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Case Report

Primary cutaneous marginal zone B-cell lymphoma

原發性皮膚邊緣帶 B 細胞淋巴瘤

NPY Chan 陳佩瑤 and WY Lam 林永賢

A 47-year-old Chinese female patient presented with a two-year history of erythematous plaques over the face, axillae and abdomen. Two biopsies were performed before the diagnosis of primary cutaneous marginal zone B-cell lymphoma was made. No evidence of systemic involvement was present at the time of diagnosis. She was subsequently commenced on cyclical chlorambucil.

47歲華人女患者兩年來於臉，腋下及腹部出現紅色斑塊。經兩次活檢診斷為原發性皮膚邊緣帶B細胞淋巴瘤。診斷時無証據顯示有系統性受累。患者其後接受週期性苯丁酸氮芥治療。

Keywords: Chinese, primary cutaneous marginal zone B-cell lymphoma

關鍵詞：華人、原發性皮膚邊緣帶 B 細胞淋巴瘤

Introduction

Primary cutaneous marginal zone B-cell lymphoma (PCMZL) is classified under the 'cutaneous B-cell lymphoma' in the latest WHO-EORTC classification for cutaneous lymphoma.[1] It is a low grade B-cell lymphoma in which systemic spread is rare. Diagnosis is based on consistent clinical features, histopathology, immunological profile and cytogenesis studies. The condition has an excellent prognosis with a 90-100% 5-year survival.[2]

Case report

A 47-year-old female patient presented with a two-year history of multiple erythematous plaques over her face, axillae and abdomen which were occasionally pruritic (Figures 1 & 2). There was no associated photosensitivity. She had no systemic symptoms, including fever, weight loss, joint pain or alopecia. Her travel, drug and past medical histories were unremarkable. She was a non-smoker and non-drinker who worked on construction sites.

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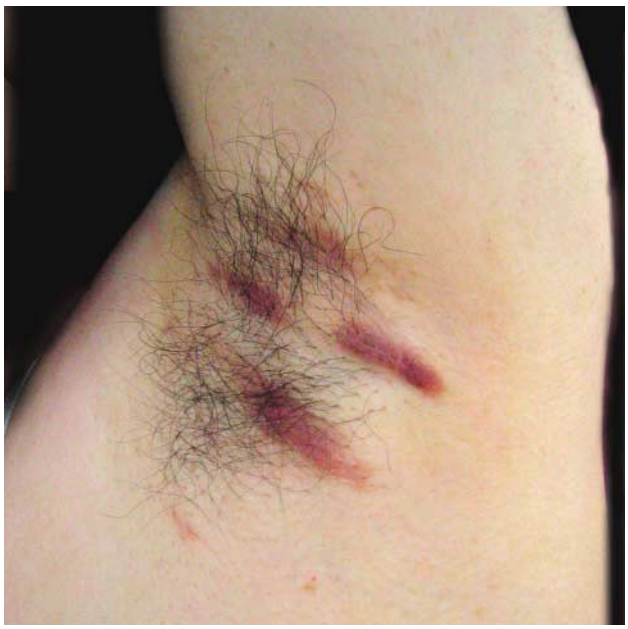

Figure 1. Brown linear plaques over the left axillae.

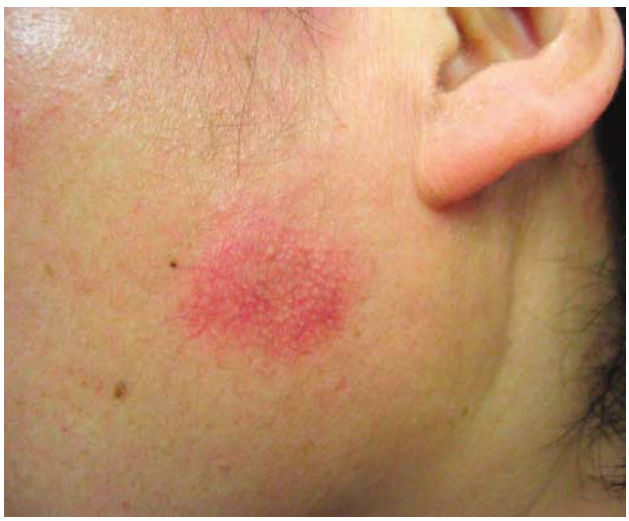

Figure 2. An erythematous nodule over the left cheek.

Physical examination showed multiple non-tender, fairly well-defined, roundish erythematous nodules and plaques over the forehead, temporal region and cheek. Telangiectasia was noted over some of the lesions, but there was no ulceration, scaling, follicular plugging or atrophy. Diascopy was negative. Similar, but smaller, lesions were present over the abdomen and right thigh. Several brown linear plaques were identified over both axillae. Her extremities and back were spared. There were no nail changes, lymphoadenopathy or hepatosplenomegaly. Examination of other systems were unremarkable. The main clinical differential diagnoses included discoid lupus erythematosus, lupus erythematosus tumidus, Jessner's lymphocytic infiltration of the skin, lymphocytoma cutis, cutaneous lymphoma and lupus vulgaris.

Blood tests including complete blood picture, renal and liver function tests were within normal limits. ESR was mildly raised at 24 mm/1 hr. Anti-nuclear antibody was negative.

An incisional skin biopsy was performed over the forehead. It showed non-specific changes of perivascular lymphocytic infiltration with a rich plasma cell component, which would be consistent with connective tissue disease. The patient was put on a trial of topical 1% hydrocortisone cream, and later 0.1% mometasone furoate cream, without improvement. A second biopsy was performed over the left axillary plaque (Figures 3 & 4). It showed dense, demarcated, lymphoplasmacytic infiltrates around blood vessels and skin appendages in the dermis. The infiltrates included centrocyte-like cells. Follicle formation was present. The epidermis was unremarkable and dermal mucin was not increased. PCR for immunoglobulin Fr3/JH gene rearrangement was demonstrated, which suggested monoclonal B-cell proliferation. The overall morphology was consistent with cutaneous marginal zone B-cell lymphoma. The patient was referred to the medical team for workup of any systemic involvement. Bone marrow examination and CT imaging showed no extracutaneous involvement. The diagnosis of primary cutaneous marginal zone B-cell lymphoma (WHO-EORTC) was made. The patient was commenced on cyclical chlorambucil 10 mg daily for 2 weeks.

Discussion

PCMZL is a low grade B-cell lymphoma which is

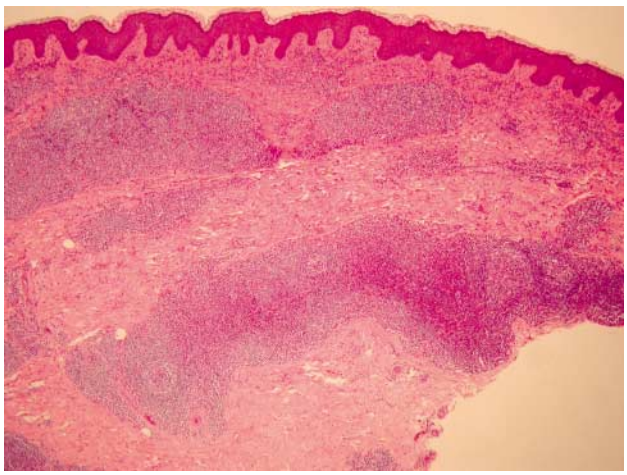

Figure 3. Dense, well demarcated lymphoplasmacytic infiltrates around the bloods vessels and skin appendages. Follicle formation is noted. (H&E, Original magnification x 10).

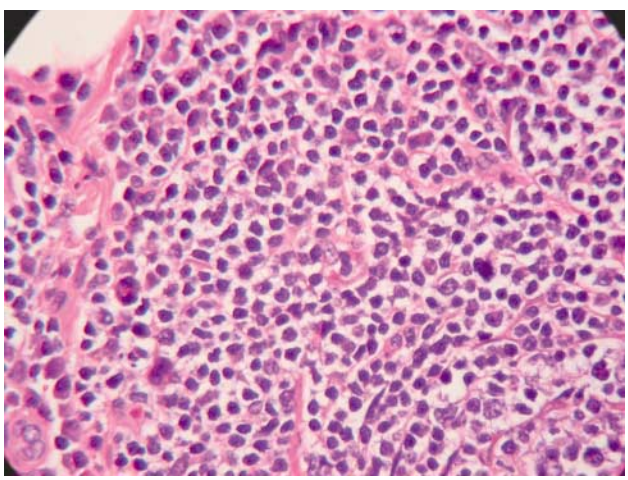

Figure 4. The marginal zone cells have abundant pale cytoplasm and irregular indented nuclei. The nucleoli are inconspicuous. (H&E, Original magnification x 40).

the second most common primary cutaneous B-cell lymphoma after primary cutaneous follicle centre lymphoma. It is a distinct entity and shares histological and clinical characteristics with mucosa-associated lymphoid tissue lymphomas (MALT). Under the European Organization for Research and Treatment of Cancer Classification (EORTC), it is equivalent to 'marginal zone B-cell lymphoma/primary cutaneous immunocytoma'. Whereas under the World Health Organization Classification (WHO), it is equivalent to 'extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoma tissue (MALT lymphoma)'. The latest WHO-EORTC classification for cutaneous lymphoma uses the term 'primary cutaneous marginal zone B-cell lymphoma' to unify the various entities above when they occur primarily in the skin.[1]

PCMZL is characterised by a clonal proliferation of small B lymphocytes, including marginal zone (centrocyte-like) cells, lymphoplasmacytoid cells, and plasma cells showing monotypic cytoplasmic immunoglobulin light-chain expression. Apart from case reports and small case series, there have been no large studies looking at the clinical characteristics, optimal treatment and clinical outcome of this entity. PCMZL represents 2-15% of all cutaneous lymphoma. With gene rearrangement analyses and immunohistochemical studies, an increasing number of PCMZL are now being diagnosed. PCMZL shows no gender preponderance and most patients are above forty years old.

The pathogenesis of PCMZL is not fully understood. *Borrelia burgdoferi* is associated with a significant minority of the European cases,[3] but it has not been reported in any Asian[4] or US[5] cases. It is postulated that PCMZL arises from chronically stimulated lymphoid tissue acquired in the skin in response to *B. burgdoferi* infection. This phenomenon is analogous to *H. pylori* infection in gastric MALT lymphoma. Clinically, PCMZL are typically found over the trunk, upper limbs, chest, axillary folds and back. The head and neck regions are less commonly involved. The lesions are red to violaceous papules, nodules or plaques. Ulceration is uncommon. Multifocal lesions are often present at the time of diagnosis. PCMZL tends to recur in skin, but dissemination to extracutaneous sites is rare. However, it is necessary to look for extracutaneous involvement when the diagnosis is initially made, especially of the gastrointestinal

tract, lung, lymph nodes, breasts, thyroid glands and salivary glands.

The diagnosis of PCMZL is based on histopathology, immunoprofile and gene rearrangement studies. Histologically, there are typically dense polymorphous lymphocytic infiltrates in the dermis, and occasionally in the subcutaneous fat. The infiltrates are composed of small to medium-sized marginal zone cells (centrocyte-like) or monocytoid cells. They are arranged mostly in a nodular pattern, but can also be diffuse. There is a variable number of lymphoplasmacytoid cells and plasma cells at the margins of the infiltrate. Dutcher bodies, which are intranuclear PAS positive pseudoinclusions, are commonly seen in the plasma cells. Reactive germinal centres are also frequently identified. The epidermis is usually uninvolved. Histologically, PCMZL needs to be differentiated from primary cutaneous follicle centre lymphoma, cutaneous pseudolymphoma, and non-Hodgkin's B-cell lymphoma with secondary involvement of the skin. This differentiation is not always easy, and can be assisted by immunoprofile and cytogenetic studies. In PCMZL, the marginal zone B-cells express CD19, CD20, CD22, CD79a and bcl-2. They are negative for CD5, CD10, bcl-6 and CD23. The lymphoplasmacytoid cells and plasma cells show monotypic expression of Ig light chains (K/λ) on paraffin sections. Cytogenetic studies show clonal rearrangement of the immunoglobulin heavy chain (IgH) genes. Recent studies suggest the presence of the t(14;18)(q32;q21) involving the *IGH* gene on chromosome 14 and the *MLT* gene on chromosome 18, and t(3;14)(p14.1;q32) involving *IGH* and *FOXP1* genes, in a proportion of PCMZLs.[6,7]

The most appropriate therapy for PCMZL has not been established. The management depends on whether the lesion is solitary or multifocal, and whether the disease is at its initial presentation or recurrence. If only a few lesions are present, the choices include radiotherapy or surgical excision. However, there is a high rate of local relapse for patients receiving only local therapy. Therefore, some argue that systemic or combined modality therapies may be preferable to local therapy. Systemic therapies are also used for more extensive multifocal lesions. They include chemotherapy (chlorambucil,[8] cyclophosphomide, doxorubicin, vincristine and prednisolone), anti-CD20 antibody (Rituximab)[9] and interferon α-2a.[10] In recurrence, a wait-and-see strategy can be adopted since the disease has a low mortality. Nevertheless, palliative treatment (e.g. radiotherapy) can be used for larger or disturbing skin lesions. It is also worth noting that a trial of systemic antibiotics for possible *B. burgdoferi* infection in endemic regions can be considered. Overall, as PCMZL is a relatively indolent lymphoma, the benefits of treatment should be weighed against any possible side-effects.

The prognosis is PCMZL is excellent with a 90-100% 5-year survival. Spontaneous resolution of skin lesions have been reported in some cases. Complete remission is usually achieved after initial treatment, but relapse and local recurrence is seen in 30-48% of cases.[11] Although systemic spread is rare, reports of large B-cell transformation and extracutaneous dissemination have been reported. At this stage, prognostic parameters for PCMZL are still to be determined.

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