Multiple Nodular Swellings in an Adult Male

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Sir,

Histiocytoses are a heterogeneous group of disorders characterized by aggregation of reactive or neoplastic histiocytes in various body tissues. Histiocytoses disorders are grouped into four classes. We present a rare case of xanthoma disseminatum (XD), a class IIa non Langerhans cell histiocytosis in which cells with the phenotype of dermal dendrocytes accumulate in the skin and other tissues. A 44-year-old man presented with multiple yellowish and reddish brown papulonodular lesions distributed all over the body with preferential location on the flexures for the last 14 years [Figure 1]. The size of the lesions varied from 5 to 20 mm. The nodules present over the trunk and the limbs were asymptomatic and firm in consistency. There were multiple painful and tender papules and nodules distributed on both the palms [Figure 2]. He had single papular lesion in the oral cavity. New crops of papulonodular lesions appeared while the old persisted. Lesions distributed in the flexures coalesced to form plaques. There were no secondary changes in the form of pustulation, necrosis or ulceration. His systemic and ocular examination was normal. There was no history to suggest immunosuppression. We considered clinical possibilities of XD, generalized eruptive histiocytoma and sarcoidosis.

A punch biopsy taken from a forearm lesion on histopathological examination showed acanthotic epidermis

with diffuse and nodular histiocytic infiltration in mid and deeper dermis [Figure 3a]. Occasional Touton giant cells were seen. Immunohistochemistry showed CD68 positivity in the histiocytic cells [Figure 3b] and they were negative on staining for S100 protein. On further investigation, his lipid profile was normal and blood investigations (blood glucose levels-96 mg/dL, bicarbonate levels-26 mEq/L, and calcium-9.4 mg/dL) and urine analysis (urine specific gravity-1.014, urine osmolarity-560 mOsm/kg) done to detect diabetes insipidus did not reveal any abnormality. Complete hemogram, liver function test, kidney function test, and MRI of the brain were also normal. Serum electrophoresis did not show M band and urine test for Bence-Jones proteins was negative. On the basis of clinical, histopathological, biochemical and imaging studies, a diagnosis of XD was reached.

XD is a rare benign normolipemic non-Langerhans cell histiocytosis. In this disorder, the skin is infiltrated by proliferating monocytes/macrophages and lipid deposition is a secondary event. XD is considered a reaction pattern rather than a neoplastic process occurring as a result of superantigen triggered pathologic macrophage response.[1] It preferentially affects males during childhood and is characterized by the insidious appearance of hundreds of red brown to yellow brown papules and nodules which are discrete and disseminated over the trunk, face and the limbs particularly involving the flexures. Swellings present in the flexures can coalesce to form sheets of thick yellow skin. Around one third of affected individuals show lesions involving the mucosa including the oral, conjunctival, genital mucosa and the airways.[2] Extra-mucocutaneous lesions involve central nervous system (CNS) and bone. CNS involvement occurs in 40% of affected people due to histiocyte overgrowth on the meninges. This usually leads to vasopressin sensitive diabetes insipidus while some patient may also manifest with seizures. Other visceral involvement is uncommon.

Most of the cases are normolipemic though some may have mildly raised cholesterol and triglyceride levels. Some

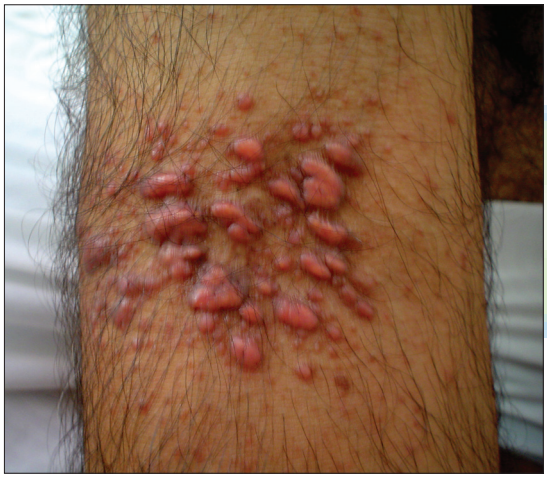

Figure 1: Clustering of papular and nodular lesions on the flexure (cubital fossa)

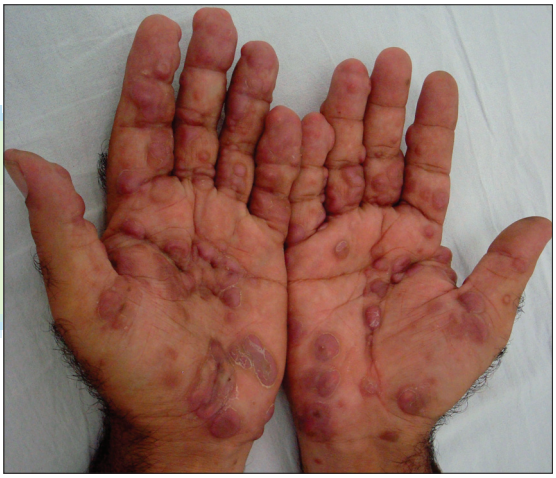

Figure 2: Multiple reddish brown papules and nodules present over both the palm

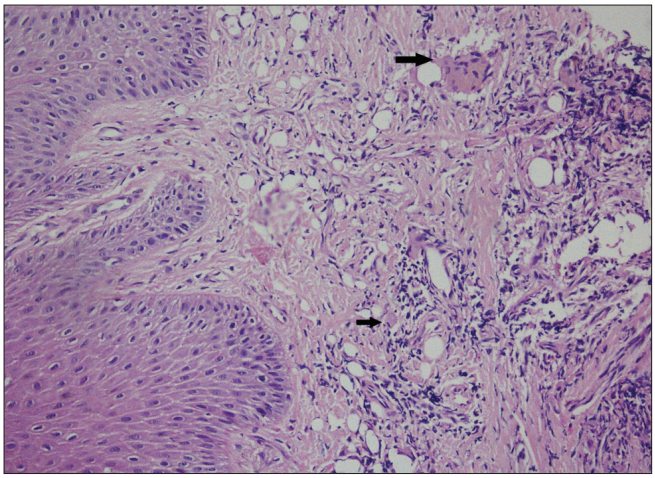

Figure 3a: Microphotograph showing histiocytic (small arrow) infiltration in dermis and occasional Touton giant cell (big arrow) (H and E, ×40)

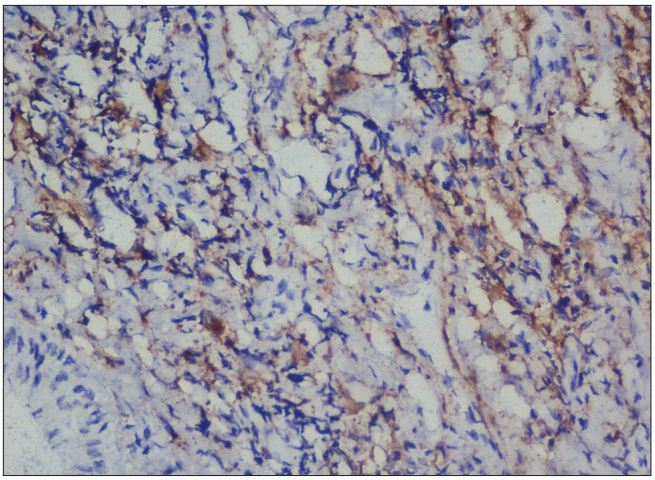

Figure 3b: Immunohistochemistry showing CD68 positivity in histiocytic cells (IHC, ×40)

cases may also have associated monoclonal gammopathy, Waldenstrom's macroglobulinemia and multiple myeloma.

Histologically, XD is characterized by early infiltration of the dermis with spindle shaped mononuclear cells, foamy histiocytes, giant cells, lymphocytes, polymorphs and eosinophils. Spindle cells have irregular scalloped borders with extensive cytoplasm and ovoid vesicular nuclei. Cells stain with CD68, factor XIIIa and KP1 and are negative for S100.

The course of the disease is variable. It may be self-limiting with spontaneous clearance or stable persisting for many years, or may show progressive course. There are reports of successful treatment with antilipemic drugs like simvastatin,[3] fenofibrate, glucocorticoids, chlorambucil and cyclophosphamide,[4] and 2-chlorodeoxyadenosine.[5] Eisendle *et al*.[6] treated a case of XD with combination of rosiglitazone (4 mg once daily), simvastatin (10 mg once daily), and acipimox (250 mg twice a day) and the patient had partial response. Those who develop diabetes insipidus have to be given desmopressin in addition. Gangopadhyay *et al*.[7] reported a young adult male patient of XD with typical lesions mainly over flexures, mucosal lesions involving conjunctiva, oral mucosa, pharynx, and larynx, bony lesion in the form of three osteolytic lesions in skull bones and with history suggestive of mild, self- limiting diabetes insipidus and appearance of gynaecomastia.

XD is a rare disorder, shows poor response to treatment and every XD patient should be investigated for diabetes insipidus and underlying hematological dyscrasias.

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