

Sweet's Syndrome Associated with *Salmonella typhimurium* Infection

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A 41-year-old woman presented with the typical clinical and pathohistological features of acute febrile neutrophilic dermatosis (AFND). The disease had been preceded by diarrhoea and vomiting for 2 weeks. Stool cultures proved positive for *Salmonella typhimurium* infection. Antibiotic therapy and tapering oral steroids led to a complete remission of skin lesions within 2 weeks. To our knowledge, this is the first report of Sweet's syndrome associated with salmonellosis. Key words: Acute febrile neutrophilic dermatosis; Salmonellosis.

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Acute febrile neutrophilic dermatosis (AFND) was first described by Sweet in 1964 as a distinctive entity (1). In 7 out of 8 cases listed in the original article, the disease was preceded by an upper respiratory tract infection. In the meantime there have been numerous reports on the association of AFND with other conditions, of which malignancies were most important (2). The association of Sweet's syndrome with a salmonellosis, however, has not been previously reported.

CASE REPORT

A 41-year-old woman was referred to our Department with painful plaques in a generalized distribution. Skin lesions had started on the left wrist 2 days prior to admission. Further history revealed diarrhoea (five loose stools/day) and recurrent vomiting for the past 2 weeks resulting in a 3 kg weight loss. Although stool cultures for pathogenic bacteria had proved negative, the patient was treated with trimethoprim-sulfamethoxazole for 2 days. Medication was then discontinued by the patient because of gastric side effects.

Further treatment of diarrhoea with loperamide and metoclopramide was ineffective. Six days prior to admission, all medication had been discontinued. Past medical history was insignificant for any serious illnesses.

On physical examination we found tender erythematous plaques, some of them edematous. They were up to 1.5 cm in size and were located on wrists, extensor sites of upper

arms, thighs, back and neck (Fig. 1). Temperature was 39.6°C. Further examination was unremarkable.

Pathological laboratory findings included: hemoglobin 10.0 mg% (normal > 12 mg%), serum iron 19 mg% (normal > 70 mg%), serum copper 262 mg% (normal < 140 mg%), ESR 80/120 mm (60/120 min); the WBC count was slightly elevated (11,000, normal < 10,000/ μ l) with a differential of 75% PMNs. The stool culture proved positive for *Salmonella typhimurium* but negative for other pathogenic bacteria including *Yersinia* spp. and *Campylobacter* spp. Stools were repeatedly positive for occult blood. The remainder of an extensive laboratory work-up was negative. A chest X-ray and an abdominal ultrasound scan also showed no pathological findings.

Histopathological examination of one of the plaques (Fig. 2) revealed a normal epidermis, a marked edema of the papillary dermis and a scattered infiltrate in the upper and mid-dermis. It mainly consisted of neutrophils but also contained some lymphocytes, histiocytes and eosinophils. Blood vessels were dilated and showed endothelial swelling but no signs of vasculitis. Direct immunofluorescence was negative (standard technique).

Under the clinical diagnosis of Sweet's syndrome the patient was treated with Flucortolon 50 mg p.o./d. The dosage was gradually tapered over a period of 3 weeks. Skin changes improved rapidly and fever resolved promptly. Hypochromic anemia was treated with oral iron administration. After we had received the bacteriological



Fig. 1. Right upper arm: Multiple erythematous and edematous plaques.

report, ciprofloxacin 750 mg/d was given for 6 days. Repeated post-treatment stool cultures proved negative for *Salmonella typhimurium*. After a one-year follow-up period, the patient is in good health, anemia has resolved completely and all laboratory parameters have become normal.

DISCUSSION

There is no doubt that our patient suffered from Sweet's syndrome. The following cardinal features were present: 1) an acute onset of the disease, 2) fever, and 3) painful erythematous plaques in a characteristic distribution. On pathohistological examination, 4) a dense dermal infiltrate was found, mainly consisting of PMNs. Moreover, 5) the condition responded rapidly to oral steroids. As pointed out by Sweet himself, one might not always find the whole spectrum of symptoms typical of AFND (3). Thus, in our patient, a marked polymorphonuclear leukocytosis was missing.

The etiology of AFND is still unknown. Sweet already assumed that it was a reactive rather than an infectious condition (1). However, it is not understood how various antigens, including viruses, bacteria or tumour-derived antigens, can induce this disease.

There have been numerous reports that Sweet's syndrome may be associated with certain other conditions. In most cases a preceding upper respiratory

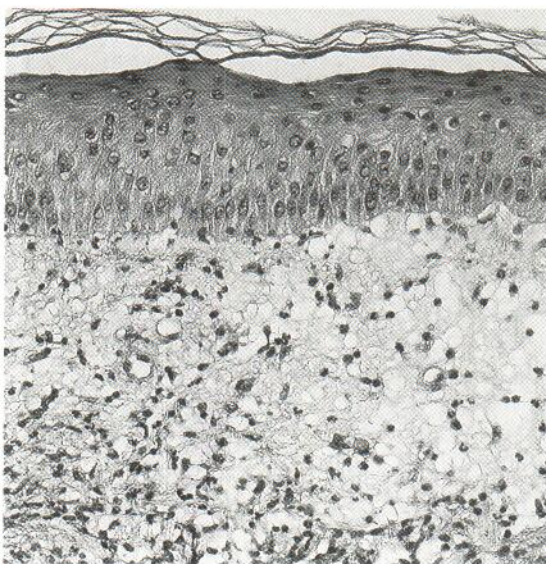


Fig. 2. Normal epidermis, marked edema of the papillary dermis. Scattered infiltrate in the upper and mid-dermis, consisting mainly of neutrophils. H&E, $\times 200$.

tract infection is encountered. The association of Sweet's syndrome with malignancies is very important. They occur in 10–15% of reported cases (4, 5). Most often an acute myelogenous leukemia is found, while solid carcinomas are less frequent (2). Skin lesions may precede the diagnosis of the malignancy by months or even years (2, 5). In addition, there have been reports of several autoimmune conditions associated with AFND, such as subacute cutaneous lupus erythematosus (6), rheumatoid arthritis (7), ulcerative colitis (1), Crohn's disease (8), Dressler's syndrome (9), Behçet's disease (10) and subacute thyroiditis (11). The list of associated infectious diseases other than upper respiratory tract infection includes *Yersinia enterocolitica* infection (12), *Escherichia coli* septicemia (13) and toxoplasmosis (14).

That salmonella infection may also induce AFND is strongly suggested by our case. The patient was in good health before the onset of gastrointestinal complaints, followed by the skin eruption. A thorough work-up revealed no other underlying disease than salmonellosis. After successful antibiotic and steroid therapy there was no flare-up of skin lesions. On the other hand, a recurrence of Sweet's syndrome would be expected if the inducing agent was not eliminated.

Before the skin lesions started, the patient had taken three different drugs to cure the diarrhea. It cannot be completely excluded that these drugs were associated with the Sweet's syndrome. However, their administration was of short duration (maximum 4 days) and all medication had been discontinued 6 days prior to the skin eruption.

With this report we extend the list of conditions associated with AFND. We suggest that in patients with Sweet's syndrome presenting with gastrointestinal symptoms, the diagnostic work-up should include stool cultures to rule out salmonellosis.

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