Dermatopathic lymphadenitis in a patient with pemphigus vulgaris

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CASE REPORT

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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 physician's 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 deposits 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...
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, and characterized by Pautrier and Woringer, DL is also known as Pautrier-Woringer disease, or lepromelanic reticuloendotheliosis, due to its characteristic fat and melanin deposition.4,5 Hurwitt coined the term dermatopathic lymphadenitis in 1942.3 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 atrophoderma 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 histopathology 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 MF/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
which cerebriform lymphocytes do not occur in a large sheet, MF/SS partially or totally obliterates the lymph node architecture. Nevertheless, additional immunohistochemistry or molecular studies, such as the loss of pan-T-cell marker expression and monoclonal T-cell receptor gene rearrangements in MF/SS, are sometimes needed to distinguish DL from MF/SS.4,7 F-18 fluoro-deoxyglucose (FDG) positron emission tomography/CT scanning is an ideal screening tool to detect internal lymphoma or lymph node involvement in MF/SS. However, a potential limitation in F-18 FDG positron emission tomography/CT evaluation of lymphoma, is that DL may also show intensely FDG-avid lymph nodes.9 Coexisting pemphigus and MF are seldom reported.10 However, chronic PV resulting in hyperpigmented skin lesions would make early skin lesions of MF/SS harder to detect. Therefore, careful physical examination is necessary.

There are no consensus guidelines for treating DL.8 Since DL is a benign reactive disease, controlling the underlying skin disease is prudent. No further intervention is necessary, unless there is local

Figure 3 (A) Prominent pigment deposition adjacent to expanded T-zone (hematoxylin and eosin, 40×). (B) High-power magnification shows twisted nuclei and abundant cytoplasm of interdigitating dendritic and Langerhans cells, with multiple, scattered, pigment-containing histiocytes and eosinophils (hematoxylin and eosin, 400×). (C) Melanin fills histiocytes’ cytoplasm (Fontana-Masson stain, 200×). (D) Hemosiderin-laden histiocytes (Prussian blue stain, 200×).

Table 1 Differential diagnosis of dermatopathic lymphadenitis (DL).4,7

<table>
<thead>
<tr>
<th>Clinical manifestation</th>
<th>Lymph node</th>
<th>Histopathology</th>
<th>Immunohistochemistry and molecular findings</th>
<th>Additional features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ordinary bacterial lymphadenitis</td>
<td>Constitutional symptoms of infection</td>
<td>Enlarged, soft, tender, localized, or generalized</td>
<td>Perilymphadenitis, infiltration of neutrophil leukocytes and macrophages, suppurative foci</td>
<td>Gram stain for bacteria</td>
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<tr>
<td>DL</td>
<td>History of exfoliative or pruritic dermatoses; peripheral eosinophilia</td>
<td>Enlarged, firm, nontender, usually localized</td>
<td>Architecture preserved, follicular hyperplasia, expand paracortical palely stained area; infiltration of melanin-, hemosiderin-, and lipid-laden macrophages, plasma cells and eosinophils</td>
<td>Increased histiocytes and specialized cells: IRCs (S100+, CD1a–), LCs (S100+, CD1a–)</td>
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<tr>
<td>MF/SS with LN involvement</td>
<td>Primary skin lesion (patch, plaque, tumor, or erythroderma); peripheral Sézary cells</td>
<td>Enlarged, nontender, more generalized</td>
<td>Early stage: resemble DL; Late stage: partial or total obliteration of LN (distortion of nodal architecture); polymorphic infiltrate with small (Lutzewer) to large (Sézary) atypical lymphocytes</td>
<td>CD4+, CD8– (75% of cases); CD2+, CD3+, CD5+, CD45R0+ (can be aberrantly dim, bright, or absent), CD7– (often); monoclonal TCR gene rearrangements</td>
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IRCs — interdigitating reticulum cells; LCs — Langerhans cells; LN — lymph node; MF — mycosis fungoides; SS — Sézary syndrome; TCR — T-cell receptor.
compression or malignancy is suspected. In a series of 12 cases with prolonged follow-up, there was no progression and the lymphadenopathy disappeared in one case.

We report a new case of DL with underlying PV in Taiwan. According to Cooper et al., DL may be much more common than has been reported, due to its reactive nature. Therefore, DL should always be considered in cases of asymptomatic lymphadenopathy in patients with chronic dermatitis. Alternatively, physicians should maintain a high index of suspicion for potential secondary lymph node infiltration by MF/SS in patients with DL, which correlates with poorer prognosis. Therefore, we recommend thorough physical examination and long-term follow-up.

References


