

Answer to Dermacase *continued from page 1249*

2. Sweet syndrome

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, was originally described in 1964 by Dr Robert Douglas Sweet.¹ It affects mostly women and is typically observed in adults between 30 and 50 years of age; however, younger adults and children can also be affected.² No racial predilection has been reported. The pathogenesis is not entirely understood, although cytokines might play a role.² Sweet syndrome is classified into 3 clinical subgroups: classic or idiopathic, malignancy-associated or paraneoplastic, and drug-induced.

Classic or idiopathic Sweet syndrome is the most common manifestation. Most cases are isolated, although association with infection (especially of the upper respiratory or gastrointestinal tract), inflammatory bowel disease, and pregnancy has been reported.² Other associated conditions include sarcoidosis, rheumatoid arthritis, erythema nodosum, Behçet syndrome, and autoimmune thyroid disease (Graves disease and Hashimoto thyroiditis).³

Malignancy-associated or paraneoplastic Sweet syndrome is less common but not rare either. The estimated incidence of malignancy in Sweet syndrome patients ranges from 10% to 20%.³ Most malignancies are hematologic, with a substantial number being acute myeloid leukemia.^{3,4} Solid tumours are also associated with Sweet syndrome, albeit less frequently; these are predominantly carcinomas of the genitourinary tract, breast, and gastrointestinal tract.³ In approximately two-thirds of patients, the cutaneous lesions of Sweet syndrome appear before or together with the discovery of a malignancy.³ In addition, it is not uncommon for recurrence of cutaneous disease to be the first sign of recurrent malignancy.²

Drug-induced Sweet syndrome is uncommon. Granulocyte-colony stimulating factor is undoubtedly

the most common culprit.⁵ Other implicated medications include all-trans retinoic acid, oral contraceptives, and antibiotics, such as trimethoprim-sulfamethoxazole, minocycline, and nitrofurantoin.^{5,6}

The classic cutaneous eruption of Sweet syndrome presents as multiple well-defined, tender, erythematous and edematous papules that frequently coalesce into larger plaques. The typical distribution includes the upper extremities, face, and neck, although the trunk and lower extremities can also be involved.² Occasionally, patients might have bullous or ulcerated lesions; this is more often noted in malignancy-associated Sweet syndrome.³ Two less-common presentations include a single tender erythematous plaque with a predilection for the face and periorbital area⁷ and a pustular dermatosis predominantly restricted to the dorsa of the hands (neutrophilic dermatosis of the dorsal hands).² Oral mucosal ulcers have also been observed in some patients, typically those with associated hematologic malignancy.⁸

Systemic symptoms might accompany the cutaneous eruption, and in those cases patients can appear quite ill. Fever is the most common symptom; occasionally, it can precede the onset of cutaneous disease by several days to weeks.⁸ Other symptoms include myalgia, arthralgia, headache, and general malaise.⁹ In addition, some patients can experience specific symptoms related to extracutaneous disease, as Sweet syndrome can (albeit uncommonly) affect the eyes, bone, muscles, kidneys, intestines, liver, spleen, heart, lungs, and central nervous system.⁸

Diagnosis

Diagnostic criteria have been established for Sweet syndrome (Table 1).^{6,10} Several conditions can mimic the cutaneous eruption; hence, the clinical differential diagnosis is extensive. It includes reactive erythemas (erythema multiforme, erythema nodosum, and

Table 1. Diagnostic criteria for Sweet syndrome

TYPE OF SYMPTOMS	MAJOR CRITERIA	MINOR CRITERIA
Classic and malignancy-associated* symptoms	<ul style="list-style-type: none"> • Abrupt onset of painful erythematous plaques or nodules • Histopathologic evidence of dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis 	<ul style="list-style-type: none"> • Fever > 38°C • Association with an underlying hematologic or solid tumour malignancy, inflammatory disease, or pregnancy, or preceded by an upper respiratory or gastrointestinal infection • Excellent response to treatment with systemic corticosteroids • Abnormal laboratory values at presentation (3 of 4): <ul style="list-style-type: none"> -ESR > 20 mm/hr -CRP positive -leukocytes > 8000/μl -neutrophils > 70%
Drug-induced† symptoms	<ul style="list-style-type: none"> • Abrupt onset of painful erythematous plaques or nodules • Histopathologic evidence of dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis 	<ul style="list-style-type: none"> • Fever > 38°C • Temporal relationship between drug ingestion and clinical presentation, or temporally related recurrence after oral challenge • Temporally related resolution of lesions after drug withdrawal or treatment with systemic corticosteroids

CRP—C-reactive protein, ESR—erythrocyte sedimentation rate.

*Diagnosis of classic or malignancy-associated Sweet syndrome requires the presence of both major criteria and 2 of the 4 minor criteria.¹⁰

†Diagnosis of drug-induced Sweet syndrome requires the presence of all 5 criteria.⁶

urticaria), as well as a variety of infectious disorders (cellulitis, erysipelas, syphilis, tuberculosis, herpes simplex virus infection, varicella-zoster virus infection, viral exanthem, etc), inflammatory disorders (pyoderma gangrenosum, Behçet syndrome, systemic lupus erythematosus, bowel bypass syndrome, etc), neoplastic disorders (leukemia cutis, lymphoma, metastatic tumour, etc) and vasculitic disorders.^{2,8}

Laboratory findings can support the diagnosis. An elevated erythrocyte sedimentation rate is a consistent finding in most patients. C-reactive protein levels can also be elevated. Peripheral neutrophilic leukocytosis is a frequent finding in those with the classic form of the syndrome. Anemia, abnormal platelet count, a normal or low neutrophil count, or abnormalities of the leukocyte differential might be observed in patients with an underlying malignancy.³

A skin biopsy is required to confirm the diagnosis of Sweet syndrome. Histopathologic findings are characterized by a dense dermal infiltrate of mature neutrophils and pronounced dermal edema without evidence of vasculitis.⁸ The histologic differential diagnosis includes other neutrophilic dermatoses, such as pyoderma gangrenosum, bowel bypass syndrome, and rheumatoid neutrophilic dermatitis, as well as infectious disorders, especially abscess and cellulitis.² A culture of skin biopsy tissue should be considered to rule out bacterial and fungal infection.

Treatment

Without treatment, the cutaneous lesions can persist for weeks or even months. Spontaneous resolution has been described in some patients. Moreover, in cases of malignancy-associated or drug-induced Sweet syndrome, prompt resolution has occurred following successful treatment of the underlying malignancy or discontinuation of the causative medication.¹¹

Sweet syndrome responds well to treatment. Systemic corticosteroids are the treatment of choice for most

patients. Therapy with prednisone is initiated at a daily dose of 30 to 60 mg. This can usually be tapered to 10 mg within 4 to 6 weeks.² Cutaneous disease and systemic symptoms begin to improve within 48 hours. Complete resolution of cutaneous disease frequently occurs at 7 to 10 days after onset.¹¹ Potassium iodide and colchicine are also considered first-line agents; they are especially useful when corticosteroids are contraindicated. Other effective but less commonly employed treatment options include indomethacin, clofazimine, cyclosporine, and dapsone.^{8,11} Individual case reports also document success with certain systemic antibiotics, such as those in the tetracycline family. Localized lesions can be treated with high-potency topical corticosteroids (eg, 0.05% clobetasol propionate) and intralesional corticosteroids (eg, triamcinolone acetonide).¹¹ Recurrence of Sweet syndrome is not uncommon. About 30% of patients will experience relapse of cutaneous disease following spontaneous or therapy-induced remission.² Recurrence is more frequent in those with an associated malignancy.

Dr Prajapati is a first-year dermatology resident at the University of Alberta in Edmonton. **Dr Barankin** is a dermatologist in Toronto, Ont.

Competing interests

None declared

References

1. Sweet RD. An acute febrile neutrophilic dermatosis. *Br J Dermatol* 1964;76(4):349-56.
2. Cohen PR, Kurzrock R. Sweet's syndrome: a neutrophilic dermatosis classically associated with acute onset and fever. *Clin Dermatol* 2000;18(3):265-82.
3. Cohen PR, Kurzrock R. Sweet's syndrome and cancer. *Clin Dermatol* 1993;11(1):149-57.
4. Cohen PR, Kurzrock R. Sweet's syndrome and malignancy. *Am J Med* 1987;82(6):1220-6.
5. Saez M, Garcia-Bustinduy M, Noda A, Dorta S, Escoda M, Fagundo E, et al. Drug-induced Sweet's syndrome. *J Eur Acad Dermatol Venerol* 2004;18(2):233.
6. Walker DC, Cohen PR. Trimethoprim-sulfamethoxazole-associated acute febrile neutrophilic dermatosis: case report and review of drug-induced Sweet's syndrome. *J Am Acad Dermatol* 1996;34(5 Pt 2):918-23.
7. Fitzgerald RL, McBurney EI, Nesbitt LT Jr. Sweet's syndrome. *Int J Dermatol* 1996;35(1):9-15.
8. Cohen PR, Kurzrock R. Sweet's syndrome revisited: a review of disease concepts. *Int J Dermatol* 2003;42(10):761-81.
9. Callen JP. Neutrophilic dermatoses. *Dermatol Clin* 2002;20(3):409-19.
10. Von den Driesch P. Sweet's syndrome (acute febrile neutrophilic dermatosis). *J Am Acad Dermatol* 1994;31(4):535-56.
11. Cohen PR, Kurzrock R. Sweet's syndrome: a review of current treatment options. *Am J Clin Dermatol* 2002;3(2):117-31.