DERMATOLOGICA SINICA 31 (2013) 86–89

Contents lists available at SciVerse ScienceDirect

Dermatologica Sinica

journal homepage: http://www.derm-sinica.com

CASE REPORT

Dermatopathic lymphadenitis in a patient with pemphigus vulgaris

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ARTICLE INFO

Article history:
Received: Nov 29, 2011
Revised: Apr 15, 2012
Accepted: Jun 25, 2012

Keywords:
dermatopathic lymphadenitis
lepomelanotic reticulosis
mycosis fungoides
Pautrier-Woringer disease
pemphigus vulgaris
Sézary syndrome

ABSTRACT

Dermatopathic lymphadenitis (DL) is a reactive lymphoid hyperplasia that commonly involves the regional lymph nodes in patients with chronic dermatoses, such as exfoliative dermatitis, toxic-shock syndrome, pemphigus, psoriasis, eczema, and, in severe cases, mycosis fungoides. Diagnosis of DL depends on the histopathologic characteristics of paracortical T-zone expansion with melanin, hemosiderin, or lipid-laden macrophages. Lymphadenopathies in patients with chronic dermatoses may be due not only to infections or malignancy, but also to reactive disorders such as DL. We describe the case of a 31-year-old woman with pemphigus vulgaris who has characteristic manifestations of DL.

Introduction

Lymphadenopathies in patients with pemphigus vulgaris (PV) have been attributed to several causes, including infections, malignant melanoma, Castleman's disease, or lymphoma.[1,2] Reactive lymphadenopathy in association with pemphigus such as dermatopathic lymphadenitis (DL) has rarely been reported, with only one case found in the literature.[3] DL is a histopathologic diagnosis of reactive lymph node hyperplasia, which is characterized by increased numbers of interdigitating reticulum cells, Langerhans cells, and histiocytes with lipid and melanin deposits.[4] The lymph nodes are usually moderately enlarged and not tender. DL is typically associated with exfoliative or eczematoid inflammatory erythrodermas.[3] Importantly, the early lymph node involvement of mycosis fungoides or Sézary syndrome (MF/SS) may be difficult to differentiate from the features of DL.[4] Awareness of DL and its potential relationship with MF/SS may be crucial to improving prognosis.

Case report

A 31-year-old woman was diagnosed with PV 8 years ago. She was prescribed systemic corticosteroid, cyclosporine, azathioprine, and methotrexate; however, control of PV was irregular, because she stopped taking her medications as directed. She also took unknown Chinese herbs and folk remedies without her physicians' knowledge. Consequently, she suffered from recurrent flaccid vesicles, erosions, desquamations and crusts over the face, scalp, neck, trunk, and limbs. Her skin lesions occasionally worsened to erythroderma. Repeat skin biopsies showed intraepidermal blisters with intercellular depositions of C3 and IgG in the lower epidermis. PV was confirmed.

She presented with gradually enlarging masses over the groin, which had been evident for 2 months. Physical examination revealed several movable, elastic-firm nodules (1–2 cm in diameter) without tenderness over the bilateral inguinal areas (Figure 1A). Erosive wounds and flaccid bullae over the bilateral legs and insteps were also present. The infectious disease consultant first suspected cutaneous wound infection with lymphadenopathies; however, the lymphadenopathies persisted after several weeks of antibiotic treatment. On referral to our care, we performed a lymph node biopsy and other examinations to investigate the cause.

Laboratory examinations showed normal white blood cell counts, with 15.8% eosinophilia but no other atypical lymphocytes. C-reactive protein, lactate dehydrogenase, renal function, and liver function were normal. Computed tomography (CT) revealed multiple lymph nodes of varying size in the bilateral inguinal regions, but detected no definite lymphadenopathies or tumors in the pelvic cavity (Figure 1B). A gallium scan showed no significant lymphoma, inflammation, or infection foci in the internal organs.

Low-power lymph node histopathology showed hyperplastic follicles, preserved nodal structure, and a paracortical T-zone

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1027-8117/$ – see front matter
http://dx.doi.org/10.1016/j.dsi.2012.09.003

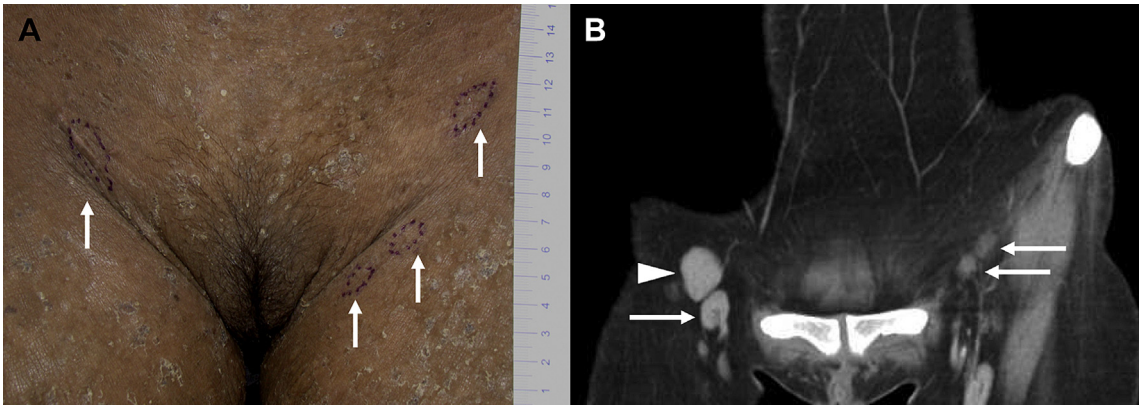

Figure 1 (A) Several movable, elastic-firm nodules without obvious tenderness in bilateral inguinal areas apparent for 2 months (arrows). (B) Pelvic computed tomography showed multiple enlarged lymph nodes over the bilateral inguinal area (arrows and arrowhead). We biopsied the largest lymph node over the right inguinal area (arrowhead).

expanded by numerous pale-stained cells (Figure 2), with prominent adjacent pigment deposition (Figure 3A). High-power magnification showed twisted nuclei and abundant cytoplasm characteristic of interdigitating dendritic and Langerhans cells. Multiple, scattered, pigment-containing histiocytes and eosinophils were present in the paracortical area (Figure 3B). Fontana-Masson stain and Prussian blue stain confirmed the presence of melanin and smaller deposits of hemosiderin (Figure 3C, and D). There were no atypical lymphocytes in the paracortical zone. Immunohistochemistry revealed polyclonal proliferation, with mixed CD4+ and CD8+ lymphocytes.

Given her history of chronic relapsing exfoliative PV and slowly enlarging lymph nodes with characteristic histopathology, we diagnosed DL. After 3 months of intensive treatment for PV with systemic and topical steroid, physical examination showed slightly smaller inguinal lymph nodes (the largest remaining lymph node decreased in size from 1.5 cm to 1.0 cm) with no new lesions. Long-term follow-up is still warranted.

Discussion

First described by Wise, in 1917,[5] and characterized by Pautrier and Woringer, DL is also known as Pautrier-Woringer disease, or lepomelanotic reticulosis, due to its characteristic fat and melanin deposition.[4,5] Hurwitt coined the term dermatopathic lymphadenitis in 1942.[3]

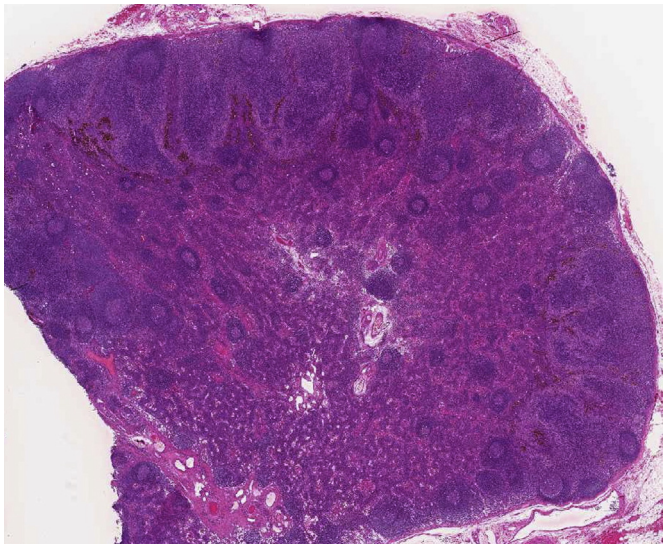

Figure 2 Low-power magnification shows palely-stained areas in the paracortical regions and hyperplastic lymphoid follicles. Nodal architecture is preserved (hematoxylin and eosin, 20×).

DL is a morphologically distinct form of reactive lymphoid hyperplasia; it often involves regional lymph nodes in patients with benign exfoliative or eczematoid chronic dermatoses, toxic-shock syndrome, pemphigus, psoriasis, neurodermatitis, eczema, or atrophia senilis.[3–6] However, it may also be idiopathic and is common in patients with MF/SS. The incidence of DL without skin disease is estimated at 12.5–34.0%.[5,6] DL affects patients of all ages, and is more frequent among women than men.[7] DL most often involves axillary and inguinal lymph nodes and rarely occurs in the head and neck.[8] The enlarged lymph nodes are usually freely-movable, firm, and relatively painless. The duration of skin manifestations preceding a positive biopsy of DL varies from 6 months to more than 6 years.[3,7] Peripheral eosinophilia, sometimes as high as 35%, can also be a constant feature.[3]

DL has characteristic histopathology, with marked paracortical expansion by irregularly-shaped, pale-staining patches of interdigitating reticulum cells, Langerhans cells, and phagocytic histiocytes. Hyperplastic lymphoid follicles are always present. Some phagocytic histiocytes may contain cytoplasmic lipid and appear foamy; others are heavily laden with pigment, mostly melanin and occasionally hemosiderin. A mixture of plasma cells with a scattering of eosinophils may also be apparent. Notably, there is no distortion of the lymph node structure.[3–7] One hypothesis is that DL is a reaction to barrier disruption of dependent skin, that subsequently results in massive transport of melanin to the lymph node.[4]

Gould et al devised a grading system for DL to classify histopathology findings, which ranges from Grade 0 (sparse or no obvious histiocytes or dendritic cells with or without pigment deposition) to Grade 4 (sheets of these cells with invariable pigment deposition), with proportionally more concomitant skin disease the higher the grade.[6]

Localized inguinal lymphadenopathy in patients with PV is usually caused by infection, reactive change (e.g., DL), or malignancy (e.g., MF/SS; Table 1).[4,7] It is very difficult to distinguish DL associated with MF/SS from DL without MF/SS. In the early stages of lymph node involvement, MF/SS may have similar histopathlogy to DL, because both exhibit a diffusely-distributed area of pale cells interspersed with varying numbers of atypical cerebriform lymphocytes. The earliest diagnostic clue for MS/SS is increased size of cerebriform lymphocytes within the expanded paracortical area. As medium to large-sized atypical lymphocytes multiply in advanced MF/SS, they invade the medulla and sinus and form sheets of infiltrating monomorphic lymphoid cells. Unlike DL, in