

Chronic idiopathic Sweet syndrome: A report of 2 cases



Asha Gowda, MS,^a Misha A. Rosenbach, MD,^b Robert G. Micheletti, MD,^b and William D. James, MD^b
Toledo, Ohio and Philadelphia, Pennsylvania

Key words: chronic Sweet syndrome; idiopathic Sweet syndrome; neutrophilic dermatoses; Sweet syndrome.

Sweet syndrome (SS) is classified as a neutrophilic dermatosis based on its chief clinicopathologic findings: sudden onset of painful, tender erythematous skin lesions (papules, plaques, and nodules) and a diffuse infiltrate of mature neutrophils in the dermis.^{1,2} The skin eruptions, which most frequently present on the face, neck, trunk, and upper extremities, are generally accompanied by signs of systemic inflammation including pyrexia, malaise, and arthralgia.³

First-line therapy for SS is systemic corticosteroids, which typically yield immediate relief from pyrexia and rapid resolution of skin lesions.³ Alternatives include saturated solution of potassium iodide (SSKI), colchicine, dapsone, indomethacin, sulfapyridine, and tumor necrosis factor antagonists.^{1,3,4}

This report discusses 2 women who had SS for a period longer than expected. There were no factors such as malignancy or SS-inducing medication discovered to be the cause of SS in these patients. Both women responded well to treatment with prednisone; however, skin lesions returned immediately upon attempts to taper the medication. We believe that these cases represent a chronic variant of classical SS, which may be considered in patients who have persistent SS-characteristic skin lesions for over 4 months.

CASE REPORTS

Case 1

A 50-year-old woman presented with a 4-month history of annular and arcuate red papules on her back, neck, chest, arms, and thighs. The patient was afebrile and reported mild pruritus and facial edema. Initially, 2 skin biopsies found neutrophil-rich dermal inflammation consistent with SS. Vasculitis was not seen. Skin lesions regressed with prednisone, but the

Abbreviations used:

MDS: myelodysplastic syndrome
SS: Sweet syndrome
SSKI: saturated solution of potassium iodide

patient experienced severe flares when tapering the medication to less than 40 mg/d (Fig 1). Routine examinations for malignancy, including complete blood counts and serum protein electrophoresis, and autoimmune disease were negative. Outbreaks of SS consisted of fever, annular erythematous patches, or blood-filled bullae. Periodically, she complained of facial edema, hand swelling, and arthralgia. She stopped treatment with prednisone for about 8 months, during which time the patient continued to experience low-grade activity of SS. A biopsy performed during a flare confirmed active SS. Laboratory tests found elevated white blood cells and neutrophils. Such flares were treated with prednisone (40 mg/d). Medical history was notable for pulmonary hyalinizing granuloma, with biapical pleural masses and mediastinal adenopathy. The biopsy specimen showed classic features of this rare disease, with no evidence of malignancy, granulomas, amyloid, or IgG4 staining. This condition has been stable for more than 10 years and has no association with SS. She stopped Dapsone, SSKI, colchicine, and topical steroids because they were ineffective or not tolerated. Currently she is treated with sulfapyridine. After 5 years of follow-up, there is no evidence of malignancy despite a thorough workup.

Case 2

A 73-year-old woman presented for evaluation of a 9-month history of skin eruptions involving her

From the University of Toledo College of Medicine^a and the Department of Dermatology, University of Pennsylvania.^b

Funding sources: None.

Conflicts of interest: None declared.

Correspondence to: William D. James, MD, 2 Maloney Building, 3600 Spruce St, Philadelphia, PA 19104. E-mail: William.james@uphs.upenn.edu.

JAAD Case Reports 2016;2:227-9.

2352-5126

© 2016 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<http://dx.doi.org/10.1016/j.jdc.2016.03.012>



Fig 1. Well-demarcated edematous pink papules on the face and neck. Rare ecchymotic patches at sites of prior lesions are also shown.

trunk, extremities, and face. Physical examination found numerous red macules and plaques, some with a bullous appearance, and scattered hyperpigmented macules. She reported no associated fever. Skin biopsy found neutrophil-rich dermal infiltrate with papillary dermal edema (Fig 2), and SS was diagnosed. Laboratory values for white blood cells and neutrophils were elevated. Persistence of the eruption despite termination of all medications eliminated the possibility of drug-induced Sweet syndrome. The patient had lung cancer diagnosed 5 months after her initial visit and malignant melanoma 19 months later. These diseases could have supported a diagnosis of malignancy-associated Sweet syndrome; however, active SS skin lesions confirmed through skin biopsy persisted even after tumor excision and cancer remission. Intermittent evaluations for malignancy over the ensuing 22 months (lung cancer) and 8 months (melanoma) were negative, as were autoantibody screenings. Serum protein electrophoresis found no evidence of an M-spike. Skin lesions resolved promptly with prednisone. When prednisone was tapered to less than 40 mg/d, the patient flared and had burning skin eruptions with swelling, painful serous-filled bullae, edematous patches and plaques, and vesiculopustules on edematous and erythematous skin. Doxycycline, SSKI, dapsone, colchicine, anakinra, indomethacin, and topical corticosteroids were ineffective or not tolerated. Sulfapyridine was instituted as a steroid-sparing drug, which allowed for tapering of prednisone to 10 mg/d. This combined treatment allowed for low-grade activity of SS with asymptomatic skin lesions. To date, she has been followed up and treated for SS for more than 4 years.

DISCUSSION

Aside from the unusual duration of symptoms, the 2 patients in this report had typical clinical, laboratory, and histopathologic features of SS; responded

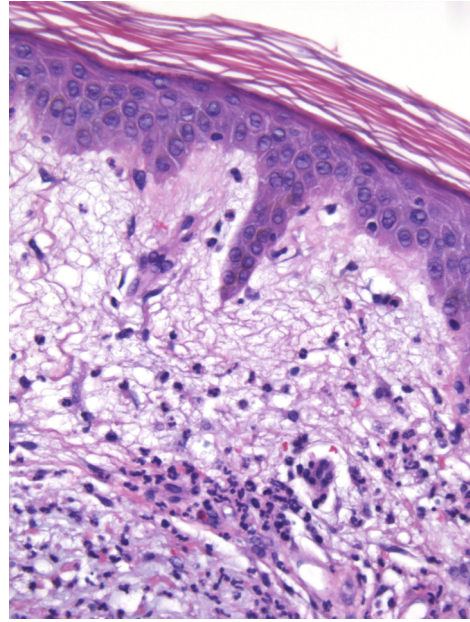


Fig 2. Papillary dermal edema with underlying neutrophilic infiltrate.

rapidly to systemic corticosteroids; and flared off treatment. Generally, SS patients are expected to remit within several weeks of treatment unless there is evidence of an underlying illness or use of disease-associated medication.³ The cases in this report represent chronic SS with no identifiable triggers including connective tissue disease or autoimmune syndromes.

Typically, SS can be explained by cytokine stimulation, either via medications (granulocyte colony-stimulating factor), malignancy (myelodysplastic syndrome [MDS]/leukemia), or postinfection (viral upper respiratory infections or viral gastroenteritis), with resultant immune stimulation.^{3,5,6} Patients with chronic SS may have underlying higher levels of proneutrophil cytokines or chemotaxins that drive neutrophil migration to the skin or may have an aberrant, hyperactive cytokine response to minor skin trauma (ie, pathergy caused by innocuous skin pressure or trauma). However, the mechanism of chronic inflammation remains unclear.

In recent years, there has been mention of patients with chronic SS in whom MDS developed years later.⁷⁻⁹ Initial skin biopsies of those patients were often histologically atypical and found lymphocytic or histiocytoid infiltrates, as opposed to SS-characterizing neutrophilic dermal infiltration. Despite the visualization of myeloperoxidase-positive lymphocytic or histiocytic infiltrates, chronic SS was diagnosed without an underlying cause. It is important to note that these studies explored the

association between chronic SS and subsequent MDS, which was diagnosed up to 13 years after the diagnosis of SS. We have not considered downstream MDS as an explanation for chronic SS in our patients because there was no evidence of histologically atypical skin lesions, and complete blood counts and peripheral smears were normal. Both patients were referred to hematologists for further evaluation, and a bone marrow biopsy was deemed unnecessary.

Chronic SS may present as a lone entity. The women presented in this report continue to be treated for SS more than 4 years after diagnosis. Despite the rapid and complete resolution of skin lesions with prednisone, the medication could not be tapered without the recurrence of severe skin eruptions.

REFERENCES

1. Cohen PR, Kurzrock R. Sweet's syndrome: a review of current treatment options. *Am J Clin Dermatol.* 2002;3(2):117-131.
2. Jindal SR, Kura MM. Classical Sweet's syndrome. *Indian Dermatol Online J.* 2014;5(1):107-108.
3. Cohen PR. Sweet's syndrome-a comprehensive review of an acute febrile neutrophilic dermatosis. *Orphanet J Rare Dis.* 2007;2:34.
4. Weenig RH, Bruce AJ, McEvoy MT, Gibson LE, Davis MD. Neutrophilic dermatosis of the hands: four new cases and review of the literature. *Int J Dermatol.* 2004;43(2):95-102.
5. Alavi A, Sajic D, Cerci FB, Ghazarian D, Rosenbach M, Jorizzo J. Neutrophilic dermatoses: An update. *Am J Clin Dermatol.* 2014; 15(5):413-423.
6. Cohen PR, Kurzrock R. Sweet's Syndrome: a neutrophilic dermatosis classically associated with acute onset and fever. *Clin Dermatol.* 2000;18(3):265-282.
7. Kulasekararaj AG, Kordasti S, Basu T, Salisbury JR, Mufti GJ, du Vivier AW. Chronic relapsing remitting Sweet syndrome: a harbinger of myelodysplastic syndrome. *Br J Haematol.* 2015; 170(5):649-656.
8. Vignon-Pennamen MD, Juillard C, Rybojad M, et al. Chronic recurrent lymphocytic Sweet syndrome as a predictive marker of myelodysplasia: a report of 9 cases. *Arch of Dermatol.* 2006; 142(9):1170-1176.
9. Kakaletsis N, Kaiafa G, Savopoulos C, et al. Initially lymphocytic Sweet's syndrome in male patients with myelodysplasia: a distinguished clinicopathological entity? Case report and systematic review of the literature. *Acta Haematol.* 2014; 132(2):220-225.