

A Case of Dermatopathic Lymphadenopathy Associated with Hypereosinophilic Syndrome

Dear Editor,

A 42-year-old man presented with a 4-week history of erythematous, maculopapular rash over his whole body (Fig.1), shortness of breath and generalised lymphadenopathy for 1 week. Clinical examination showed erythroderma with multiple lymph nodes in the cervical, axillary and groin areas. The lymph nodes were firm, mobile, non tender and were not attached to underlying structures. The lymph nodes were about 3.0 cm by 2.0 cm in size. Clinical examination of the respiratory system showed prolonged expiratory phase with diffuse wheeze over both lungs. There was no evidence of hepatosplenomegaly.

Complete blood picture showed a raised absolute eosinophil count of 1.6 k/ul. His immunoglobulin (Ig) E was raised at 5380 IU/ml (normal range 0 to 165). His liver biochemistry, urea and electrolytes were all unremarkable. Repeated stool for ova and parasites (4 samples) were negative. His erythrocyte sedimentation rate, C-reactive protein, antineutrophilic cytoplasmic antibody, anti-nuclear antibody, complement 3, complement 4, IgA, IgG, IgM, rheumatoid factor, anti-extractable antibody, anti-cardiolipin antibody, serum tryptase, chest x-ray, urine for microscopy and urine for porphyrin were all unremarkable or within the normal range. The patient was also negative for hepatitis B surface antigen, hepatitis C antibody and Epstein Barr virus DNA.

Whole body positron emission tomography-computerised

tomography showed clusters of enlarged lymph nodes in the bilateral inguinal, axilla, jugular chains and occipital regions. These lymph nodes were minimally hypermetabolic lymphadenopathy. The standardised uptake value (SUVmax) of all these lymph nodes was 2.33. No enlarged lymph nodes were detected in the mediastinum, hilar, retroperitoneum or pelvic cavity. No hypermetabolic focal lesions were detected within the solid organs to suggest the presence of 18F-fludeoxyglucose-avid neoplasm.

On computerised tomography, prominent lymph nodes were seen in the bilateral cervical, subsegmental regions, bilateral axillary regions and bilateral inguinal regions. The largest lymph node was located in the right inguinal region at 3 cm in diameter. No abnormality was detected in the thorax, abdomen, pelvis and skeleton.

A skin biopsy showed a minimally inflamed skin tissue with increased eosinophil in the superficial dermis. The eosinophils were 25/high-powered field (Fig. 2). Focal mild increase in vascularity was noted in the dermal papillae. Serial step sectioning did not show any evidence of vasculitis. There was also no abnormal lymphoid infiltrate seen.

Biopsy of the right inguinal lymph nodes was subsequently performed. The 2 inguinal lymph nodes showed prominent sinus histiocytosis together with many pigmented macrophages. Mild follicular hyperplasia was observed. These appearances were typical of dermatopathic



Fig. 1. Erythematous, maculopapular rash over the back.

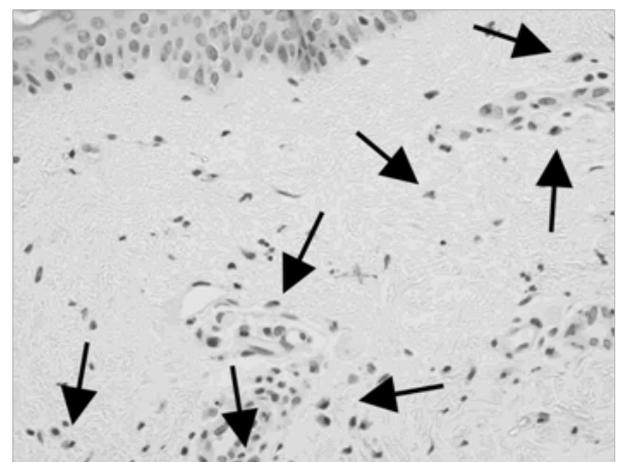


Fig. 2. Skin biopsy showing eosinophils (up to 25 per high-powered field) in the superficial dermis (arrows indicating eosinophils).

lymphadenopathy (DLA). There was no evidence of granulomata or giant cells in the lymph nodes. And, no atypia or malignancy was seen (Fig. 3).

The gentleman was finally diagnosed with hypereosinophilic syndrome after examination of his bone marrow biopsy for chromosome 4Q12 deletion; and the presence of tyrosine kinase created by fusion of the FIP1-like (FIP1) gene and platelet-derived growth factor receptor α (PDGFRA) gene.

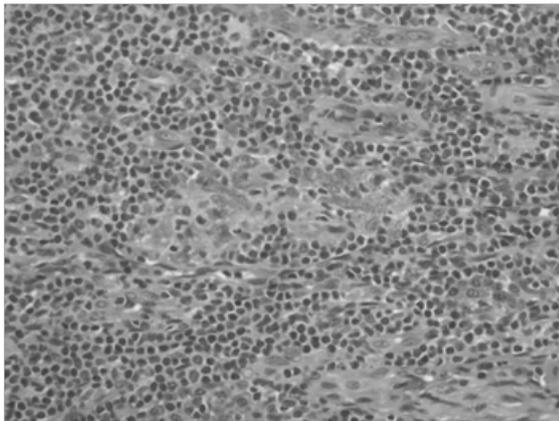


Fig. 3. Lymph node showing pigmented macrophages in the sinus (400X). All slides by haematoxylin and eosin staining.

Discussion

DLA can present in various ways; such as breast mass, parotid mass or neck infection. It can also be associated with elevated erythrocyte sedimentation rate and hypereosinophilia. In a study by Kojima *et al*,¹ they found that DLA was associated with peripheral eosinophilia in 50% of their patients. Although there are many known causes of DLA, this is the first documented case of hypereosinophilic syndrome manifesting as erythroderma complicated by DLA.^{2,3}

The patient in this case report presented with an increase in peripheral eosinophilia and skin lesions; and was subsequently diagnosed with hypereosinophilic syndrome. Hypereosinophilic syndrome is a disorder where there is an increase in eosinophils in the peripheral blood and also infiltration of eosinophils into the organ. The diagnostic criteria for hypereosinophilic syndrome are peripheral eosinophilia of more than 1500/ μ L for 6 consecutive months, no evidence of parasitic, allergic or other causes of eosinophilia and organ involvement.⁴

Cutaneous manifestations of hypereosinophilic syndrome usually consist of itchy erythematous and maculopapular rashes, urticaria or angioedema in 27% to 53%.^{4,5} A common histological finding on skin biopsy would be diffuse eosinophilic infiltration.

Hypereosinophilic syndrome is characteristically

associated with the deletion of chromosome 4Q12. The characteristic mutation for hypereosinophilic syndrome is an 800 kb deletion between FIP1L1 gene and the PDGFRA gene.⁴ This fusion of FIP1L1 gene and the PDGFRA genes will result in the creation of a new fusion protein, tyrosine kinase.⁴

The initial therapy for hypereosinophilic syndrome is systemic corticosteroid.^{4,5} However, resistance cases to high dose corticosteroid have been reported.⁶ In steroid resistant cases, the use of imatinib has been shown to be effective.⁶

He was started on systemic steroid at 1 mg/kg/day. His generalised lymphadenopathy resolved 2 weeks after commencement of systemic steroid while his skin rash resolved completely after 4 weeks.

In conclusion, this is the first reported case of hypereosinophilic syndrome manifesting as erythroderma complicated by DLA. In those with DLA and peripheral eosinophilia, hypereosinophilic syndrome is one of the differential diagnoses that clinicians have to keep in mind.

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