Giant Cellulitis-like Sweet Syndrome, a New Variant of Neutrophilic Dermatosis

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**Background:** Neutrophilic dermatoses comprise a wide spectrum of inflammatory diseases with overlapping features characterized histologically by the presence of an aseptic neutrophilic infiltrate in the epidermis, dermis, and/or hypodermis and are often associated with systemic inflammatory and neoplastic disorders.

**Observations:** We describe 3 patients with an unusual neutrophilic dermatosis characterized by relapsing episodes of fever, widespread infiltrated plaques with bullous appearance, and variable involvement of the arms, legs, abdomen, and/or trunk. Light microscopy studies showed marked edema of the papillary dermis with an inflammatory infiltrate consisting mainly of mature neutrophils. All 3 patients were morbidly obese, and workup revealed underlying cancer in 2 cases: myeloma and breast carcinoma. Management of the underlying disease resulted in long-term remission of the skin disease.

**Conclusions:** The clinicopathologic features in our 3 cases best correspond to a widespread giant cellulitis-like form of Sweet syndrome. Knowledge of this newly observed unusual variant of Sweet syndrome within the broad spectrum of neutrophilic diseases is important for its prompt and proper management.


**NEUTROPHILIC DERMATOSES**

Neutrophilic dermatoses comprise a wide spectrum of diseases, including Sneddon-Wilkinson disease (subcorneal pustulosis), Sweet syndrome (acute febrile neutrophilic dermatosis), pyoderma gangrenosum, erythema elevatum et diutinum, eccrine neutrophilic hidradenitis, and neutrophilic panniculitis. These disorders, characterized histologically by the presence of an aseptic neutrophilic infiltrate in the epidermis, dermis, and/or hypodermis, frequently show overlapping features. Neutrophilic dermatoses are commonly associated with systemic inflammatory and neoplastic disorders, including Crohn disease, rheumatoid arthritis, and hematologic malignant neoplasms. Neutrophilic dermatoses have been increasingly associated with extracutaneous neutrophilic infiltrates: lung, articular, skeletal, liver, spleen, lymph node, ocular, and gastrointestinal involvement have been described. On the basis of these observations, the term neutrophilic diseases has been proposed.

Sweet syndrome is characterized by the sudden development of tender inflammatory cutaneous lesions, abundant dermal neutrophilic inflammatory infiltrate evident on histopathologic examination, as well as an increase of inflammatory markers in the blood.

We report 3 cases of a novel neutrophilic dermatosis bearing a resemblance to Sweet syndrome that is unusual for the development of giant widespread infiltrated inflammatory plaques.

**REPORT OF CASES**

**CASE 1**

A 62-year-old man developed painful erythematous plaques involving his left leg, buttocks, and trunk as well as fever and malaise. During the preceding 2 years, the patient had experienced 8 similar episodes of variable intensity, which regressed spontaneously within 4 weeks. There had been no drug therapy preceding these episodes. On examination, he had an extensive erythematous infiltrated plaque involving the left lower leg, more than 60 cm in diameter. The lesion was sharply delimited, warm, and strongly infiltrated with a vesicular or bullous appearance. Purpuric lesions were also present...
ent. In addition, the patient exhibited discrete, erythematous, slightly infiltrated plaques of up to 50 cm in diameter on the thighs, trunk, and buttocks (Figure 1). He was obese, with a body mass index of 51 (calculated as weight in kilograms divided by height in meters squared). Light microscopy studies of a biopsy specimen revealed marked edema of the papillary dermis with an inflammatory infiltrate of the upper dermis consisting mainly of mature neutrophils. There was no evidence of leukocytoclastic vasculitis. Periodic acid–Schiff and Ziehl-Neelsen stains were negative for fungi and mycobacteria, respectively. Direct immunofluorescence microscopy study results also were negative. A complete blood cell count showed leukocytosis (white blood cells, 10,600/μL [to convert to ×10^9/L, multiply by 0.001]) and a platelet count of 96,000 × 10^9/μL (1:1 conversion to ×10^9/L). The C-reactive protein level was 279 mg/L (reference, <5 mg/L; to convert to nanomoles per liter, multiply by 0.9524). Electrolyte levels and results of renal and hepatic function tests were within normal limits. Bacteriologic examinations and repeated cultures of wound swabs did not yield any growth of bacteria. Testing for antinuclear antibodies was negative. Serum electrophoresis with immunofixation showed hypergammaglobulinemia and an inflammatory infiltrate of the upper dermis consisting mainly of mature neutrophils. There was no evidence of leukocytoclastic vasculitis. Periodic acid–Schiff and Ziehl-Neelsen stains were negative for fungi and mycobacteria, respectively. Results of bacteriologic examination and culture of the wound swabs, as well as direct immunofluorescence microscopy studies, also were negative. Laboratory examinations revealed leukocytosis (white blood cells, 24,000/μL) and high C-reactive protein levels (429 mg/L). Extensive workup did not find any evidence of an underlying solid tumor or lymphoproliferative disorder. The patient was given prednisone, 1 mg/kg/d, with dose reduction across several weeks. With this treatment, the cutaneous and systemic manifestations were controlled for 7 months, when the patient suddenly died of myocardial infarction with heart failure.

CASE 2

A 48-year-old woman developed skin lesions on her legs associated with fever, with temperatures up to 39.5°C, and malaise. The patient had similar recurrent, self-resolving, painful skin lesions associated with fever during the past 8 years. On examination, the obese patient (body mass index, 46.8) had extensive sharply limited, painful, warm, and strongly infiltrated erythematous plaques on the right lower leg and knee as well as on the extensor side of her left arm, the buttocks, and the trunk. Some lesions had a bullous appearance with a purpuric component (Figure 2). Light microscopy revealed marked edema of the papillary dermis with a dense inflammatory infiltrate of the upper dermis consisting mainly of mature neutrophils without leukocytoclastic vasculitis (Figure 3). Periodic acid–Schiff and Ziehl-Neelsen staining results were negative for fungi and mycobacteria, respectively. Results of bacteriologic examination and culture of the wound swabs, as well as direct immunofluorescence microscopy studies, also were negative. Laboratory examinations revealed leukocytosis (white blood cells, 24,000/μL) and high C-reactive protein levels (429 mg/L). Extensive workup did not find any evidence of an underlying solid tumor or lymphoproliferative disorder. The patient was given prednisone, 1 mg/kg/d, with dose reduction across several weeks. With this treatment, the cutaneous and systemic manifestations were controlled for 7 months, when the patient suddenly died of myocardial infarction with heart failure.

CASE 3

A 68-year-old woman developed painful erythematous plaques on her right leg associated with temperatures up to 39°C and malaise. The patient had 3 similar episodes during a 3-month period. On examination, she had several extensive, sharply limited erythematous plaques more than 50 cm in diameter involving the suprapubic region and the right thigh, leg, and foot. Some lesions had a vesicular or bullous appearance as well as a purpuric component (Figure 4). Her body mass index was 35. Light microscopy revealed marked edema of the papillary dermis with a dense inflammatory infiltrate of the upper dermis consisting mainly of mature neutrophils without evidence of leukocytoclastic vasculitis. Periodic acid–Schiff and Ziehl-Neelsen staining results were negative for fungi and mycobacteria, respectively. The patient developed leukocytosis (white blood cells, 11,300/μL) with a C-reactive protein level increased to 235 mg/L. Bacteriologic examinations and repeated cultures of the wound

**Figure 1.** Lesions associated with Sweet syndrome in patient 1. A, Erythematous infiltrated plaque with a bullous appearance involving the left leg. B, Erythematous, slightly infiltrated plaques on the abdomen. C, Similar lesions on the back and buttocks.
swabs or tissue samples did not yield any bacteria or fungi. No monoclonal immunoglobulin was detected by immunofixation. Topical corticosteroid therapy was started, with a transient improvement followed by a relapse. On reevaluation at that time, breast carcinoma was diagnosed. After surgical removal of the tumor, the patient did not develop any further skin lesions during the 12-month follow-up.

Figure 2. Lesions associated with Sweet syndrome in patient 2. A, Erythematous infiltrated plaques on the back and buttocks. B, Erythematous plaques with bullous appearance and a purpuric component. C, Plaque on the right thigh and the knee.

Figure 3. Light microscopy and histologic examination results in patient 2. A, A dense inflammatory infiltrate of the upper dermis and middermis consists mainly of mature neutrophils and marked edema of the papillary dermis (hematoxylin-eosin, original magnification ×100). B, Neutrophils in perivascular distribution without leukocytoclasia and interstitial edema (hematoxylin-eosin, original magnification ×400).
Our 3 patients developed severe relapsing eruptions with giant inflammatory lesions ranging from erythematous, slightly infiltrated lesions to painful indurated plaques with vesicular, bullous, or even hemorrhagic appearance. Lesions developed asymmetrically on the legs or arms, trunk, abdomen, and face. Their size was impressive—up to 100 cm in diameter. Clinical and histopathologic features best fit the diagnosis of Sweet syndrome. Su and Liu first proposed a set of criteria for Sweet syndrome, which were subsequently revised. When the 2 major criteria and at least 2 of the 4 minor criteria are fulfilled, classic Sweet syndrome can be diagnosed. Our patients fulfilled the major criteria as well as 3 or 4 minor criteria. Search for an underlying associated disease disclosed, in 2 patients, cancer. Two patients responded promptly to systemic corticosteroids, and the third patient experienced improvement with high-potency topical corticosteroids. Finally, the disease went into remission in 2 patients after management of the underlying malignant disease, with no further recurrence.

In classic Sweet syndrome, lesions usually affect the head, neck, and upper extremities. Lesions may be single or multiple and consist of erythematous papules and plaques with a pseudovesicular appearance. The lesions may coalesce to form irregularly shaped plaques. Concurrent fever, with temperatures up to 39°C, occurs in as many as 80% to 90% of patients. The evolution of the syndrome is chronic and relapsing in up to one-third of the cases. As observed in 2 of our patients, the cutaneous eruption can resolve spontaneously without specific therapy. Malignancy-associated Sweet syndrome shows some distinctive features compared with idiopathic Sweet syndrome. Lesions in the malignancy-associated syndrome tend to have a more widespread distribution, including involvement of the lower limbs. Furthermore, lesions tend to be more frequently bullous, hemorrhagic, and ulcerated and show some overlap with or bear close resemblance to pyoderma gangrenosum, as observed in our cases. Anomalies of the blood cell count are found in 50% to 80% of cases as in our first patient. Such atypical features in Sweet syndrome should prompt the search for an associated undiagnosed cancer or for tumor recurrence in a patient with a history of cancer. In 2 of our patients, dermatosis preceded the discovery of an underlying malignant neoplasm, either a solid tumor or a myeloproliferative disease.

Sweet syndrome is characterized histopathologically by the presence of a large nodular dermal infiltrate of mature neutrophils together with marked edema in the upper dermis. Fragmented nuclear “dust” of neutrophils (leukocytoclasia) in “top-heavy” fashion may be present, but the histologic signs of a primary leukocytoclastic vasculitis are absent. In the overlying epidermis, a variable degree of neutrophilic spongiosis or intraepidermal neutrophilic abscess formation can be occasionally observed. In our first patient with relapsing episodes, light microscopy revealed strong dermal edema with only mild neutrophilic infiltrate. Such images with few neutrophils have been described in cases of Sweet syndrome with chronic relapsing lesions. Noteworthy, in Sweet syndrome associated with hematologic malignant neoplasms, the infiltrate may also consist of immature myeloid or leukemic cells.

In our review of the English-language literature, including major textbooks, we were unable to find a description of Sweet syndrome of similar extent as in our patients. The severe widespread, relapsing eruption made us consider the possibility of an as-yet unrecognized novel variant of Sweet syndrome associated with giant cellulitis-like plaques. Strikingly, all 3 patients were morbidly obese, with body mass index higher than 35, which may have favored the development of such giant lesions. Our cases differed from a newly described variant of Sweet syndrome mimicking necrotizing fasciitis. This report described 3 patients who were septic, had a hematologic malignant neoplasm, and developed a localized, tender, indurated erythematous-violaceous plaque after therapy with granulocyte colony-stimulating factor. The inflammatory infiltrate composed of neutrophils further extended into the deep soft tissue and the muscle. Several differential diagnoses were further discussed; the first was an acute infectious cellulitis. However, microbiologic analysis results of tissue smears and biopsy specimens, as well as blood cultures, remained sterile, and oral and intravenous broad-spectrum antibiotics had no effect. Nevertheless, triggering of Sweet syndrome and other neutrophilic diseases by bacteria and other infectious agents

Figure 4. Large erythematous infiltrated plaques involving the hip region, the right leg, and the right foot in patient 3.
used. 8,18 fazimine, and cyclosporine have been among therapies line alternatives for treatment. Finally, indomethacin, clo-
dide, dapsone, and colchicine represent valuable first-
and calcineurin inhibitors may be tried. Potassium io-
the lesions are few and localized, topical corticosteroids
inflammation and at the same time should be tried. 8,18

Recognition and diagnosis of Sweet syndrome and other
neutrophilic dermatoses is important not only in
the search for underlying disease1,2,7,10 but also for the ini-
tial assessment of the patient. First, differential diag-
agnosis should be considered, including infectious
conditions (such as cellulitis), systemic inflammatory
response syndrome, drug eruptions, and, less frequently,
autosomal recessive neutrophilic dermatoses. 8,18

Consistent with a neutrophilic disease.

In conclusion, we describe a new variant of Sweet syn-
drome characterized by relapsing widespread giant le-
sions. The eruption invariably occurred in morbidly obese
patients. It is likely that this giant cellulitis-like variant
of Sweet syndrome is not so rare; rather, it has simply
remained unreported or unrecognized.

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