Eosinophilic Cellulitis

"Thesis"

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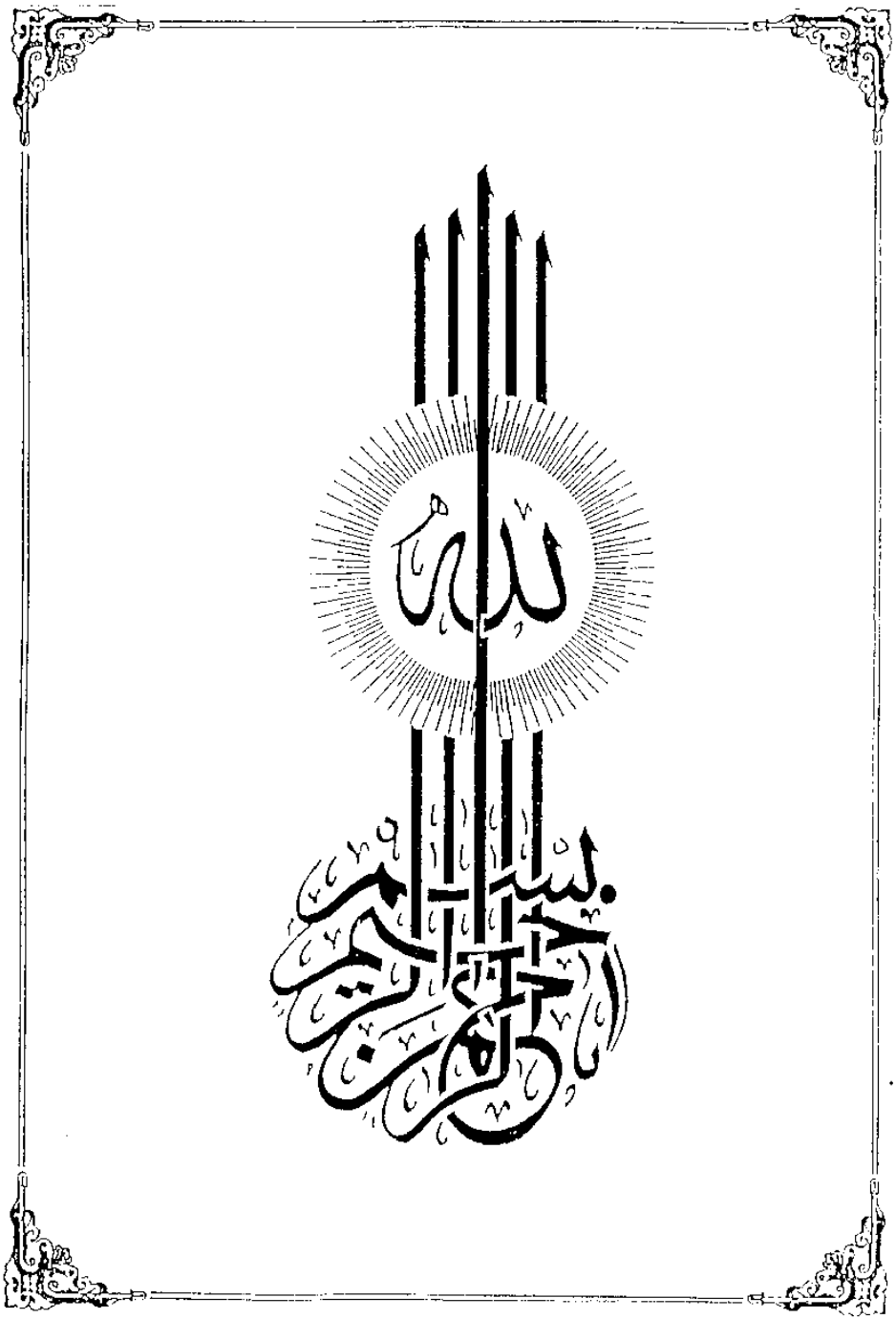

Abstract

- Eosinophilic cellulitis is an idiopathic disease limited to the skin. Wells reported the first four cases, in 1971 under the term "recurrent granulomatous dermatitis with eosinophilia" then he and Smith, in 1979, proposed the simpler term of eosinophilic cellulitis in reporting eight additional cases.

The etiology is unknown, it appears to be a hypersensitivity reaction to variovs antigen including, drugs, insect bites and dermatophyte infection.

The disease is rare, it can effect both sexes usually adults.

Clinically and histopathologically :

There are three stages

1- Acute stage : "eosinophilic cellulitis".

2- Subacute stage : "granulomatous dermatitis".

3- Stage of resolution.

A peripheral blood eosinophilia is present in half of cases during the active phase of the disease.

Systemic corticosteriods suppress and appear to shorten the course of the disease in most cases.

List of abbreviations

- Eosinophil chemotactic factor of anaphylaxis : ECFA.
- Platelet activating factor : PAF.
- Eosinophil stimulation promotor : ESP.
- Eosinophil activating factor : EAF.
- Monocyte - derived eosinophil cytotoxicity enhancing factor : M-ECEF.
- Interleukin 5 : IL-5.
- Major basic protein : MBP.
- Eosinophil cotionic protein : ECP.
- Eosinophil derived neurotoxin : EDN.
- Eosinophil peroxidase : EPO.
- Slow reacting substance of anaphylaxis : SRS-A.

CONTENTS

I	Introduction	
II	Semantics of eosinophilic, cellulitis.	1
III	Historical view	3
IV	Etiology of eosinophilic cellulitis	8
V	Clinical Picture.	19
VI	Histopathogical picture.	24
VII	Diagnosis of eosinophilic cellulitis.	32
VIII	Differential diagnosis.	42
IX	Treatment of eosinophilic cellulitis.	60
X	Appendix I	65
XI	Summary.	68
XII	References	
XIII	List of pictures	
XIV	Arabic Summary	

Eosinophilic cellulitis

Introduction

Eosinophilic cellulitis is an idiopathic disease limited to the skin. Wells reported the first four cases, in 1971 under the term "recurrent granulomatous dermatitis with eosinophilia" then he and Smith, in 1979, proposed the simpler term of eosinophilic cellulitis in reporting eight additional cases.

The etiology is unknown; it appears to be a hypersensitivity reaction to various antigens. Parasitic infection, dermatophyte infection, insect bites, and drugs have been proposed as eliciting factors in selected cases. The finding of complement within blood vessel walls in two cases suggests that vascular damage is involved (Well's and Smith, 1979).

The disease is rare, only 29 cases being reported untill 1988. Both sexes can be involved usually adults although children have also been affected (Champion, 1992).

Clinically and histopathologically :

There are three stages :

1- An acute stage "eosinophilic cellulitis

There is pruritic erythematous edema that resembles cellulitis. At times, blisters develop over the affected area. Histologically, one can find dermal edema and dense infiltration with eosinophilia.

2- Subacute stage : "granulomatous dermatitis".

The cellulitis gradually resolves but the area become indurated and remain slate coloured for several weeks. Biopsies show eosinophilia, large pale histiocytes between collagen bundles and flame figures.

3- Stage of resolution :

The skin becomes slate grey and appears atrophic resembling morphea. Histologically, histiocytes and giant cells are interposed between collagen bundles, flame figures are still pominent.

A peripheral blood eosinophilia is present in half of cases during the active phase of the disease. In most patients, the condition becomes chronic or recurrent with eventual spontaneous resolution over the course of a year or two (Steffen, 1986).

Eosinophilic cellulitis has to be differentiated from cellulitis, urticaria, and toxocara infection which may resemble it both clinically and histo-pathologiclly (Champion, 1992).

Flame figures and infiltration of the dermis with eosinophilia and histiocytes are pesent in diverse other disease such as, bullous diseases, eczema, prurigo of unknown cause (Well s and Smith, 1979).

Systemic corticosteroids suppress and appear to shorten the course of the disease in most cases but the dose equivalent to 50-60 mg/ day of prednisone may be required. Griseofulvin therapy was associated with temporary resolution in two patients with suspected dermatophyte

infection. (Wells and Smith, 1979). In addition some patients may clear spontaneously (John and White, 1985).

The Semantics "Eosinophilic Cellulitis"

Ehrlich Enigmatic Eosinophil

Paul Ehrlich identified eosinophils in 1879 (Gleich, 1988). In the same year, he found abundant eosinophils in the bone marrow of a patient with leukemia. By the early twentieth century, eosinophils were known to be important in parasitic and allergic diseases. Currently, eosinophils are recognized in many skin reactions (Ackermann, 1978).

Eosinophils may appear early, as a primary response, or late, as part of a mixed inflammatory reaction often following a neutrophil response. There are conditions in which eosinophils seem incidental, yet on occasion may be prominent and confuse the diagnostic picture. Even in conditions in which eosinophils are almost always present, the reaction patterns are not unique. For example, eosinophilic spongiosis is a cardinal feature of the vesicular stage of incontinentia pigmenti, yet it may be found in such common diseases as allergic contact dermatitis, insect bites and bullous pemphigoid as well as pemphigus and eosinophilic cellulitis.

Fortunately, a good deal has been learned about eosinophils in recent years (Gleich, 1988).

The semantics of eosinophilic cellulitis :

Eosinophilic infiltrates seem to share a fate of semantic confusion. Eosinophilic fasciitis, for example, is a misnomer, since eosinophils need not to be a conspicuous part of the fasciitis (Ackermann, 1978).

Eosinophilic panniculitis is best considered a histologic description and not a disease entity (Winkelmann and Frigas, 1986).

Eosinophilic cellulitis seems to mean exactly what an author chooses it to mean either a synonym for Wells syndrome or a synonym for eosinophilic infiltrates with flame figures or both (Melski, 1990). Wells (1971) originally used eosinophilic cellulitis to refer to the acute stage of "recurrent granulomatous dermatitis with eosinophilia" a disease that he previously called "recurrent cutaneous swelling with necrobiosis and eosinophilia" In that report, flame figures were not a part of eosinophilic cellulitis. Subsequently Wells and Smith (1979) used eosinophilic cellulitis to refer to all three stages.

They also referred to the "characteristic histological features of eosinophilic cellulitis" including flame figures even though they described nine cases of other diseases with the same histology versus eight with eosinophilic cellulitis. Some of the 46 cases of eosinophilic cellulitis published by Panizzon (1989), probably belong to the other diseases category of Wells and Smith .

Melski (1990), have seen the characteristic histology in bullous hypersensitivty to benzocaine and in eosinophilic ulcer of the tongue.

It may be preferable to refer to such cases as showing eosinophilic infiltration with flame figures rather than eosinophilic cellulitis (Wood et al, 1986).

Eosinophilic cellulitis

Historical view

Wells, in 1971 , described four patients under the title of recurrent granulomatous dermatitis with eosinophilia who had been observed over a period of ten years and had shared in common specific clinical picture as a striking histopathology. Clinically,those lesions began as an area of redness and swelling that spread rapidly over a few days and evolved into large lesions with a distinct rosy and violaceous border with edema.

Wells noted an early resemblance to erythema multiforme and with evolution, some resemblance to morphea. All four patients had peripheral blood eosinophilia. Some had recurrent lesions, and bullae developed in two of the four patients.

Histopathologically, Wells and Smith (1978), described an early massive dermal infiltration with eosinophils which are massed in and around small venules. This is followed by an infiltration of eosinophils and pale histiocytes between connective tissue bundles and the presence of characteristic flame figures. These flame figures consist of a central core of collagen bundles coated with eosinophilic debris. This eosinophilic flame- like mass may in turn be surrounded by a palisade of large histiocytes and giant cells of the foreign body type in the late stages of the lesion. Early lesions may show only a few leukocytes, predominantly eosinophils, in and around small venules

(Schorr et al, 1984).

Wells (1971), in his original paper, stated that he focus on the most striking feature of the histopathology characteristic of all of his cases, the phagocytic flame figures.

Schorr (1978), while in England saw a presentation by Dr. Wells (1978) at the Nottingham Annual Meeting of the British Association of Dermatologists and was impressed that the cases of eosinophilic cellulitis diagnosed by Wells had some similarities to erythema chronicum migrans Afzelius.

Wells and Smith (1978), stressed the persistent erythematous and urticarial nature of these lesions, which were frequently annular and would persist for several weeks.

Wells and Smith (1979), again emphasized the annular or circinate character of these plaques and proposed the shortened name of "eosinophilic cellulitis". In their publication, they briefly described eight additional cases and noted similar flame figures in one case of bullous pemphigoid, one of herpes gestationis, three of eczema, two of prurigo of unknown cause but with lesions resembling insect bites. In addition, they recorded a case of diffuse erythema and a tinea pedis sharing the histopathology of eosinophilic cellulitis.

They stated that it seems likely that in eosinophilic cellulitis a number of different triggers such as insect bites, fungus infections or drug eruptions may fire off a hypersensitivity mechanism.

They noted similarities between flame figures and the Splendore - Hoeppli deposits occuring around parasites or around colonies of deep fungus such as sporotrichosis (Symmers 1978).

In the same year (1979) , Spigel and Winkelman reported two additional cases of eosinophilic cellulitis under the title of Wells syndrome . These authors recorded involvement of muscle and fascia. Their second patient had a clinical picture consistent with fixed drug eruption as well as that of an acute infective cellulitis. Bone marrow eosinophilia was present in both patients . They concluded that on the basis of histopathological findings , recurrent granulomatous dermatitis with eosinophilia is a distinct disease and is part of the eosinophilic syndromes involving the skin.

Nielsen et al (1981) , under the title of eosinophilic cellulitis described an eleven-years old boy who developed pruritic grouped papules on the face , abdomen and upper extremities with fever resembling erythema multiforme . They noted confluent infiltrated urticaria like lesions with some serous and hemorrhagic bullae . During hospitalization , this boy developed sharply demarcated heavily infiltrated , erythematous lesions on his extremities . He also developed joint pains and swellings. Clinically , the annular plaque greatly resembled erythema chronicum migrans . They stated that the cause of eosinophilic cellulitis remains unknown . It was important to note that their child differed from

other reported cases by scalp ulceration with scarring alopecia, the presence of disseminated fibrinoid necrosis and a positive antinuclear antibody (ANA). They did not record the titre of the positive ANA nor the pattern of the fluorescence, so its significance was difficult to ascertain.

Schorr et al (1984), described five patients with the clinical and histopathologic picture, including flame figures of eosinophilic cellulitis. Two of them had documented tick bites, a third patient had a clinical picture suggestive of a tick bite reaction but stated that she was stung by a small garden bee at the involved site, the fourth patient removed a spider from the site of a spider bite and the fifth patient was presented with papular urticaria of flea bites. They suggested that the characteristic flame figures of eosinophilic cellulitis are not diagnostic of a specific disease entity but rather a striking and peculiar histopathologic response to multiple factors of which arthropod bites (ticks, bees, fleas and spiders) represent one definite etiology.

Dijkstra et al (1986), also concluded that eosinophilic cellulitis was not an entity as such but instead represented a severe urticarial hypersensitivity reaction to various stimuli.

Wells (1986), commented on these possibilites saying that he and Smith reported a unique clinical picture which they called eosinophilic cellulitis. The lesion had a characteristic flame figures and giant cell phagocytosis.