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ACUTE FEBRILE NEUTROPHILIC DERMATOSIS (SWEET'S SYNDROME)

Report of Two Cases and Review of the Literature

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Abstract. Two further cases of acute febrile neutrophilic dermatosis (Sweet's syndrome) are described. These are the first patients reported from Scandinavia. One of them has a monoclonal paraproteinemia, probably benign, with unclear relation to the syndrome. The other had a streptococcal sore throat preceding the dermatosis. As this dermatosis is probably not so uncommon, and the response to corticosteroids is excellent, its recognition is important. The differential diagnoses are discussed.

In 1964 Sweet reported 8 cases with a clinically and histopathologically distinct syndrome of unknown etiology (4). It is characterized by an acute onset of high fever, raised painful red plaques on the face and limbs, increase of blood polymorphonuclear neutrophilic leucocytes, a high erythrocyte sedimentation rate and a quick and complete response to corticosteroids. He suggested the name of Acute febrile neutrophilic dermatosis. Since then 10 further cases have been published, also from England (1, 3, 5, 6). Probably the syndrome is not as rare as is indicated by the very small number of reported cases. As it may cause considerable diagnostic difficulties, and when recognized the result of the proper treatment is excellent, we want to describe the first cases reported from Scandinavia.

CASE REPORTS

Case 1

House-wife aged 51. In 1965 she had a temporary, uncharacteristic rash. In the summer of 1969 a moderate essential hypertension was diagnosed. She has since been on chlorothiazide, 50 mg daily, and a betareceptor blocking agent, Aptin®. On 9 November 1969, she had a sore throat, a moderate fever of 38°C and she noticed a reddened skin infiltration on her right upper arm. On 12 November oral penicillin was instituted. Despite this her fever rose slowly to 40°C, she developed more skin eruptions and 14 November she was admitted to hospital.

Physical examination on admittance: a tired, high-febrile (39.8°C) woman who gave the impression of being severely ill. Except for the striking, cutaneous changes and a slight redness of the throat the physical examination was essentially normal. On the arms and the legs, especially the extensor sides, and the back of the neck there were approximately 10, from 0.5 x 0.5 cm to 5 x 5 cm large, well-defined blue-red slightly infiltrated and rather tender plaques (Fig. 1). Some of the plaques, especially on the legs, had a rough, mamillated surface resembling a "relief map of a mountain range".

Histopathology. Epidermis is normal microscopically. In the upper part of the corium there are moderate perivascular infiltrates of neutrophilic granulocytes, lymphocytes and histiocytes. No signs of a vasculitis.

Laboratory findings. Haemoglobin conc. 11.9 g/100 ml. White blood count 18 000 (neutrophilic leucocytes 82%, monocytes 3%, lymphocytes 15%). Thrombocytes 296 000. ESR 114 mm/h. Liver function tests: alkaline phosphatases 16 units (upper normal limit 10 units); bilirubin, thymol S-GOT and S-GPT, normal. After 1 week, alkaline phosphatases 6 units. Serum electrolytes and serum creatinine, normal. Antistreptolysin-0 and antistaphylolysin titres, normal. Wasserman and Waaler-Rose tests, negative. Transitory proteinuria the first 2 days. No glucosuria. Paper electrophoresis of serum: albumin 2.6, alfa-1-globuline 0.5, alfa-2-globulin 1.0, beta-globulin 1.0 and gamma-globulin 2.0 g/100 ml. Immune electrophoresis of serum: IgG 1 450 (normal), IgA 378 (increased) and IgM 195 mg/100 ml (increased). A paraprotein belonging to IgM globulin could be demonstrated in repeated blood samples. Bacteriological cultures from the throat, blood and urine were negative.

Course and treatment. Initially, a drug reaction from penicillin or the antihypertensive drugs was suspected. These medicaments were withdrawn. However, the first 4 days in hospital the patient remained acutely ill, febrile, and her skin changes and the leucocytosis did not improve. Now the diagnosis of acute, febrile neutrophilic dermatosis was considered. Even the histopathological picture was in accordance with this syndrome. As there were no signs of any infection, prednisolone 30 mg daily

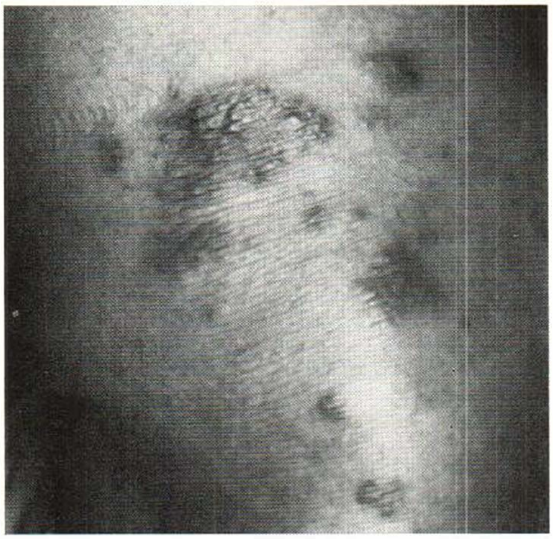

Fig. 1. Close-up view of lesions on the thigh (case 1).

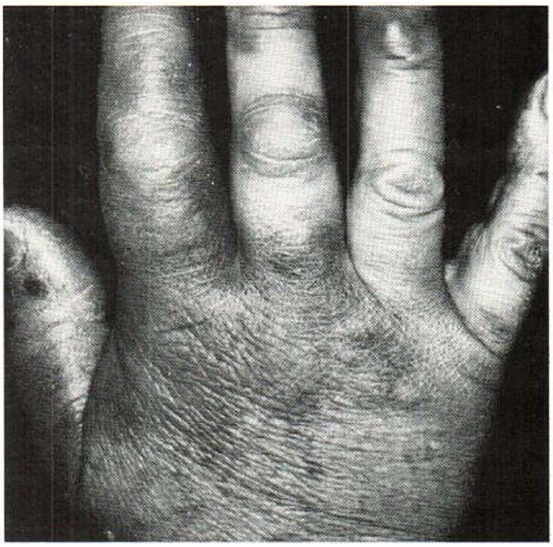

Fig. 3. Swollen blue-red plaques on the right hand (case 2).

was instituted. This had a dramatic effect: after 1 day the woman's general condition was greatly improved and she had no longer any fever. The skin changes were paler and less swollen. The leucocyte count was now 6 600, and the proportion of neutrophilic polymorphonuclears 66%. After 1 week the prednisolone dose was reduced to 20 mg daily. Within 1 day the fever returned (38.6°C) the skin changes were redder and the leucocyte count was 14 200 with 67% neutrophilic polymorphonuclears. The corticosteroid dose was increased to 30 mg daily, and within 2 days she was again in the same state as before the prednisolone dose reduction. During the following 6 weeks the prednisolone was slowly reduced without complications. She is now in a good health and has no signs of any skin or septic disease. The blood cell count is normal, and ESR has fallen to 21 mm/h. The paraproteinemia is stationary and investigations at the medical department has shown no signs of multiple myelomatosis or macroglobulinemia (Waldenström). It is regarded as a form of benign monoclonal essential gammapathy (Waldenström). Its relation to the dermatosis is not clear at present.

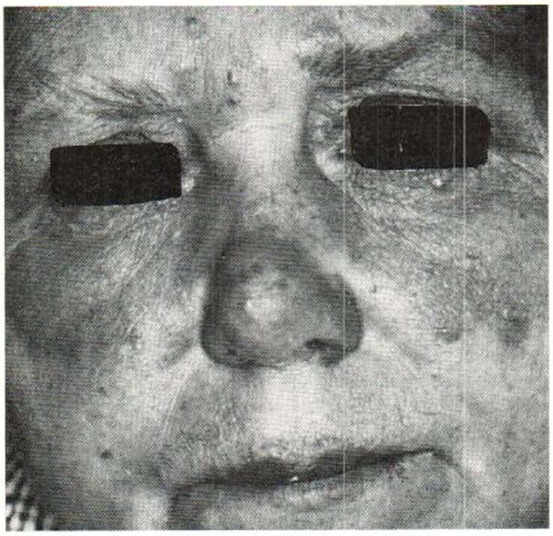

Fig. 2. Skin lesions on the face (case 2). The picture was taken 2 days after the institution of corticosteroids. The lesions are therefore less swollen and paler than before the beginning of the treatment.

Case 2

A 59-year-old woman with venous insufficiency and leg ulcers since 1956. Patch testing in 1966 because of a hypostatic eczema demonstrated an allergy against tape, balsam of peru, neomycin, jodochlorhydroxyquin and lanolin. In the beginning of April 1970 she had a sore throat and a moderate fever for 3 days. She recovered without treatment. One week after the first throat symptoms she developed swollen and painful red areas around her left eye, and felt feverish. The next day the skin around the right eye was swollen too. An X-ray of the paranasal sinuses was normal. She was admitted to hospital because of a suspected erysipelas.

Physical examination was essentially normal except for a fever of 39.2°C and the skin changes around the eyes. The skin on the left upper and lower lids and the neighbouring parts of the cheek and the right upper lid was well-marginated dusky red, tender and heavily swollen (Fig. 2). The left eye could not be seen because of the oedema. An ophthalmological investigation was normal.

Histopathology. No epidermal changes. In the corium there are intense and moderate perivascular infiltrates, which are almost completely composed of neutrophilic

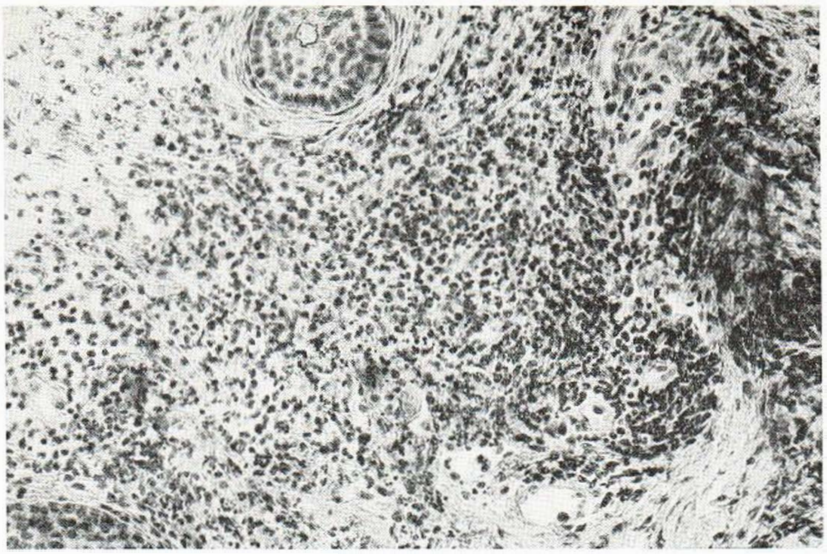

Fig. 4. Histologic section from the left shin showing perivascular infiltrates of neutrophilic granulocytes (case 2).

granulocytes (Fig. 4). No bacteria can be seen in the tissue. No signs of a vasculitis.

Laboratory findings. Haemoglobin conc. 11.6 g/100 ml. White blood count, 17 000 (neutrophilic leucocytes 83%, monocytes 1%, lymphocytes 16%). Thrombocytes 223 000. Sternal bone marrow normal. ESR 50 mm/h. Liver function tests: bilirubin, alkaline phosphatase, thymol, S-GOT and S-GPT, normal. Serum creatinine, normal. Antistreptolysine-O titre 1 600 u/ml and antistaphylolysin titre, normal. Wasserman and Waaler-Rose tests, negative. No LE-cells were found. The urine analysis was normal. Paper electrophoresis of serum: albumin 2.7, alfa-1-globulin 0.2, alfa-2-globulin 1.1, betaglobulin 0.8 and gammaglobulin 1.5 g/100 ml. Immune electrophoresis of serum: IgG 2 400 (increased), IgA 296 (increased) and IgM 100 mg/100 ml (increased). No paraprotein could be found in repeated blood samples. Bacteriological cultures from the blood were negative. X-ray of the lungs: nothing noteworthy.

Course and treatment. At first an erysipelas was suspected. Penicillin (3 mill. IU daily perorally) and 3 days later tetracycline (2 g daily perorally) was instituted. The fever rose in spite of the massive antibiotic therapy, the patient's general condition was worsened, the skin lesions around the left eye extended over the middle line and in a symmetric way encircled the right eye too, and there developed new skin lesions on the right hand and the left shin of the same type as in the face (Fig. 3). Her right fourth finger was so swollen that when strangulation was imminent, her rings had to be cut off. ESR increased to 91 mm/1 h. With the first patient in mind, the diagnosis of Sweet's syndrome was now made and 30 mg prednisolone daily prescribed. Within 1 day, the temperature was normal and the skin lesions paler and less swollen. The corticosteroid was then slowly reduced as we had learnt from our first patient and the literature, and there were no break-through or rebound phenomena. After 2 weeks, the skin lesions had completely disappeared, and 2 weeks later the patient was free from steroids. She has since remained in good health. ESR is now 16 mm/1 h, and AST-0 400 u/ml. Judging from the AST-0 titre changes, the sore throat that preceded the patient's dermatosis was probably of a streptococcal origin.

DISCUSSION

Our 2 cases are in all respects characteristic of the acute febrile neutrophilic dermatosis (Sweet's syndrome). Eighteen patients have now been reported in the literature, all from England, and only one of them is a male. Our 2 patients are also females. In Table I the symptoms and signs of the cases described in the literature are compared with those of our patients. An extensive review of the syndrome has recently been published by Crow et

Table I. *Clinical features in 18 cases of Sweet's syndrome from the literature and the 2 present cases.*

	Positive/ investigated	Case I	Case II
Acute infection preceding the onset	11/16	+	+
Fever	13/15	+	+
Neutrophilic leucocytosis	14/16	+	+
ESR increased	9/9	+	+
Dermal neutrophilic infiltration	18/18	+	+
Excellent response to systemic steroids or ACTH	12/12	+	+
Recurrences	6/18		

al. (1969). The skin lesions are located mostly on the face and limbs, and often have a typical surface, which reminds one of "a relief model of a mountain range" (1). The response to systemic corticosteroids or ACTH treatment is usually dramatically good. When no steroids are given there will be a spontaneous remission after about 6–8 weeks.

The often dramatically ill patient with fever, a high erythrocyte sedimentation rate, leucocytosis and prominent, strange, blue-red skin eruptions have in many cases led to suspicions of a *septic state*. Sometimes the skin lesions are restricted to only one area of skin, most often the face (5, 6). These cases are often misdiagnosed as *erysipelas*. Thorough bacteriological and virological investigations of the blood and the skin lesions are, however, negative and antibiotics are without any effect. An acute exacerbation of a "*collagenosis*" may also be suspected initially but no serological clues supporting this diagnosis have been found. The lack of involvement of internal organs and the spontaneous course of the disease exclude systemic lupus erythematosus, polyarteritis nodosa, etc. We believe that some of these cases earlier have been diagnosed as atypical forms of *erythema multiforme* or *erythema nodosum*, especially as in many cases an acute infection precedes the skin eruption. It is possible that these two diseases and Sweet's syndrome may represent a hypersensitivity reaction to non-specific infective agents (1, 4). No cases of Sweet's syndrome caused by drugs, tuberculous infection, sarcoidosis or malignant tumours have been published yet. The syndrome of acute febrile neutrophilic dermatosis is differentiated from erythema exsudativum multiforme by its asymmetric distribution of the skin lesions and their often characteristic surface, tenderness, the often more pronounced skin infiltration and the absence of lesions of the mucous membranes. Laboratory investigations will show a high erythrocyte sedimentation rate and a more pronounced leucocytosis in Sweet's syndrome than in erythema multiforme (2). The response to corticosteroids is more dramatically good in Sweet's syndrome.

Histopathologically the intense neutrophilic infiltration is an important sign of Sweet's syndrome. The deep cutaneous infiltration may sometimes resemble erythema nodosum especially when localized to the shins (4). The complete clinical picture will, however, exclude this disease. Histopathologically there is a close resemblance between Sweet's syndrome and an early stage of erythema elevatum diutinum (4), but the clinical picture is quite different.

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