Corticosteroid-resistant Sweet syndrome in the setting of acute myeloid leukemia with monosomy 7 and 5q deletion

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INTRODUCTION

Sweet syndrome (SS), otherwise known as acute neutrophilic febrile dermatosis, typically manifests in the fourth or fifth decade of life and is characterized by fever and a cutaneous eruption of painful erythematous and edematous papules, plaques, or nodules. Histopathologically, the cutaneous manifestation is characterized by a predominant neutrophilic dermal infiltrate with associated papillary dermal edema. Three subtypes of SS have been recognized in the literature: classic, malignancy associated and drug induced. The malignancy-associated subtype of SS is most commonly reported in the setting of acute myeloid leukemia (AML) and may precede, coincide, or follow the malignancy. We present an unusually severe case of AML-associated SS, recalcitrant to standard treatment with corticosteroids and with a concomitant, rare genetic mutation.

CASE REPORT

A 52-year-old man with a medical history remarkable for type 2 diabetes presented with a 1-week history of a painful, pruritic facial rash that subsequently spread to the trunk and bilateral upper and lower extremities. The rash continued to progress despite 4 days of methylprednisolone (4 mg) and cephalexin (500 mg) prescribed by his primary care physician for presumed acute folliculitis prior to dermatology referral. Review of systems was remarkable for malaise, fatigue, dizziness, headache, epistaxis, easy bruising, and a 10-pound unintentional weight loss in the previous 2 months. Examination was significant for pink, deep red, and purple edematous nodules and plaques on the scalp, face, trunk, and bilateral upper and lower extremities (Fig 1). The initial differential diagnosis included SS, leukemia cutis, lymphoma, and a disseminated cutaneous bacterial or fungal infection. Punch biopsies for histopathology and tissue cultures were obtained, as were laboratory studies, including a complete blood count with differential. The patient was started on daily oral prednisone (80 mg) and twice-daily triamcinolone ointment (0.1%) for suspected SS while awaiting the laboratory, microbiology, and histopathology results.

Histopathology from 2 punch biopsies of lesions on the left upper arm and shoulder showed papillary dermal edema, with a diffuse neutrophilic infiltrate in the reticular dermis, consistent with SS (Fig 2). Tissue cultures were ultimately negative for bacteria, fungus, and mycobacteria. His initial complete blood count showed pancytopenia; a manual differential found 9% blasts in the peripheral blood. He was referred urgently to the oncology department for suspected myeloid malignancy, and subsequent bone marrow biopsy confirmed a diagnosis of AML. Cytogenetic analysis found a 5q deletion and monosomy 7.

The patient was admitted to the hospital for induction chemotherapy. Upon admission, it was
noted that his rash continued to progress despite 8 total days of oral corticosteroid therapy. Given the lack of response to treatment, he was started on daily colchicine (0.6 mg) and transitioned to daily intravenous methylprednisolone (90 mg) during his hospitalization. His colchicine was increased to 1.2 mg/d for 2 weeks, and he was discharged home on a prednisone taper (reduction by 20 mg every 3-5 days).

Clinical improvement was noticed on day 7 of chemotherapy and week 3 of systemic corticosteroids. His SS showed significant improvement after 32 days of chemotherapy with liposomal daunorubicin and cytarabine (44 mg/m²) and 6 weeks of systemic corticosteroids (Fig 1, B).

DISCUSSION

SS has been reported in 1% of AML cases.5 The mainstay of treatment for SS is a systemic corticosteroid, which in most cases induces a rapid and complete response.4 Other commonly used treatments include topical corticosteroids, colchicine, dapsone, and indomethacin.6 Previously reported cases of AML-associated SS have responded well to standard therapy.3,7 A retrospective study of 77 patients with SS, 35% of whom had an associated malignancy, found complete response after treatment initiation in 82% of patients and partial response in 17% of patients treated with a systemic corticosteroid.4 Our patient provides a rare case of AML-associated SS, resistant to systemic corticosteroid therapy.

Treatment of SS is typically initiated at 1 mg/kg/d of an oral corticosteroid and tapered within 4 to 6 weeks.6 Generally, this regimen leads to remission of general malaise within hours and skin lesions within 2 to 5 days.6 Intravenous corticosteroids may be necessary for refractory cases of SS at a dose of up to 1000 mg/d for 3 to 5 days and concluding with a tapering course of an oral corticosteroid or another immunosuppressant agent.7 The use of colchicine for SS has reportedly been effective in 80% of patients for resolution of fever, skin lesions, and
arthralgia. The typical usage involves a starting dose of 0.5 mg, which can be increased to 1.5 mg/d for 10 to 12 days. The typical response to colchicine therapy is relatively rapid in 2 to 5 days with complete resolution occurring in 1 to 2 weeks.

Our patient’s case is unique for the unusually severe and symptomatic nature of the skin lesions. Ultimately, he required both high-dose intravenous corticosteroids and adjunctive colchicine to halt progression, and his cutaneous lesions began to regress only after a combination of increased intravenous corticosteroids, colchicine, and chemotherapy induction. His underlying AML likely contributed to his severe clinical presentation and delayed systemic steroid response.

The cytogenetic features found in our patient are also unique. Of the few published reports on the genetics of AML-associated SS, the most commonly reported gene mutations are de novo in an active disease state and involve a normal or intermediate karyotype. Our patient’s cytogenetic analysis found karyotype abnormalities constituting a complex cytogenetic profile. AML patients with monosomy 7 have a 10-year overall survival rate of 8% after chemotherapy induction, compared with 38% in those with a normal karyotype. Although the 5q deletion has been reported as a common karyotype abnormality in AML-associated SS, to our knowledge, there are no reports of AML-associated SS patients with concomitant monosomy 7 abnormalities. These adverse cytogenetic features may also have contributed to the severe clinical presentation observed in our patient.

We present this case to serve as a vivid clinical example of severe SS in the setting of AML and as a reminder to clinicians to evaluate for an underlying hematologic malignancy in patients presenting with treatment-resistant SS.

REFERENCES
1. Sweet RD. An acute febrile neutrophilic dermatosis. Br J Dermatol. 1964;76:349-356.
2. Nelson CA, Stephen S, Ashchyan HJ, James WD, Micheletti RG, Rosenbach M. Neutrophilic dermatoses: pathogenesis, Sweet syndrome, neutrophilic eccrine hidradenitis, and Behçet disease. J Am Acad Dermatol. 2018;79(6):987-1006.
3. Nelson CA, Noe MH, McMahon CM, et al. Sweet syndrome in patients with and without malignancy: a retrospective analysis of 83 patients from a tertiary academic referral center. J Am Acad Dermatol. 2018;78(2):303-309.e4.
4. Rochet NM, Chavan RN, Cappel MA, Wada DA, Gibson LE. Sweet syndrome: clinical presentation, associations, and response to treatment in 77 patients. J Am Acad Dermatol. 2013;69(4):557-564.
5. Kazmi SM, Pemmaraju N, Patel KP, et al. Characteristics of Sweet syndrome in patients with acute myeloid leukemia. Clin Lymphoma Myeloma Leuk. 2015;15(6):358-363.
6. Cohen PR. Sweet’s syndrome—a comprehensive review of an acute febrile neutrophilic dermatosis. Orphanet J Rare Dis. 2007:2:34.
7. Zheng S, Li S, Tang S, et al. Insights into the characteristics of Sweet syndrome in patients with and without hematologic malignancy. Front Med (Lausanne). 2020;7:20.
8. Maillard H, Leclech C, Peria P, Avenel-Audran M, Verret JL. Colchicine for Sweet’s syndrome. A study of 20 cases. Br J Dermatol. 1999;140(3):565-566.
9. Amouri M, Masmoudi A, Ammar M, et al. Sweet’s syndrome: a retrospective study of 90 cases from a tertiary care center. Int J Dermatol. 2016;55(9):1033-1039.
10. Grimwade D, Hills RK, Moorman AV, et al. Refinement of cytogenetic classification in acute myeloid leukemia: determination of prognostic significance of rare recurring chromosomal abnormalities among 5876 younger adult patients treated in the United Kingdom Medical Research Council trials. Blood. 2010;116(3):354-365.