EOSINOPHILIC CELLULITIS AND RECURRENT GRANULOMATOUS DERMATITIS WITH EOSINOPHILIA (WELLS SYNDROME)

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A 21-year-old male developed 4 recurrences of Wells syndrome with highly characteristic recurrent indurated urticarial plaques, circulatory eosinophilia, arthralgia, episodic asthma and histopathological flame figures. Direct immunofluorescence revealed perivascular deposits of C_3 and IgM. A good response to corticosteroid was noticed.

Key words : Eosinophilic cellulitis, Recurrent granulomatous dermatitis with eosinophilia, Wells' syndrome.

Ever since Wells report of recurrent granulomatous dermatitis with eosinophilia in 1971,[1] and the later description eosinophilic cellulitis in 1978,[2] not more than 30 cases have been reported in the ever enlarging group of eosinophilic dermatoses.[3-11] At present Wells syndrome is considered a rare but distinct clinical entity characterised clinically by the sudden onset of acute, urticarial, itchy, erythematous, indurated plaques persisting for 4 to 8 weeks before spontaneous resolution and later recurrences.[12] Histopathological hallmark is unusual flame figure.[11] We are reporting a case of Wells syndrome.

Case Report

A 21-year-old male student had a slowly enlarging, itchy, dusky, indurated plaque on the anterolateral aspect of the left thigh. During the following 2 weeks, the lesion enlarged further involving the skin overlying the left knee, limiting its movements. The lesion was firm, nontender, 15 cm × 10 cm, with a smooth shiny skin and well-defined margins. It resembled early morphoea, was hot to touch, the overlying skin could not be easily pinched into folds. General physical and systemic review was within normal limits. There was no response to repeated courses of systemic antibiotics and topical corticosteroids; but 40 mg/day prednisolone for 3 weeks led to resolution within $2\frac{1}{2}$ months leaving behind brownish discoloration. Marked peripheral eosinophilia was detected. Four recurrences at the same site with variable intervening periods and circulating eosinophilia were observed for two years, controlled on each occasion with a short course of oral prednisolone. Arthralgia, malaise and episodic bronchospasm occurred on two occasions which also responded to oral corticosteroids.

Haemoglobin, WBC, platelet and reticulocyte counts, PCV, ESR, blood chemistry profile including electrolytes, urea, creatinine, uric acid, cholesterol, proteins, bilirubin, transaminases, alkaline phosphatase, glucose, amylase, calcium, serum electrophoresis, chest skiagrams, three consecutive stool samples repeated on three visits, antiamoebic serology and blood film for microfilariae were normal. Collagen profile was normal. Serum C_3 concentration was 74 mg% (normal 112 mg%). The differential cosinophilic counts were 44, 42 and 14% on three separate visits with absolute eosinophilic counts of 3825, 3402 and 588/cmm respectively. The histopathological examination of deep biopsies including subcutaneous fat on 3 occasions showed a similar picture. Epidermis was normal. Large areas of reticular dermis and subcutaneous fat were infiltrated by a dense, angiocentric, predominently eosinophilic infiltrate (Fig. 1). Two biopsies taken at an advanced

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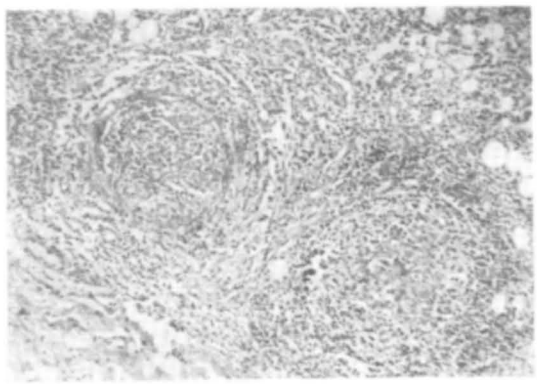

Fig. 1. Dense perivascular predominently eosinophilic infiltrate invading the vessel wall with occlusion of the lumen (H&E X55)

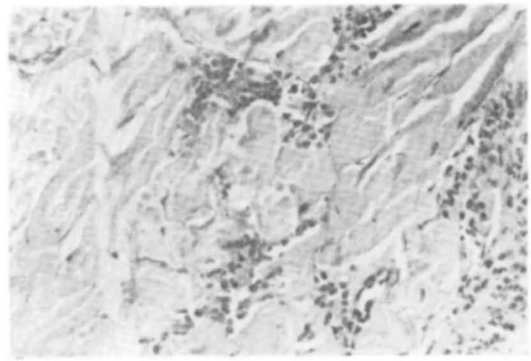

Fig. 2. Flame figures (H&E X140)

stage showed typical flame figures consisting of an intensely eosinophilic collagen bundles surrounded by extruding eosinophils, granules, nuclear dust and histiocytes (Fig. 2). The infiltrate also invaded deeper interlobular septae of subcutaneous tissue. Direct immunofluorescence examination of the frozen sections demonstrated complement (C_3) deposits in small capillaries. Variable degree of faint to intense IgM staining was seen in the small capillaries and blood vessels.

Comments

Wells originally reported four cases.[1] The lesions were described to undergo an evolution through two clinical and three histopathological phases.[3,5,8,10,12] The first clinical phase, described by Wells as eosinophilic cellulitis, consists of a rapidly spreading erythematous urticarial oedema resembling acute cellulitis, or an annular infiltrated plaque with central clearing, and occasionally there may be vesicles, haemorrhagic blisters and ulceration. The progressive infiltration of the plaque results in the second stage of granulomatous dermatitis represented by a woody indurated, early morphoea-like lesion, which eventually heals with non-scarring greyish discoloration. Recurrences at the same or other sites are not uncommon. Peripheral circulatory eosinophilia in the range of 10 to 48% is a rule during the acute stage and may be accompanied by systemic features such as fever, asthma and arthralgia.[8] Lesions are usually seen on the extremities and trunk, rarely on the face. There is no sexual predilection. Most cases occur in adults, two cases have been reported in childhood.[5,13] Response to corticosteroids is unequivocal, dapsone has also been found to be useful.[4]

The histopathological features have been a continual focus of interest and undergo three classical stages of metamorphosis.[3,8,11,12] The first stage is characterised by dermal oedema, massive, mainly angiocentric predominently eosinophilic infiltrate, disintegrating eosinophils with abundant extruded granules and an occasional subepidermal blister. The intermediate subacute stage corresponds clinically to the induration. Most conspicuous phenomenon during this stage are flame figures and microgranulomatous infiltrate of histiocytes and giant cells. The flame figures consist of a core of collagen coated with extruded eosinophilic granular debris surrounded by a palisading of histiocytes, giant cells and eosinophils representing a phagocytic response to the products of disintegrating eosinophils.[11] Recent, immunofluorescence findings have supported the view that the flame figures are focal necrobiotic areas

produced by direct cytotoxic effect of eosinophilic granules on the main component (50%) of major basic protein (MBP) of the collegen fibres.[14] The third and final stage corresponds to the atrophic discoloured lesion consisting of a few remaining eosinophils and flame figures.

The aetiology of Wells syndrome is not clear, it is considered a non-specific cutaneous reaction triggered by different agents.[1,8] The main event is presumably an immune complex mediated reaction leading to a strong eosinophilotactic phenomenon.[11] Frequent demonstration of C_3, IgM, IgA, IgD and fibrin in and around the vessel walls supports this pathophysiologic process, though eosinophilic chemotaxis has been found to be normal.[3,5,11,14] The anti-human major basic protein (MBP) induced strong immunofluorescence inside the flame figures suggests that MBP mediated cytotoxic injury of collagen produces the characteristic lesions.[14] Leukotrienes C_4 and D_4, the components of slow reacting substance of anaphylaxis (SRS-A) and potent mediators of inflammation have been recently shown to be increased by the suction bulla technique of the involved tissue.[15] They are generated by eosinophils and may contribute to the tissue injury. The patient under report displayed typical clinicopathological features as described by Wells and was followed through all the clinical and pathological stages. A rare feature of this case was the corticosteroid responsive episodic asthma. The presence of systemic symptoms may prompt inclusion in the hypereosinophilic syndrome, however, the complete criteria of such a diagnosis require marked (more than 1500/cmm) persistent eosinophilia of more than 6 months duration, exclusion of parasitic and allergic diseases and features consistent with organ infiltration.[12] The Wells syndrome could certainly be considered a minor variant of the clinical spectrum of hypereosinophilic syndrome.

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