Hong Kong J. Dermatol. Venereol. (2005) **13**, 222-226

Case Report

Primary cutaneous follicular lymphoma: report of a rare disease in the Chinese

原發性皮膚濾泡型淋巴瘤：罕有華人病例報告一宗

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A 53-year-old man presented with an infiltrated red patch over nose. Histopathology showed malignant lymphoid infiltrate with neoplastic lymphoid follicles. Immunohistochemical staining showed CD20+ bcl-6+ B cells. This is a case of follicular lymphoma.

53 歲男患者患有鼻部紅色斑片。組織病理顯示惡性淋巴樣細胞浸潤及腫瘤性淋巴樣濾泡。免疫化學染色法顯示 CD20+ bcl-6+ B 淋巴細胞。此例為濾泡型淋巴瘤。

Keywords: Chinese, Follicular lymphoma

關鍵詞：華人，濾泡型淋巴瘤

Case report

A 53-year-old Chinese male noted an asymptomatic patch over the nose for six months. The lesion progressively increased in size. There was no weight loss or systemic upset. The past history was unremarkable except that he underwent an appendicetomy in 1985. On examination, an erythematous, oedematous infiltrative plaque was found over the nose tip and ala nasi on the right side (Figure 1). There was no epidermal change. In addition, there were no sensory loss or lymphadenopathy.

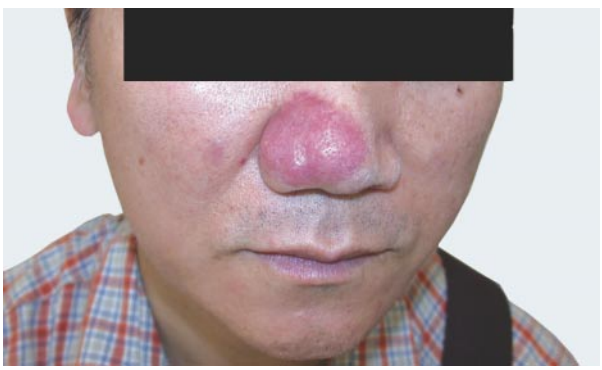

Figure 1. An erythematous infiltrated plaque over the nose.

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The differential diagnoses include rosacea, granuloma faciale, lymphocytoma cutis, Jessner's lymphocytic infiltrate, lupus erythematosus, lupus pernio, lupus vulgaris, and leprosy.

Laboratory investigations showed a slightly raised ALT 66 U/L which normalised subsequently. HBsAg was negative, ANA titre 1:80. Chest X-ray showed no significant abnormality. The lung fields appeared clear. A skin biopsy was done, and histopathology showed a dense lymphoid infiltrate in the dermis (Figure 2). The infiltrate had a mixed follicular and diffuse pattern. The lymphoid follicles consisted of a mixture of large round centroblasts and medium-sized and small irregular centrocytes, and there was a lack of tingible body macrophages (Figure 3). In the diffuse areas and the interfollicular areas, the lymphoid infiltrate consisted of a mixture of small lymphocytes and medium-sized and large cells, some with nuclear irregularity (Figure 4). Immunohistochemical staining showed that the lymphoid infiltrate consisted of sheets of CD20 positive B cells; in both the follicular and diffuse areas. The lymphoid follicles were negative for bcl-2 expression. Bcl-6 positive cells were found both within and focally outside the follicles. The features were compatible with follicular lymphoma (grade 2).

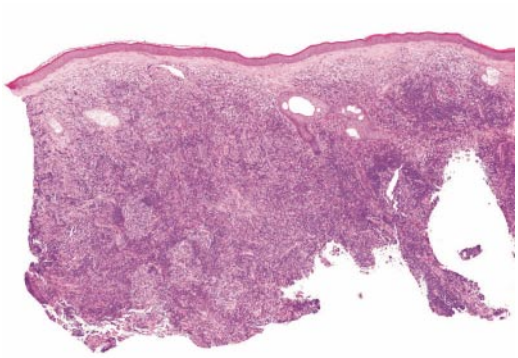

Figure 2. The skin biopsy shows a dense dermal lymphoid infiltrate with neoplastic lymphoid follicles identified near the base (H & E, Original magnification x 40).

Discussion

According to the European Organization for Research and Treatment of Cancer (EORTC) definition of primary cutaneous lymphoma (PCL), the lesion has to be present in the skin, with no evidence of extracutaneous disease at the time of diagnosis and within the first 6 months after

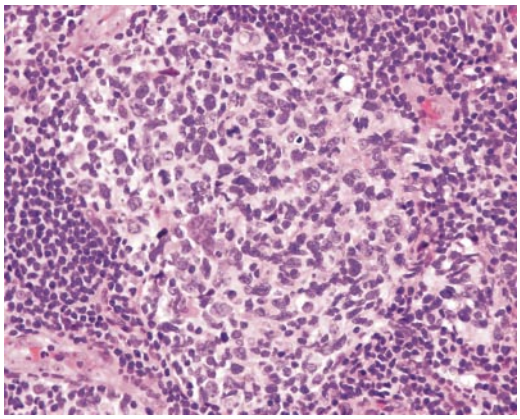

Figure 3. The neoplastic follicle consist of a mixture of large round centroblasts and medium-sized and small irregular centrocytes. Tingible body macrophages are not seen (H & E, Original magnification x 400).

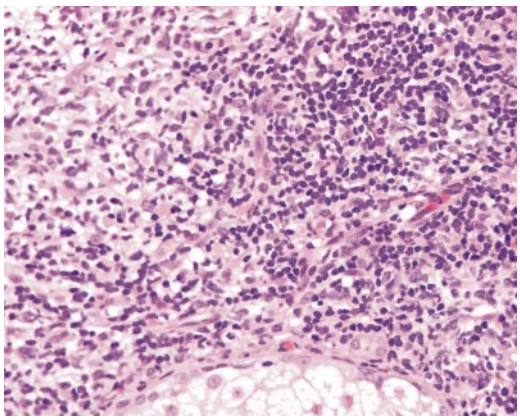

Figure 4. In the diffuse area of the lymphoid infiltrate, there is a mixture of small lymphocytes and medium-sized and large cells, some with nuclear irregularity (H & E, Original magnification x 400).

diagnosis (with the exception of classical mycosis fungoides and Sézary syndrome).[1]

PCL is the second most common extranodal lymphomas, after gastrointestinal lymphomas.[2] According to the WHO-EORTC classification for PCLs, PCLs are classified as follows: cutaneous T-cell and NK-cell lymphomas; cutaneous B-cell lymphomas; and precursor haematologic neoplasm.[3] Primary cutaneous B-cell lymphoma (PCBCL) (WHO-EORTC) comprises 20-25% of all PCLs.[3] For all PCBCLs, primary cutaneous follicle centre lymphoma (including all cases of cutaneous follicular lymphoma and some cases of diffuse large B-cell lymphoma by other classifications) makes up 48%; while the remaining ones are primary cutaneous marginal zone B-cell lymphoma (30%) and primary cutaneous diffuse large B-cell lymphoma (leg type and others) (22%).[3]

The systemic form of Follicular lymphoma (FL) is an indolent B-cell lymphoma but widespread disease is frequent. It is a common type of non-Hodgkin lymphoma (NHL) in adults, and is predominantly a nodal disease. It accounts for 35% of all NHL in the United States and 22% in the world.[4] Ethnic differences exist in this entity: this condition is uncommon in Hong Kong (Asia), only comprising 8% of all NHL.[5] It remains incurable for the majority of patients, despite its initial responsiveness to a variety of therapeutic modalities. The 5-year overall survival rate is 72%, the 5-year failure-free survival rate is 40%, and the survival rate continues to drop after 5 years.[6]

The genetic hallmark of FL is the reciprocal t(14;18)(q32;q21), which is the most common chromosomal translocation in lymphoid neoplasms. It is identified in a majority of FL cases (70-95%).[7,8] The t(14;18) juxtaposes the *bcl-2* oncogene with the immunoglobulin heavy chain (IgH) joining region, resulting in the constitutive overexpression of the antiapoptotic *bcl-2* gene, a key early event in the oncogenesis of FL. The translocation is detectable in roughly 70% of cases by polymerase chain reaction (PCR). Other methods of detection include Southern blotting (the gold standard) and fluorescence *in situ* hybridisation (FISH).

FL displays a growth pattern that recapitulates germinal centre-like structures. It composes of germinal centre-derived B cells (centrocytes and centroblasts) that display pan-B-cell markers (CD19, CD20, CD22, and CD79a) monotypic surface light chains and frequently express the follicle centre cell-associated antigens, CD10 and bcl-6 protein. Primary cutaneous FL involves adults of both genders. It presents with erythematous papules, plaques, nodules, and tumours, usually non-ulcerated. It occurs mostly on the head and neck and on the trunk. It usually clusters at a single site, but may be multiple at different sites. The histopathology of primary cutaneous FL consists of variable proportions of centroblasts and centrocytes (germinal centre-derived B-cells) with variable proportions of follicular and diffuse areas. Similar to systemic FL, there is also expression of pan-B-cell markers (CD19, CD20, CD22, CD79a) and follicle centre cell-associated antigens (CD10 or bcl-6).

In a study of 17 patients suffering from primary cutaneous FL, the median age at diagnosis was 63 years.[9] The initial presenting skin lesions were localised to the head and neck region (n=16) or rarely the trunk (n=1). CD10 expression was found in 90% (27 of 30) of cases, while bcl-6 was found to be expressed in all cases tested. Bcl-2 expression was found in 57% (17 of 30) of the cases, and t(14;18) translocation was noted in 31% (4 of 13) of the patients with primary FL. Seven of 17 (41%) patients had cutaneous relapse, 4 multiple relapses and 1 nodal disease. Extra-cutaneous relapse was rare.[9] t(14;18) IgH/BCL-2 translocation was found in the majority of systemic nodal FL. While several studies reported a uniform lack of this translocation in primary cutaneous FL,[10,11] other investigators noted this occurred in 13% to 40%.[9,12-14] The reason for the difference is not certain. Most series

agree that its detection is lower compared with systemic FL. In secondary disease and grade 1 or 2 primary cutaneous FLs, the detection rate of the translocation was higher. Concerning bcl-2 protein expression, it was detected in the majority of nodal FLs, approaching 100% in grade 1 and 75% in grade 3 lesions in one study.[15] However, the expression rate in primary cutaneous FL (PCFL) varied widely from 0% to 86%.[9-14] Most series agreed that its detection in PCFL is lower than its systemic counterpart.

Most PCBLs are unilesional or localised. Radiotherapy is usually used as first-line therapy. The choice of other treatment options depends on the age of the patient, the location, the histological subtype, the number of lesions, body surface area, and the general health condition. The options include surgical excision, INF-alpha, and chemotherapy. Recently, rituximab, a chimeric anti-CD 20 monoclonal antibody, was reported to have good effect.[16,17] A recent study reported the use of intralesional injections of rituximab into some but not all cutaneous lesions in a patient with multiple primary cutaneous follicular centre B-cell lymphoma. All lesions disappeared at 6 months, even for the lesions that had not been injected. It was hypothesised that there was systemic diffusion of rituximab from injected sites despite the low doses injected locally, or the induction of a specific anti-tumour immune response acting systemically.[18]

The prognosis of PCFL is much better than systemic FL and the disease-specific 5-year survival rate is greater than 95%.[3] Whether clinical differences exist between cases that are bcl-2 and/or t(14; 18) positive and those that lack these features remain to be determined.

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