

Sweet's Syndrome Masquerading as Facial Cellulitis

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Sweet's syndrome, or acute febrile neutrophilic dermatosis, is a cutaneous condition that typically occurs as tender red plaques or nodules. However, atypical presentations may occur and, in our case, Sweet's syndrome masqueraded as facial cellulitis and soft tissue infections of the extremities in a sporotrichoid pattern. Despite treatment with broad-spectrum antibiotics, the cutaneous lesions progressed. Results of skin biopsy specimens of the facial plaque and a nodule on the right upper extremity were diagnostic of Sweet's syndrome. Simultaneous to diagnosis, the patient also was found to have acute myelogenous leukemia (AML).

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We present the case of a woman with skin lesions originally diagnosed as facial cellulitis and multiple soft tissue infections of the extremities in a sporotrichoid pattern. The importance of an accurate diagnosis is essential because Sweet's syndrome responds to immunosuppressive agents instead of antimicrobial therapy. In addition, recognition of Sweet's syndrome is crucial, as it may occur in the context of underlying hematologic or autoimmune diseases.¹

Case Report

A 54-year-old white woman presented with left facial erythema, swelling, and pain. The patient was well

except for the onset of oral ulcers (canker sores) over the previous month. Despite the presence of these ulcers on the left side of her oral mucosa, she underwent an elective right molar root canal. Within 24 hours of the procedure, left facial erythema, swelling, and pain developed. The initial diagnosis was facial cellulitis. Even with the administration of intravenous antibiotics, the erythema progressed, and fevers developed, necessitating hospitalization.

On admission, the patient was febrile (temperature, 38.8°C) and appeared ill. Physical examination revealed a sharply demarcated erythematous plaque that extended from the left maxillary area to just below the mandible (Figure). This area had woody induration on palpation and sharp palpable margins. There was scant, yellow serous drainage from the lesion, along with mild skin denudation. Crepitus and lymphadenopathy were not present. Along the left side of the lower lip, there were 2 raised plaques with vesicles on the surface. Examination of the oral cavity showed numerous small (<2 mm) erosions on the left buccal mucosa. The site of the dental procedure was unremarkable. The findings from ophthalmologic and neurologic examinations were normal. Three erythematous nodules (2–4 cm in diameter) were present on her right forearm in a linear sporotrichoid pattern. There was a single tender nodule on her left forearm. The patient reported that each nodule had occurred at previous venous puncture sites over the past 3 days.

Results of laboratory studies yielded the following values: white blood cell (WBC) count, 6700/ μ L; hemoglobin level, 9.1 g/dL; erythrocyte sedimentation rate, 135 mm/h; and platelets, $11.3 \times 10^3/\mu$ L. The automated WBC differential count was 65% neutrophils, 11% lymphocytes, 22% monocytes, 1% eosinophils, and 1% basophils. A computed tomographic scan of the head, sinuses, and neck revealed soft tissue swelling of her left face involving both subcutaneous and cutaneous tissues. No osseous involvement or abscess formation was noted.

Even after aggressive antimicrobial therapy that included piperacillin/tazobactam, clindamycin, and acyclovir, she remained febrile, and the soft tissue

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Figure not available online

Facial erythematous exudative plaque extending from the left maxillary area to just below the mandible. Vesicular lesions are present on the lower lip.

lesions progressed. Also, the patient developed nodules on the extensor surfaces of both lower extremities in a sporotrichoid pattern. In addition to blood cultures, bacterial and viral cultures of the skin lesions and an antistreptolysin O titer were negative. Given the progressive nature of these lesions, negative culture results, and lack of response to antimicrobial agents, biopsies of the facial plaque and a nodule on the right upper extremity were performed. Results of skin biopsy specimens revealed dense neutrophilia, leukocytoclasia, and marked dermal edema with bullae formation. No evidence of vasculitis was identified, and results from stains for microorganisms were negative. Because of the lack of leukocytosis with presumed infection and anemia, a manual blood smear was examined. Results showed that several blasts were missed by the automated WBC count. Subsequently, a biopsy of the bone marrow was diagnostic for acute myelogenous leukemia (AML), M4 type. As a result, the patient was diagnosed with Sweet's syndrome associated with AML. Treatment with a saturated solution of potassium iodide, as well as chemotherapy with idarubicin and cytarabine (araC), was instituted. All skin and mucosal lesions cleared within 3 weeks of therapy, without residual scarring. Three months after bone marrow transplantation, the patient is currently in remission without recurrence.

Comment

Sweet's syndrome first was reported in 1955 in a patient with AML.² Robert Sweet subsequently reported 8 cases in 1964 and described the salient features of this new syndrome, leading to the eponym "Sweet's syndrome." The alternate name of this syndrome is *acute febrile neutrophilic dermatosis*, which describes the fevers, tender erythematous plaques, peripheral leukocytosis, and dermal neutrophilic infiltrates characteristic of the disorder.³ Diagnostic criteria were first proposed by Su and Liu⁴ in 1986, with subsequent revisions.⁵

Clinically, Sweet's syndrome is described as painful erythematous plaques or nodules that occur asymmetrically on the face, neck, and extremities. The lesions may increase in size rapidly over days and typically measure 2 to 10 cm in diameter. Sweet's syndrome also may present as other less-recognized cutaneous findings, including bullae, pseudovesicles, pustules, localized edema, or abscesslike lesions.⁶⁻⁷ In our patient, Sweet's syndrome masqueraded as cellulitis of the face and soft tissue infections of the extremities in a sporotrichoid distribution. The facial plaque was diagnosed initially as erysipelas caused by *Streptococcus pyogenes* because of the lesion's appearance and sharp palpable margins.

The nodules on our patient's upper extremities occurred at previous venous puncture sites, explain-

Conditions Associated With Sweet's Syndrome*

Type of Sweet's Syndrome	Associated Condition or Inciting Agent
Classic	Infections: upper respiratory tract (Streptococcus) and GI tract (Yersinia) Vaccine related: pneumococcal and BCG Inflammatory bowel disease: Crohn disease and ulcerative colitis Pregnancy Idiopathic
Malignancy Associated	Hematologic: most commonly, AML Solid tumor: carcinomas of the genitourinary system, breast, or GI tract
Drug Induced	Granulocyte-colony stimulating factor, [†] trimethoprim-sulfamethoxazole, minocycline, nitrofurantoin, antiepileptics (eg, carbamazepine), antihypertensives (eg, hydralazine), oral contraceptives, and retinoids

*GI indicates gastrointestinal; AML, acute myelogenous leukemia.

[†]Most common medication related to Sweet's syndrome.

ing their sporotrichoid distribution. The occurrence of skin manifestations at previous sites of trauma, known as Köbner phenomenon, may occur in Sweet's syndrome, as well as Behçet disease and pyoderma gangrenosum.⁶

Sweet's syndrome also may appear as vesicles or pseudovesicles and therefore be occasionally confused with herpetic infections of the skin and buccal mucosa.^{6,8} In our case, 2 vesicularlike lesions were noted near the lower lip, and several oral ulcers were noted on the buccal mucosa. Despite empiric therapy with acyclovir, the lesions persisted, and results from viral cultures were negative. One of the skin biopsy specimens showed a vesicle; however, viral inclusions were not identified, and results from the cultures were negative. Pseudovesicles as a presentation of Sweet's syndrome have been reported and linked to underlying malignancy.⁹

On laboratory examination, most patients present with peripheral neutrophilia and leukocytosis. Paradoxically, however, the WBC count may be normal or depressed due to an underlying condition (eg, hematologic malignancy). An elevated erythrocyte sedimentation rate, C-reactive protein, or both occurs in more than 90% of cases.

In addition to the clinical findings, the diagnosis of Sweet's syndrome requires pathologic demonstration of a dermal neutrophilic infiltrate. Leukocytoclasia, or fragmentation of neutrophil nuclei, is a

common finding.³ Classically, the epidermis is spared, and there is no evidence of vasculitis; however, a recent report suggests that vasculitis may occur as an epiphenomenon in Sweet's syndrome.¹⁰ As in our case, biopsy is extremely useful to confirm the diagnosis of Sweet's syndrome and to rule out other cutaneous conditions.

Sweet's syndrome may be associated with a variety of underlying disease processes. These conditions are divided into 3 main forms: classic, malignancy associated, and drug induced (Table).⁵ Approximately 10% to 20% of Sweet's syndrome cases are related to an underlying hematologic condition, most commonly, AML.

Treatment of malignancy-associated Sweet's syndrome consists of chemotherapeutic agents, and in drug-induced cases, the cessation of the causative medication. Systemic corticosteroids—in a dose of 1 mg/kg or 60 mg daily with a 4- to 6-week taper—are recommended. Resolution of the systemic symptoms, such as fevers, malaise, and myalgias, typically occur in 2 to 6 days; skin manifestations resolve in 2 to 3 weeks, without scarring. Corticosteroid-sparing agents, such as potassium iodide, colchicine, indomethacin, dapsone, cyclosporine, and chlorambucil, have been used with success in case reports.^{1,5-6} Currently, there are no comparison studies for these therapies, and corticosteroids remain the drugs of choice when no contraindications are present.

Potassium iodide is the most commonly utilized corticosteroid-sparing agent, with successful treatment noted in several case reports.^{11,12} In our case, corticosteroids were avoided because of the aggressive use of chemotherapeutic agents and the patient's immunosuppressed condition, though neither was considered as an absolute contraindication. Despite the severity and number of lesions, all manifestations of Sweet's syndrome resolved completely in 3 weeks with potassium iodide and chemotherapy.

The typical course of Sweet's syndrome is resolution within 2 to 8 weeks. However, recurrence of the lesions may occur in 20% to 30% of patients, especially those with underlying malignancy. In fact, a relapse of the hematologic malignancy may be preceded by a recurrence of Sweet's syndrome.

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