

Case Letter

Photoinduced Classic Sweet Syndrome Presenting as Hemorrhagic Bullae

To the Editor:

Sweet syndrome (SS) is characterized by fever; acute onset of painful erythematous papules, plaques, or nodules; peripheral neutrophilic leukocytosis; and histologic findings of a dense neutrophilic infiltrate without evidence of primary vasculitis.¹ We report a rare case of classic SS presenting with hemorrhagic bullae over photoexposed areas. Our case is notable because of the unusual nature of the clinical manifestation.

A 45-year-old woman presented with painful, fluid-filled lesions on the upper extremities of 1 week's duration. Lesions were acute in onset and associated with fever. The patient had a history of diabetes mellitus and hypertension, which were well controlled. She also had a history of minimal itching on sun exposure as well as an upper respiratory tract infection 2 months prior to presentation. There was no history of muscle weakness, pain and/or discoloration of the fingertips, or treatment with topical or systemic agents.

On physical examination, the patient was well nourished with an average build. She was febrile (temperature, 38.5°C) with a pulse of 82 beats per minute, a blood pressure of 130/80, and a respiratory rate of 14 breaths per minute. On cutaneous examination multiple erythematous plaques with central large hemorrhagic bullae were present on the extensor aspect of the forearms and dorsum of the left hand. The smallest plaque measured 4×8 cm and the largest measured 8×15 cm (Figure 1). The lesions were tender, and Nikolsky sign was negative. Considering the clinical features, a differential diagnosis of bullous

systemic lupus erythematosus, polymorphic light eruption, Jessner lymphocytic infiltrate, and SS were considered. Complete blood cell count demonstrated a hemoglobin level of 12.1 g/dL (reference range, 14.0–17.5 g/dL), total leukocyte count of 13,280/ μ L (reference range, 4500–11,000/ μ L), neutrophil count of 80% (reference range, 56%), lymphocyte count of 13% (reference range, 34%), monocyte count of 8% (reference range, 4%), and an erythrocyte sedimentation rate of 40 mm/h (reference range, 0–20 mm/h). Serum creatinine levels were 0.9 mg/dL (reference range, 0.6–1.2 mg/dL) and urea nitrogen levels were 26 mg/dL (reference range, 8–23 mg/dL). C-reactive protein was positive, antinuclear antibody was negative, and double-stranded DNA was negative. Ultrasonography of the abdomen and pelvis and a chest radiograph revealed no abnormalities.

Histopathology from a lesion on the forearm revealed a dense, predominantly neutrophilic infiltrate located in the superficial dermis as well as prominent papillary dermal edema infiltration in the dermis with vasodilatation in some areas without leukocytoclastic vasculitis features (Figures 2 and 3). Considering the clinical and histopathologic features, a diagnosis of SS was made, and the patient was started on intravenous dexamethasone (4 mg twice



Figure 1. Multiple erythematous plaques with central large hemorrhagic bullae were present on the extensor aspect of the forearms and dorsum of the left hand.

Dr. Pai is from the Department of Dermatology, Goa Medical College, India. Drs. Gupta, Athanikar, Naveen, Sori, and Shastry are from Sri Dharmasthala Manjunatheshwara College of Medical Sciences and Hospital, Sattur, Dharwad, India. Drs. Gupta, Athanikar, Naveen, and Sori are from the Department of Dermatology, and Dr. Shastry is from the Department of Pathology. The authors report no conflict of interest. Correspondence: Varadraj V. Pai, MD, Department of Dermatology, Goa Medical College, Goa 403202, India (docpai@rediffmail.com).

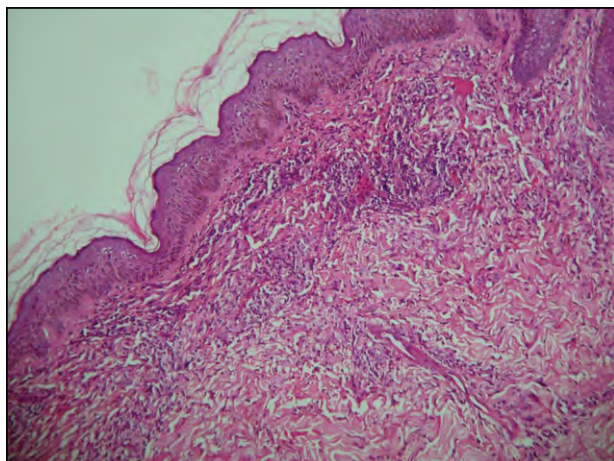


Figure 2. Neutrophilic infiltrate in the superficial dermis and prominent papillary dermal edema infiltrate in the dermis (H&E, original magnification $\times 40$).

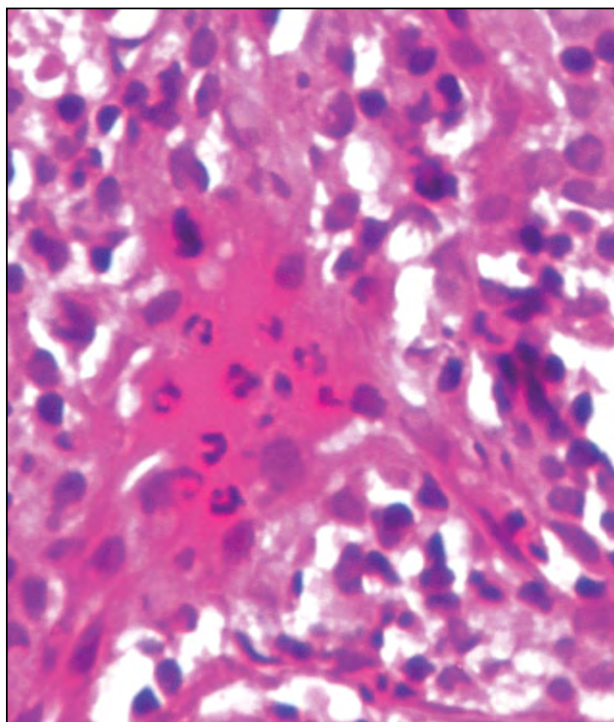


Figure 3. Polymorphonuclear neutrophilic infiltrate with multilobulated nucleus without leukocytoclasia (H&E, original magnification $\times 100$).

daily) with a dramatic response, as the lesions almost cleared within 4 to 5 days of treatment (Figure 4).

Sweet syndrome was first described in 1964 as acute febrile neutrophilic dermatosis.² Sweet syndrome can be subdivided into 3 groups depending on the clinical setting: classic or idiopathic, malignancy associated, and drug induced.³ Classic or idiopathic SS



Figure 4. Intravenous dexamethasone resulted in improvement within 4 to 5 days of treatment.

typically affects women in the third to fifth decades of life,⁴ as seen in our case. The proposed diagnostic criteria for SS state that patients must meet both of the 2 major criteria and 2 of 4 minor criteria for the diagnosis.³ The major criteria include acute onset of typical skin lesions and histopathologic findings consistent with SS. The minor criteria include fever (temperature $>38^{\circ}\text{C}$) or general malaise; association with malignancy, inflammatory disease, pregnancy, or antecedent respiratory or gastrointestinal tract infection; excellent response to treatment with systemic corticosteroids or potassium iodide; and abnormal laboratory values at presentation (3 of 4 required: erythrocyte sedimentation rate >20 mm/h; leukocyte count $>8000/\mu\text{L}$; neutrophil count $>70\%$; positive C-reactive protein). Our patient fulfilled both the major criteria and 3 of 4 minor criteria. Although the exact etiology of SS is unknown, it is widely believed that SS may be a hypersensitivity response to underlying bacterial infections such as *Yersinia enterocolitica*, viral infections, or tumors.⁵

Cytokine dysregulation also has been indicated in the pathogenesis of SS, an imbalance of cytokine secretion from helper T cells such as IL-2 and IFN- γ , which may stimulate the cytokine cascade leading to activation of neutrophils and release of toxic metabolites.⁶ The cutaneous manifestations of SS consist of erythematous to violaceous tender papules or nodules that often coalesce to form irregular plaques.⁷ Rare clinical manifestations include bullous lesions; oral involvement; glomerulonephritis; myositis; and ocular manifestations including conjunctivitis, episcleritis, and iridocyclitis.^{5,8} Photoaggravated and photoinduced syndromes also have been reported.⁹

Bullous-type SS has been reported, but all the known cases were secondary to malignancy or were drug induced^{8,10}; they did not present in a classic or idiopathic variant. Our case is unique in that it is a report of the classic SS variant with lesions including bullae over photoexposed areas, possibly indicating a causal association of sun exposure and the development of SS.

The diagnostic histopathologic features of SS include a dense, predominantly neutrophilic infiltrate located in the superficial dermis as well as prominent papillary dermal edema, which occasionally may lead to subepidermal vesiculation.^{11,12} The epidermis often is normal but spongiosis may be present, and rarely neutrophils may extend into the epidermis to form subcorneal pustules.¹³ Severe edema in the papillary dermis may cause subepidermal blistering and bullous lesions.¹⁰ Systemic steroids are the therapeutic mainstay in SS. Other treatment options include methylprednisolone, potassium iodide, colchicine, indomethacin, cyclosporine, and dapsone.

Varadraj V. Pai, MD
Gaurang Gupta, MBBS
Sharatchandra Athanikar, MD
Kikkeri Narayanasetty Naveen, MD
Tukaram Sori, MD
Dinesh Shastry, MD

REFERENCES

1. Von den Driesch P. Sweet's syndrome (acute febrile neutrophilic dermatosis). *J Am Acad Dermatol*. 1994;31:535-556.
2. Sweet RD. An acute febrile neutrophilic dermatosis. *Br J Dermatol*. 1964;74:349-356.
3. Su WP, Liu HN. Diagnostic criteria for Sweet's syndrome. *Cutis*. 1986;37:167-174.
4. Cohen PR. Pregnancy-associated Sweet's syndrome: world literature review. *Obstet Gynecol Surv*. 1993;48:584-587.
5. Cohen PR, Hönigsman H, Kurzrock R. Acute febrile neutrophilic dermatosis (Sweet syndrome). In: Wolff K, Goldsmith LA, Katz SI, et al, eds. *Fitzpatrick's Dermatology in General Medicine*. 7th ed. New York, NY: McGraw-Hill; 2008:289-295.
6. Giasuddin AS, El-Orfi AH, Ziu MM, et al. Sweet's syndrome: is the pathogenesis mediated by helper T cell type 1 cytokines? *J Am Acad Dermatol*. 1998;39:940-943.
7. Cohen PR. Sweet's syndrome—a comprehensive review of an acute febrile neutrophilic dermatosis. *Orphanet J Rare Dis*. 2007;2:34.
8. Lund JJ, Stratman EJ, Jose D, et al. Drug-induced bullous Sweet syndrome with multiple autoimmune features. *Autoimmune Dis*. 2010;2011:176749.
9. Bessis D, Dereure O, Peyron JL, et al. Photoinduced Sweet syndrome. *Arch Dermatol*. 2003;137:1106-1108.
10. Bielsa S, Baradad M, Martí RM, et al. Sweet's syndrome with bullous lesions [in Spanish]. *Actas Dermosifiliogr*. 2005;96:315-316.
11. Jordaan HF. Acute febrile neutrophilic dermatosis: a histopathological study of 37 cases and a review of the literature. *Am J Dermatopathol*. 1989;11:99-111.
12. Kemmett D, Hunter JA. Sweet's syndrome: a clinicopathologic review of twenty-nine cases. *J Am Acad Dermatol*. 1990;23(3, pt 1):503-507.
13. Wallach D. Neutrophilic disease [in French]. *Rev Prat*. 1999;49:356-358.