing papulonodular skin eruption with histologic features of a malignant lymphoma.

Primary cutaneous lymphomas can be divided into T-cell (75%) and B-cell (25%) lineages. Primary cutaneous T-cell lymphomas (CTCLs) comprise a diversified group of conditions. While the majority (65%) belongs to mycosis fungoides and its variants, primary cutaneous CD30+ lymphoproliferative disorders account for 25% of all CTCLs. In the new World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC) classification, LyP is classified as a primary cutaneous CD30+ lymphoproliferative disorder.[1] Primary cutaneous CD30+ lymphoproliferative disorder is considered to be a continuum of conditions with lymphomatoid papulosis (LyP) at the benign end and cutaneous anaplastic large cell lymphoma (C-ALCL) at the malignant end.

LyP is generally accepted as a histologically malignant, but clinically benign condition which typically runs a chronic relapsing course. LyP accounts for 12-15% of all cutaneous T-cell lymphomas (CTCLs). The median age of onset is 45 years (age range: 8 months to 84 years) and the male to female ratio is 1.5:1.[2-4] LyP is characterised by the presence of papular, nodular, and/or papulonecrotic skin lesions. Lesions may coexist at different stages of development. Red-brown papules and nodules with central necrosis, haemorrhage or scab formation are typically found. Vesicles or pustules may be present in some cases. Most lesions are smaller than 3 cm in diameter. The predominant sites of involvement are the trunk and proximal limbs. The face, palms and soles are only rarely affected. Skin lesions are usually asymptomatic and spontaneous regression of individual lesions is anticipated in 3-12 weeks after onset, leaving localised dyspigmentation and/or superficial atrophic scars. LyP is a recurrent condition and the duration of disease may vary from months up to 40 years. As many as 20% of patients with LyP have been reported to be associated with another type of malignant lymphoma including mycosis fungoides, cutaneous anaplastic large cell lymphoma and Hodgkin disease.[4] The cumulative risk of development of a malignant lymphoma is estimated to be 12-60% after 15 years and 80% after 30 years.[5] Risk factors for the development of a systemic lymphoma are unknown.

The histopathology of LyP is highly variable, and also depends on the stage of skin lesion sampled. Three histologic subtypes of LyP (types A, B, and C) have been described, which represent a spectrum with overlapping features.[4,6] Despite the diversity of the histological features, these subtypes share the same benign clinical course. In LyP type A lesions, scattered or small clusters of large CD30+ cells are typically found in a mixture of densely populated inflammatory cells, namely neutrophils, small lymphocytes, histiocytes, and/or eosinophils. Multinucleated or Reed-Sternberg – like CD30+ cell can sometimes be found in LyP type A. Epidermotropism, as in the case of mycosis fungoides (MF), is typically not featured in this subtype. LyP type B occurs in less than 10% of cases and is characterised by an epidermotropic population of small atypical cells with cerebriform nuclei as seen in mycosis fungoides (MF). In LyP type C lesions, a homogenous population of large CD30+ T cells are found with relatively few admixed inflammatory cells. This subtype has close resemblance with cutaneous anaplastic large cell lymphoma (C-ALCL) histologically. Concerning the immunostaining properties, the large atypical cells found in the LyP type A and type C lesions share the same immunophenotype as the tumour

cells in C-ALCL.[7] The atypical cells with cerebriform nuclei in the LyP type B lesions have a CD3+, CD4+, CD8- phenotype and do not express CD30 antigen. T-cell receptor genes clonality can be demostrated in 40-70% of cases of LyP.[8] The same gene rearrangements have been demonstrated in LyP lesions and the associated lymphomas.[9]

The clinical differential diagnoses of LyP include pityriasis lichenoides (PLEVA), folliculitis and arthropod bites. Histologically, cutaneous anaplastic large cell lymphoma (ALCL), systemic ALCL with skin involvement, mycosis fungoides with CD30+ transformation and other CTCLs with CD30 antigen should be considered as differential diagnoses. LyP carries a favourable prognosis. In a recent study of 118 LyP patients, only 5 (4%) patients developed a systemic lymphoma, and only 2 (2%) patients died of systemic disease over a median follow-up period of 77 months.[2]

Treatment for LyP is often unnecessary unless for symptomatic relief. Spontaneous regression of individual lesions is anticipated and no treatment modality is proven to affect the natural course of the disease. Topical or systemic corticosteroid is generally not effective. Low-dose oral methotrexate (5-20 mg/wk) is the most effective therapy to suppress the development of new skin lesions.[10] Beneficial effects have also been reported for PUVA and topical chemotherapy.[4] However, after discontinuation of treatment, the disease generally relapses within weeks or months. The short-term benefits of active treatment (such as low-dose oral methotrexate) should be balanced carefully against the potential side effects. Therefore, in patients with relatively few and non-scarring lesions, long-term follow-up to monitor development of other malignant lymphomas without active treatment should be considered.

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