Angioimmunoblastic T-cell lymphoma

Sir,

Angioimmunoblastic T-cell lymphoma is a nodal T-cell lymphoma derived from follicular helper T cells with complex dysregulation of B cells. Extranodal sites, including cutaneous lesions, are well recognized.[1,2] Cutaneous lesions may manifest as a pruritic maculo-papular eruption mimicking a viral exanthem or drug hypersensitivity reaction, urticaria, erythroderma, erosions, petechiae, purpura, papulo-vesicles, prurigo-like lesions, plaques or as tumor nodules.[3]

A 42-year-old man presented with a history of recurrent abscesses and pruritus for about 8 months accompanied by rapid weight loss, loss of appetite, and generalized weakness. He also had pain and swelling in both wrists for 1 month. There was no history of tuberculosis, diabetes mellitus or exposure to sexually transmitted diseases.

On examination, the patient was pale and poorly nourished. There were multiple abscesses on the scalp, retro-auricular region, trunk and dorsum of hands [Figure 1a, b, and d]. Deep necrotic ulcers were seen over the buttocks and scrotum [Figure 1c]. Axillary, inguinal, and femoral lymph nodes were visibly enlarged [Figure 1e], about 2 × 3 cm in diameter, soft in consistency, non-tender and mobile. He had generalized xerosis with a few keratotic papules and excoriation marks over the extremities and trunk. Examination of the abdomen revealed non-tender hepatomegaly. There was tenderness and swelling of both knee joints, wrists and hands.

Hematological investigations revealed anemia, leukocytosis with eosinophilia and absolute lymphocytosis [hemoglobin (Hb) 10.4 gm%, total count 55,700/cumm], and a raised erythrocyte sedimentation rate (ESR; 150 mm/h). Blood sugar, renal and liver function tests were within normal limits. X-ray of the involved joints was normal. Culture of pus aspirated from the abscesses revealed growth of *Staphylococcus aureus*.

Skin biopsy revealed an ulcerated epidermis with necrosis and a dense neutrophilic infiltrate. The underlying dermis showed blood vessels infiltrated by neutrophils. Scattered lymphocytes were seen in the upper dermis. Lymph node biopsy revealed diffuse effacement by an interfollicular mixed polymorphous infiltrate of small to medium-sized lymphocytes, plasma cells, eosinophils, epithelioid histiocytes, immunoblasts, and prominent arborizing high endothelial venules [Figure 2a–d]. Bone marrow biopsy

revealed an increase in myeloid, lymphoid, and plasma cells with an increased myeloid: erythroid ratio of 20:1.

Immunohistochemistry of the lymph node biopsy revealed that the majority of cells expressed CD3 and CD4. Endothelial cells expressed CD31. Follicular dendritic cells expressed CD23, while interfollicular dendritic cells expressed CD1a. Some cells expressed CD20, CD138, and CD23 [Figure 3a–e]. Immunohistochemistry of the skin biopsy did not reveal atypical cells. Serum electrophoresis showed an increase in alpha-1, alpha-2, beta, and gamma globulins.

In view of the clinical features and the hematological, histopathological and immunohistochemistry findings, a diagnosis of angioimmunoblastic T-cell lymphoma with dysproteinemia was made.

Angioimmunoblastic T-cell lymphoma is a nodal T-cell lymphoma derived from follicular helper T cells and is associated with dysregulation of B cells.[1] It is a clinico-pathologic syndrome characterized by fever, night sweats, weight loss, generalized lymphadenopathy, hepatomegaly, and splenomegaly.[4] The most common first presentation of the disease is generalized lymphadenopathy. Forty five percent of patients have extranodal cutaneous involvement.[2]

Cutaneous features are frequently observed during the course of this disease.[5,6] These consist of maculo-papular eruptions, purpura, infiltrated or urticarial plaques, papulo-vesicular lesions, nodules and erythroderma.[3] Facial edema, livedo reticularis, and drug eruption may be seen during chemotherapy. These eruptions regress spontaneously or after corticosteroid treatment.[7] Relapse may also trigger cutaneous features.

The diagnosis can be confirmed by histopathology and immunophenotyping. Lymph node biopsy shows a tumor composed of lymphoid cells with proliferation of arborizing vessels and effacement of nodal architecture.[4,8] Plasma cells, eosinophils and a dense infiltration of medium to large pleomorphic cells may be seen. Lymphoid cells are positive for CD3, CD4, and CD21 with partial positivity for CD8 and CD30.[1,9]

The histopathological features are usually non-specific and a small percentage of patients show features suggestive of a cutaneous T-cell lymphoma.[3,4,8,10] Immunophenotypic studies of the dermal lymphoid

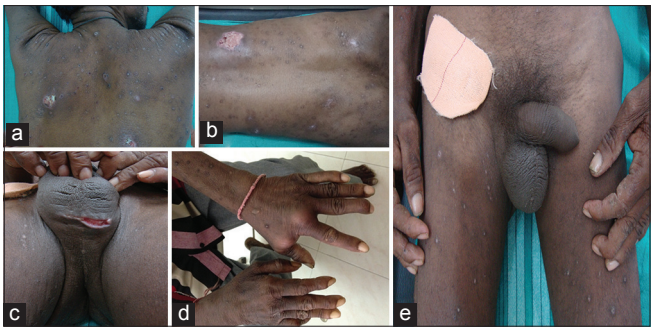

Figure 1: (a and b) Multiple necrotic ulcers over the back, (c) necrotic ulcer over the scrotum, (d) abscesses over the dorsum of left hand, (e) visibly enlarged inguinal and femoral lymph nodes

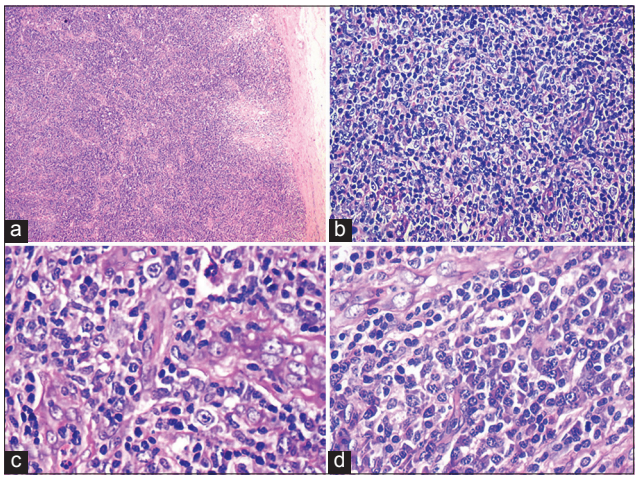

Figure 2: (a) Effacement of normal lymph node architecture, (b) abnormal lymphocyte proliferation with vesicular nuclei and prominent nucleoli, (c) prominent proliferation of high endothelial venules, (d) sheets of plasma cells

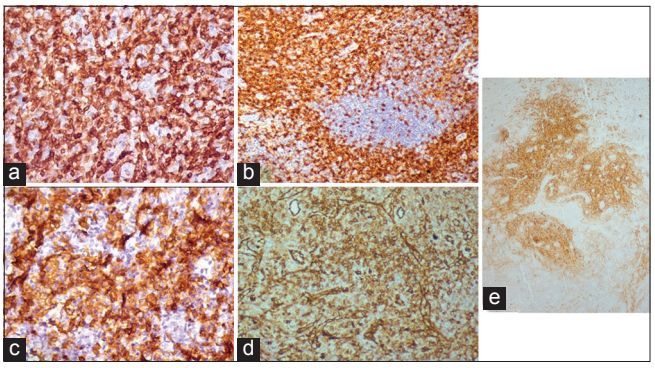

Figure 3: Immunohistochemistry (IHC) showing (a) CD3 expression by T-lymphocytes; (b) CD4 expression by T-lymphocytes; (c) Sheets of plasma cells expressing CD138; (d) High endothelial blood vessels expressing CD31; (e) Follicular dendritic cells decorated by CD23

infiltrates are poorly informative.[9,10] Martel *et al.* classified this variant of T-cell lymphoma into four histologic groups as follows: (1) non-specific pattern of mild perivascular infiltrates of eosinophils and lymphocytes with no atypia in

the superficial dermis associated with capillary hyperplasia; (2) sparse superficial perivascular infiltrates of atypical lymphocytes with pleomorphic and kidney-shaped nuclei associated with vascular hyperplasia; (3) dense pleomorphic infiltrate composed of atypical lymphocytes in the superficial and deep dermis, suggestive of cutaneous lymphoma; and (4) vasculitis without cellular atypia.[11]

Infectious diseases may be associated with this lymphoma, especially lymphotropic viruses such as Epstein–Barr virus (EBV), which is noted in a majority of lymph nodes.[12]

The molecular alterations underlying the neoplastic transformation of T-helper cells include clonal aberrations in chromosomes 3, 5, and 21.[13,14]

Treatment with systemic corticosteroids and chemotherapy has been advocated as first line therapy, including cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) based regimens. Monoclonal antibody agents such as alemtuzumab and rituximab added to such regimens may improve the clinical outcomes.[15]

The prognosis of these patients is poor with a mortality rate of 50-75% and a mean survival of 1–2 years from the time of presentation.[3]

Our patient presented with recurrent large abscesses and necrotic ulcers along with severe pruritus, arthritis, fever, significant weight loss, lymphadenopathy and hepato-splenomegaly. He was treated with cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) regimen at a cancer institute.

It is important to recognize that abscess formation and necrotic ulcers may be rare manifestations of angioimmunoblastic T-cell lymphoma in which cutaneous involvement is a poor prognostic sign.

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