Eosinophilic Cellulitis: Five Cases

RUNE LINDSKOV,[1] NIELS ILLUM,[2] KAARE WEISMANN[3] and OLE FRØKJÆR THOMSEN[4]

Departments of [1]Dermatology, and [2]Pediatrics, Rigshospitalet, University of Copenhagen, [3]Department of Dermatology, Bispebjerg Hospital, Copenhagen, and [4]Department of Pathology, Rigshospitalet, University of Copenhagen, Denmark

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Five cases of eosinophilic cellulitis or Wells' syndrome are described. While only few children have been included in earlier reports, 4 of the 5 patients in the present paper were below 10 years of age, with the youngest being only 20 months when the disease started. One of the children developed hard and tender subcutaneous swellings on the scalp, the histology of which showed extensive subcutaneous necrotizing granulomas. Similar lesions have not been described previously in connection with eosinophilic cellulitis. Eosinophilic cellulitis may be called a rare disease. However, it is important that clinician and histopathologist are both acquainted with the pathological features of this condition, as the disease often responds readily to steroid therapy. *Key words: Wells' syndrome; Eosinophils; Case study.* (Received December 10, 1987.)

R. Lindskov, Stokholmsvej 41 B, DK-3060 Espergærde, Denmark.

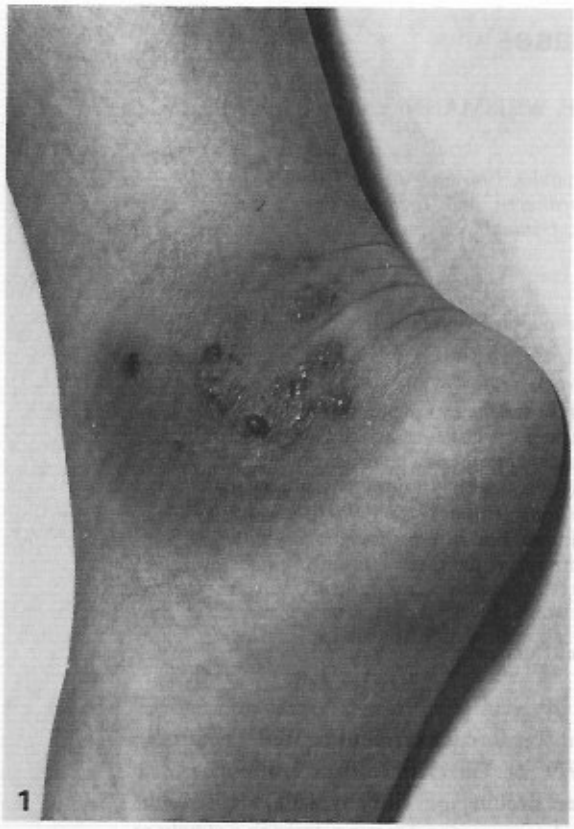
Recurrent granulomatous dermatitis, later termed eosinophilic cellulitis or Wells' syndrome, was described by Wells in 1971 (1) and later in 1979 (2). The characteristic eruption consists of cutaneous of rose-coloured and later blue–green swellings, eventually with extensive blistering, followed by hard indolent infiltration. The disease is non-scarring, leaving a slowly resolving hyperpigmentation. Massive eosinophilia in the blood is often present. Characteristic histological features are seen in the active phase of the disease.

Till now, only 22 cases of eosinophilic cellulitis have been described, to the best of our knowledge (1–9). Because it is important to recognize this disease—clinically as well as histologically—we report 5 additional cases, 4 of which were in children, one of them with unusual localization of the eruptions.

CASE REPORTS

Case 1: A 4-year-old girl was admitted with a reddish brown granulomatous infiltration, of one month's duration, on the distal part of the left arm, with severe blistering. A few papular and vesicular lesions developed in other sites as well. In the early phase the eruption was pruritic. The general health of the child was not affected. The lesions gradually disappeared over 2 months. Since the first attack, the girl had two episodes of rosy and later green–brown cellulitis as well as blisters on various parts of the trunk and extremities (Fig. 1). The eruptions subsided in 2 months and 3 weeks, respectively, and no recurrences were seen during the following year. As *Staphylococcus aureus* and haemolytic streptococci were isolated from the lesions, the patient was given systemic antibiotics, though without effect. Furthermore, oral acyclovir was tried, also with no effect. During the last attack, prednisone 15 mg once a day was given for 14 days with some improvement. The skin was treated with topical antiseptics.

Case 2: A 5-year-old previously healthy girl presented with yellowish green and purple skin infiltrations scattered on the ventral side of the trunk, the volar aspects of both wrists and the dorsal parts of the feet (Fig. 2). Some lesions were incrusted. A pronounced blistering with clear liquid content was seen. Up to about ten hard and tender subcutaneous nodules were felt on the scalp. A local tender lymphadenopathy was present. She continued to develop lesions for 2 months, after which the skin eruptions as well as the subcutaneous nodules faded away, leaving a few itching lesions on the soles of both feet. General



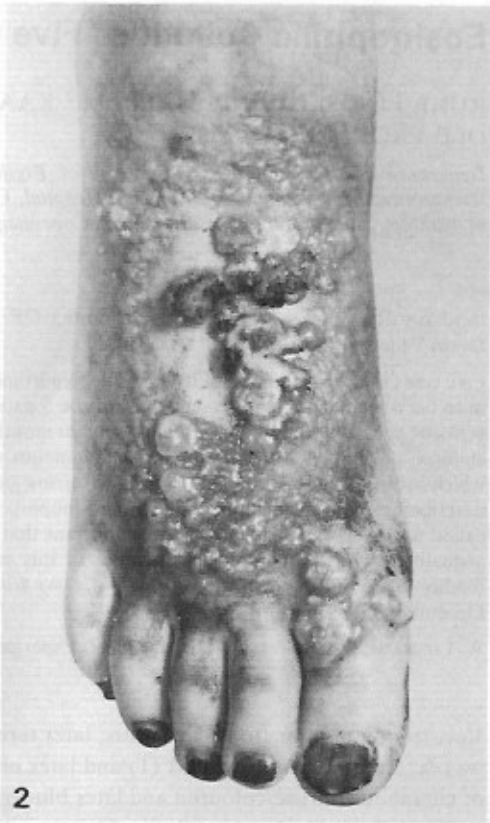


Fig. 1. Cellulitis with blisters in case 1.

Fig. 2. Pronounced blistering on the dorsum of a foot in case 2.

wellbeing was reduced during the active phase because of low-grade fever, diffuse joint pains with some stiffness and pronounced itching. The following year the girl remained symptom free. *Staphylococcus aureus* was demonstrated in the lesions. However, systemic antibiotics did not influence the course. Oral acyclovir was given, without effect. The skin was treated with topical antiseptics.

Case 3: A 20-month-old Pakistani boy, born in Denmark, was referred with a universal pruritic herpetiform papulovesicular rash. The lesions were firm, with a tendency to coalesce. Some lesions were umbilicated. Old lesions showed crustation. The most severely affected areas were face, hands and feet (Fig. 3). General health was unaffected and the boy was not febrile. The skin disease subsided slowly during 2 months of treatment with topical antiseptics. Systemic antibiotics were given, but without effect in spite of the presence of *Staphylococcus aureus* and haemolytic streptococci in the lesions. During the following 2 years the boy suffered from several minor recurrences and a few severe outbreaks.

Case 4: A 9-year-old boy was seen with an acute vesiculopapular eruption and a febrile condition. The episode lasted for 2 weeks and was diagnosed as erythema multiforme or a viral exanthema. There was no post-infectious scaling on the skin and no adenitis. Three months later he was re-admitted because of another attack lasting for about 2 weeks. For the next 2 years he remained free of symptoms until he developed a similar widespread vesicopapular exanthema, concentrated on the extremities and lower parts of the trunk and a few elements on his face. The only treatment was with topical antiseptics.

Case 5: A 56-year-old woman presented with a pruritic cellulitis-like infiltration with tense bullae on the distal parts of the left arm and the right leg. On the proximal part of the left arm a dark reddish blue scleroderma-like firmness was seen. The patient had suffered from these eruptions for one month. Apart from pruritus and pain in the most tense plaques, the general health of the patient was not affected. As

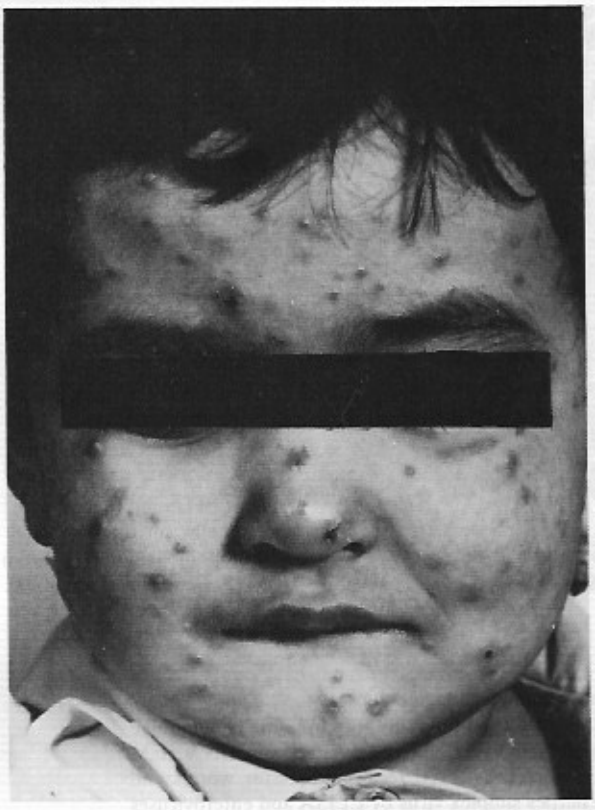


Fig. 3. Herpetiform papulovesicular rash in case 3.

Staphylococcus aureus was present in the skin lesions, the patient was given systemic antibiotics, but without effect. When betamethasone (Celeston®) 4 mg daily was given, the condition improved rapidly. Two relapses during the following year were treated with a similar beneficial effect.

Histopathology

Fundamentally, all the patients had the characteristic histological lesions of eosinophilic cellulitis in their skin biopsies. These consisted of a fairly heavy dermal leukocytic infiltration, predominantly with eosinophils. In addition, foci of dermal fibrinoid degeneration and necrosis occurred, surrounded by inflammatory cells, particularly histiocytes and giant cells of foreign body type, thus forming small dermal granulomas. Because of their characteristic appearance, these small areas of necrosis have been called 'flaming figures' (Fig. 4). The flaming figures were of varying appearance from case to case, being most prominent in case 5, whereas in case 1 they were smaller and hence less conspicuous. In close vicinity to well developed flaming figures, extracellularly dispersed eosinophilic granules could be seen, phagocytosed by histiocytes and giant cells. Besides the typical changes of eosinophilic cellulitis, the patient in case 2, in a biopsy from the scalp, moreover revealed extensive subcutaneous necrotizing granulomas, surrounded by a rim of histiocytes and a massive diffuse infiltration of partially ruptured eosinophilic cells and granules. No definite evidence of vasculitis was present in any of the cases.

Laboratory data

The eosinophil and total leukocyte counts in peripheral blood are shown in Table I. Initially, patients 2 and 3 were slightly anaemic. IgE was marginally elevated in case 3 and IgG slightly elevated in case 2. IgM was 2.5 in case 1 and 6.4 in case 2 (0.2–1.3 g/l). ESR was 62 in case 2. The varicella zoster titre was 400–1 600 in case 1 and 800–3 200 in case 2. Both children had had chickenpox, 1 and 3 years previously. A bone-marrow aspirate in case 2 showed hyperplasia with slight eosinophilia. Immunofluorescence studies demonstrated massive deposition of C 3 in dermal vessels of lesional skin in case 2, and deposits of IgM in the dermal vessel walls and at the dermo-epidermal junction in lesional skin in case 3. No deposits, however, were found in lesional or normal skin of case 5. The following laboratory data in-

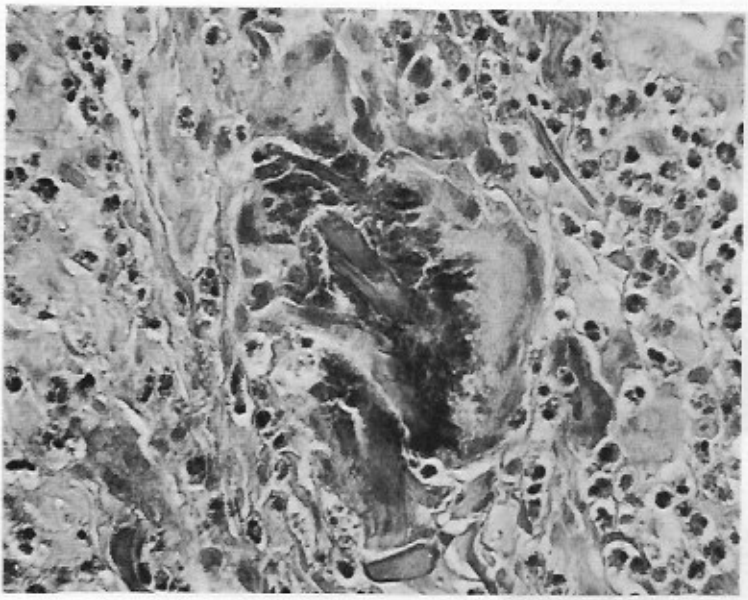


Fig. 4. 'Flaming Figure' with giant cells, surrounded by eosinophilic leukocytes. From case 5. Lendrum stain, ×400.

cluded normal or negative values of ESR, haemoglobin, platelets, alkaline phosphatase, alanine aminotransferase, AST, ASH, immunoglobulin G, A, M and E, cold agglutinin titre, mycoplasma pneumoniae titre, Paul-Bunnell titre, Borrelia titre, herpes complement, varicella zoster titre, anti-DNA, IgM rheumatic factor, hepatitis B antibody and antigen, toxocariasis IFAT, fecal cultures for worms and pathogenic bacteria, detection from vesicular fluid of herpes simplex virus by ELISA and enteroviruses by tissue culture, lymphocyte transformation tests (case 1). Lymphocyte subpopulations did not show monoclonal expansion (cases 1 and 2).

Table I. *Patient characteristics*

Case no.	Age	Type of lesion	Course (maximum duration of one attack)	Predilection site	Maximum eosinophil count leukocyte count per mm^3
1	4	Edematous plaques; bullae	3 attacks over 27 months (2 months)	Distal extremities, lower trunk	2 225 13 000
2	5	Edematous plaques, bullae; subcutaneous nodules on scalp	One attack (2 months)	Distal extremities	26 000 47 000
3	2	Herpetiform papules and vesicles	One major attack several minor do over 2 years (2 months)	Face, hands, feet	2 494 20 000
4	9	Papules, vesicles	3 attacks over 2 years (2 weeks)	Face, extremities, lower trunk	2 405 18 500
5	56	Edematous plaques, bullae, scleroderma-like firmness	3 attacks over 16 mo (6 weeks)	Distal extremities, back	588 7 900

DISCUSSION

All 5 patients had clinical features characteristic of eosinophilic cellulitis. The colour of the swellings was typical. Early lesions and the advancing border of older lesions were rose-coloured, whereas the central parts of older lesions turned green-brown to blue. Also, the typical histological changes were present in all the cases, the diagnostic features consisting of the combination of dermal eosinophilic infiltration and flaming figure granulomas (1). Presumably, the granulomas are not developed until some weeks in the course of disease, while in the beginning, only the dermal eosinophilic infiltration is present (1).

Varying degrees of eosinophilia in the peripheral blood were found in all the patients, in case 2 even up to 25000/mm^3. Moreover, this patient also presented with a bone marrow aspirate showing slightly increased numbers of eosinophils. Bone marrow eosinophilia has been described previously in connection with EC (3–5). Furthermore, this patient had 5 to 10 hard, slightly tender subcutaneous nodules on the scalp. These nodules gradually disappeared. Histology of the lesions showed extensive subcutaneous necrotizing granulomas. Similar lesions have not been described previously in eosinophilic cellulitis. Besides, in the bone marrow, extracutaneous infiltrations of eosinophils have been described in muscle and fascia of a patient with eosinophilic cellulitis localized to an arm (3).

Clinically, eosinophilic cellulitis is characterized by a substantial cutaneous edema. The eosinophilic granulocyte, can be characterized as a pro-inflammatory cell, which in several skin diseases may be pathophysiologically related to the development of cutaneous edema (10). The eosinophil's participation in the formation of flaming figures is suggested by immunofluorescence analysis of major basic protein contents of the flaming figures (7). Moreover, electron microscopic observations have revealed free eosinophilic granules coating collagen fibres in flaming figure granulomas (8).

In 2 children (cases 1 and 2) a four-fold increase in the varicella zoster titre was found. However, both had had chickenpox two and one years before the present skin disease. The moderate fluctuations in antibody titre may have resulted from an unspecific stimulation of the immune system. In none of the patients did systemic antibiotic treatment succeed in clearing the skin disease. Thus the isolated bacteria possibly represent a secondary invasion.

Deposits of the immunoreactants, IgM and C3, were demonstrated in lesional skin from 2 of the 3 patients examined. In a previous report, properdin and IgM were detected in the vessels of skin and muscle, respectively, in a patient with eosinophilic cellulitis (3). These findings suggest that circulating immune complexes are present in patients with this disease.

Of the 22 cases hitherto reported, only 4 have been below 20 years of age and of these only one below 10 years. Our series of 5 patients therefore seems to be atypical, with 4 children being less than 10 years of age and the youngest being only 20 months when the disease started.

In conclusion, we find it justified to maintain the term eosinophilic cellulitis when the patient presents with recurrent and disseminated typical lesions combined with some degree of blood eosinophilia and with the characteristic histological findings. Eosinophilic cellulitis may be called a rare disease. However, it is important that both the clinician and the histopathologist are acquainted with the pathological features of the disease and collaborate in coming to the right diagnosis, as the disease often responds readily to steroid therapy.

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