Rare disease

Sweet's syndrome in a patient with infective endocarditis: a rare clinical entity

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Summary

Sweet's syndrome, also known as acute febrile neutrophilic dermatosis, has been associated with malignancy, autoimmune disease and collagen vascular disease. The association of infective endocarditis and Sweet's syndrome is rare. The authors report a case of Sweet's syndrome in a patient with infective endocarditis. Infective endocarditis should be excluded in patients of rheumatic heart disease presenting with Sweet's syndrome. Alternatively, Sweet's syndrome should be considered as a differential diagnosis when a patient with infective endocarditis develops skin lesions.

BACKGROUND

The association of infective endocarditis and Sweet's syndrome is rare. We report a case of Sweet's syndrome in a patient with infective endocarditis. Infective endocarditis should be excluded in patients of rheumatic heart disease presenting with Sweet's syndrome. Alternatively, Sweet's syndrome should be considered as a differential diagnosis when a patient with infective endocarditis develops skin lesions. Sweet's syndrome should be considered as an extra-cardiac manifestation of infective endocarditis. Awareness of this association may guide appropriate diagnostic procedures and therapy.

CASE PRESENTATION

A 45-year-old female with a history of rheumatic heart disease for the past 30 years presented with fever of 1 week's duration, erythematous and bullous lesions on her trunk, bilateral arms and legs and abdominal pain. Fever was high grade and associated with chills, nausea and vomiting. The patient also had painful rash all over her body that had erupted suddenly about a week before presentation. The rash was non-pruritic, started on the dorsum of her hands and spread to involve her face, neck, chest and legs. She denied using any new soaps, lotions or perfumes. She did not change her bed sheets or acquire clothing in the recent past. She also denied contact with pets, recent travel, a similar rash in any other family member, or being bitten by an insect. She denied having had any similar rash in the past. She had a history of rheumatic heart disease for the past 30 years. Her previous echocardiogram showed rheumatic heart disease with mitral regurgitation and mild tricuspid regurgitation. Her medications included erythromycin which she had been taking for her condition.

INVESTIGATIONS

Tender to palpation.

Laboratory results showed an elevated white cell count of 18.7×10^9 with 76% neutrophils and 12% bands. Her erythrocyte sedimentation rate (ESR) was 64 mm/h. Her blood urea was 40 mg/dl and serum creatinine was 1.3 mg/dl. Blood cultures were positive for *Staphylococcus aureus*. Other laboratory tests, which included fungal serology, potassium hydroxide mount, gram stain, acid fast bacilli smear, fungal culture and an acid fast culture of the skin rash, were all negative. She was started empirically on intravenous vancomycin for possible methicillin-resistant *Staphylococcus aureus*, pending the results of drug sensitivity.

Echocardiography was done and revealed mitral valvular vegetations with mitral regurgitation and mild tricuspid regurgitation. There was pulmonary arterial hypertension with normal biventricular function. The left ventricle ejection fraction was 60%. The patient was diagnosed to have infective endocarditis and started on intravenous antibiotics.

The rash showed no improvement after 3 days of antibiotics. A punch biopsy of one of the skin lesions revealed dense dermal infiltrates composed predominantly of neutrophils, with no evidence of vasculitis. This was consistent with the diagnosis of Sweet's syndrome (figure 1A–E). The patient's symptoms and rash rapidly improved on treatment with systemic corticosteroids.

DIFFERENTIAL DIAGNOSIS

1. Drug induced sweet syndrome
2. Erythema multiforme
3. Pyoderma gangrenosum

TREATMENT

1. Intravenous antibiotics
2. Systemic corticosteroid

OUTCOME AND FOLLOW-UP

The patient's symptoms and rash rapidly improved on treatment with systemic corticosteroids.

Figure 1 (A, B) The punch biopsy of the skin lesion showing neutrophil infiltration in the dermis, with no evidence of vasculitis consistent with sweet syndrome (A, B-photomicrograph-40X). (C, D) The punch biopsy of the skin lesion showing neutrophil infiltration in the dermis, with no evidence of vasculitis consistent with sweet syndrome (A, B-photomicrograph-200X). (E) The punch biopsy of the skin lesion showing neutrophil infiltration in the dermis with subepidermal bullae with no evidence of vasculitis consistent with sweet syndrome (E-photomicrograph-200X).

DISCUSSION

Sweet's syndrome, also known as acute febrile neutrophilic dermatosis, was first described by Robert Douglas Sweet in 1964.¹ Sweet's syndrome is characterised by fever, neutrophilia, cutaneous eruptions consisting of erythematous papules and plaques, and a dermal non-vasculitic neutrophilic infiltration on skin biopsy.²⁻³ These plaques are painful but non-pruritic.⁴ Other skin manifestations such as pustules, vesicles, purpura, ulcers and haemorrhagic lesions have been described.¹ Seventy-five per cent of patients have some prodromal illness, most commonly an upper respiratory tract infection.⁵

Common complications of Sweet's syndrome include arthralgia, arthritis, conjunctivitis, iridocyclitis, and rarely involvement of the central nervous system.⁴ Sweet's syndrome is more common in females with a female to male ratio of 3.7:1, with the mean age of 52 years.¹

Sweet's syndrome should be regarded as a cutaneous marker of systemic disease. It has been associated with malignancies in about 20 to 25% of patients.⁶ Most malignancies are haematopoietic, especially myelodysplastic syndromes and acute myeloid leukemia. Fifteen per cent are due to solid tumours including breast, genitourinary and gastrointestinal malignancies.⁷

Only a few cases of Sweet's syndrome associated with infective endocarditis disease have been reported in the literature.¹ It appears that the syndrome is not initiated by the underlying disease but rather shares with it a concurrent pathogenic mechanism.

The pathogenesis of Sweet's syndrome is poorly understood. Cytokines, such as granulocyte colony stimulating factor (G-CSF), interleukin (IL)-1, IL-6, or IL-8, if deposited in the dermis, may be responsible for the immunopathologic and clinical manifestations of Sweet's syndrome. The fact that Sweet's syndrome can occur after G-CSF treatment shows that IL-1, which is produced by acute myelocytic leukemia cells and stimulates the G-CSF gene, plays a role in the pathogenesis of Sweet's syndrome.¹

For a definitive diagnosis of Sweet's syndrome, both major and two minor criteria should be met. The two major criteria are 1) abrupt onset of painful erythematous plaques or nodules occasionally with vesicles, pustules, or bullae and 2) neutrophilic infiltration in the dermis without leukocytoclastic vasculitis. The minor criteria are 1) skin lesions preceded by a non-specific respiratory or gastrointestinal tract infection, vaccination or associated with inflammatory diseases such as autoimmune disorders, infections, haemoproliferative disorders, solid malignant tumours or pregnancy, 2) accompanied by periods of general malaise and fever ($>38^{\circ}\text{C}$), 3) laboratory values during onset: ESR >20 mm, C reactive protein-positive, segmented neutrophils $>70\%$ in peripheral blood smear, leukocytosis >8000 (three of four of these values are necessary) and 4) excellent response to treatment with systemic corticosteroids or potassium iodide.¹⁻⁸

Sweet's syndrome is one of the groups of neutrophilic dermatoses that include pyoderma gangrenosum and whose association with ulcerative colitis and Crohn's disease is well established. Sweet's syndrome can be distinguished from pyoderma gangrenosum by the absence of vasculitis and lack of dermal necrosis, but histological features may occasionally overlap. The abrupt tendency for Sweet's syndrome to form multiple eruptions on the upper half of the body and the lack of ulceration also distinguishes the rash from pyoderma gangrenosum. However, the two conditions can occur in the same patient, as may other neutrophilic dermatosis, vesiculopapular eruptions or other cutaneous features of inflammatory bowel disease such as erythema nodosum or polyarthritis. The simultaneous occurrence of different rashes in the same person can be viewed as the dermatological expression of a neutrophilic reaction to a common stimulus.⁹

Sweet's syndrome, if left untreated, usually heals within 6 to 8 weeks.⁵ Prednisone at an initial dose of 40–60 mg per day, with gradual tapering off over 4 to 6 weeks, is the standard treatment for Sweet's syndrome.³⁻⁵ Relapses are

common if steroids are tapered too quickly. In recurrent disease, therapy with colchicine, potassium iodide, dapsone, doxycycline, indomethacin, clofazimine, isotretinoin and cyclosporine have all been described.¹⁻⁵

Potassium iodide administered orally as 300 mg enteric-coated tablets, three times each day, for a daily dose of 900 mg, or as a saturated solution of potassium iodide (Lugol's solution), beginning at a dose of three drops three times each day (nine drops/day=450 mg per day) and increasing by one drop three times per day, typically to a final dose of 21 drops/day (1050 mg) to 30 drops/day (1500 mg), usually results in resolution of fever and other symptoms within 1 to 2 days and resolution of skin lesions within 3 to 5 days of initiation of therapy. Vasculitis and hypothyroidism are potential adverse effects of potassium iodide.¹⁰

Learning points

- ▶ Sweet's syndrome should be considered as an extra-cardiac manifestation of infective endocarditis.
- ▶ Infective endocarditis should be excluded in patients of rheumatic heart disease presenting with Sweet's syndrome.
- ▶ Alternatively, Sweet's syndrome should be considered as a differential diagnosis when a patient with infective endocarditis develops skin lesions.
- ▶ Awareness of this association may guide appropriate diagnostic procedures and therapy.

Competing interests None.

Patient consent Obtained.

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