

Drug-Induced Sweet Syndrome



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A 38-year-old woman developed malaise, fever, chills, bilateral conjunctivitis, arthralgia, and a dry cough. Two days later, a tender nonpruritic rash characterized by erythematous papules, nodules, and plaques, some with apparent pustules, appeared on the extensor surface of her right arm (Figure 1) and gradually spread over her back (Figure 2) and legs as seen in the images. Seven weeks earlier, she had developed postpartum urinary retention, treated with intermittent self-catheterization and complicated by recurrent urinary tract infections. She received consecutive courses of cephalexin for 5 days, ciprofloxacin for 3

days, and, finally, trimethoprim-sulfamethoxazole (TMP-SMX), which she began 6 days before her symptoms occurred. Her vitals in the emergency room were temperature of 100.6 F (38.1°C), heart rate of 110, respiratory rate of 16 breaths/min, and blood pressure of 112/65 mm Hg. Her laboratory tests were remarkable for leukocytosis ($13.8 \times 10^3/\text{mm}^3$) with 76% neutrophils and 17% band neutrophils. A skin biopsy showed neutrophil-rich pseudobullae formation within the dermis and prominent edema, sparing of the epidermis with subepidermal clefts. TMP-SMX was discontinued; she was started on intravenous



FIGURE 1. Right arm showing erythematous nodules with vesicles.



FIGURE 2. Back showing erythematous macules, papules, and some nodules below the neck.

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methylprednisolone 120 mg and transitioned to oral prednisone, with a 2-week taper on discharge. She responded well to therapy with postinflammatory hyperpigmentation at the site of her erythematous lesions at her 2-week follow-up.

Acute febrile neutrophilic dermatosis, also known as Sweet syndrome (SS), is characterized by fever and painful erythematous papules, nodules, and plaques that can appear anywhere on the skin but typically involve the face, arms, and neck.^{1,2} Vesicles, bullae, and pustules may develop in these lesions. Some patients have extracutaneous findings, including conjunctivitis, arthralgia, and cough. SS has been typically classified into 3 categories: (1) classical SS, (2) malignancy-associated SS, and (3) drug-induced SS. About 80% of cases of classical SS occur in women, and the frequency is about 70%, 60%, and 50% in those associated with drugs, solid tumors, and hematologic malignancies, respectively. Multiple drugs may contribute to SS,^{1,2} with TMP-SMX as a frequently reported culprit.^{1,2} The interval between initial drug exposure and the onset of SS varies from days to months,¹ but most cases develop within 2 weeks.

A diagnosis of drug-induced SS entails all of the following criteria^{1,2} being met:

1. Abrupt onset of painful erythematous plaques or nodules.
2. Histopathologic evidence of dense neutrophilic infiltration of the dermis without evidence of leukocytoclastic vasculitis.
3. Fever ($>38^{\circ}\text{C}$).
4. Temporal relation between drug ingestion and onset of symptoms.

5. Resolution of symptoms after drug withdrawal or treatment with systemic steroids.

Peripheral leukocytosis with neutrophilia is a common laboratory finding. Characteristic histological findings demonstrate prominent edema in the superficial dermis, with dense neutrophil infiltrate in the dermis and the upper epidermis.

The clinical differential diagnosis of SS tends to vary with the lesion morphology. It is important to rule out infections because the clinical findings of fever, leukocytosis, and cutaneous lesions characterized by neutrophil-dense infiltrates can resemble bacterial sepsis. The erythematous and edematous lesions of SS can resemble bacterial, fungal, and atypical mycobacterial infections; special staining (eg, Gram stains/periodic acid–Schiff) of the skin biopsy can help differentiate from drug-induced SS. Other differentials such as malignancy, vasculitis, or drug eruptions must be taken under consideration in the proper clinical context of the patient. In this patient, the temporal onset of symptoms with drug ingestion and rapid improvement after drug discontinuation made alternate diagnoses unlikely.

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