Pruritic postoperative eruption

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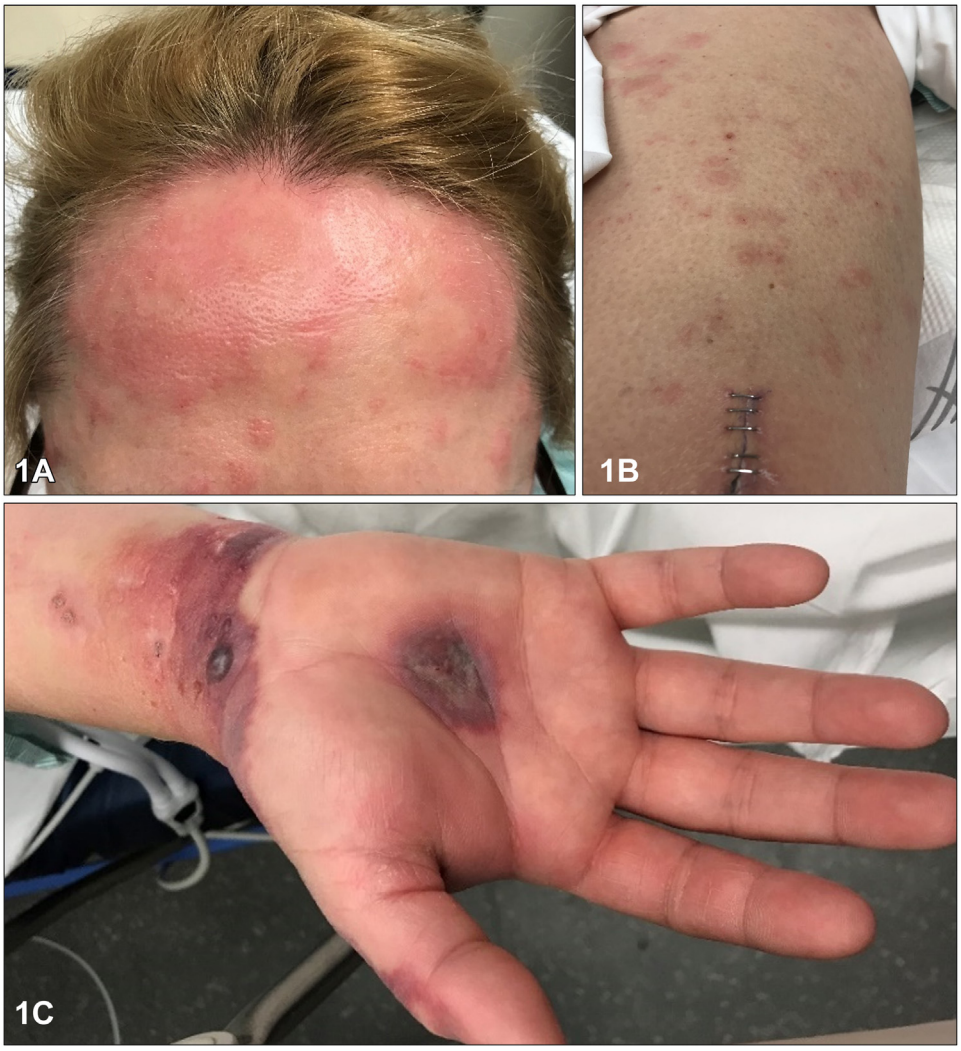

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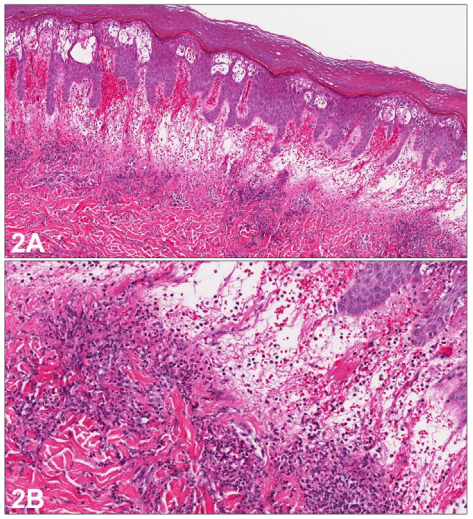

HISTORY

A 50-year-old woman presented 11 days following total knee arthroplasty with a 2-day history of an intensely pruritic rash and a reported fever of 38.3 °C. Postoperative medications included hydrocodone/acetaminophen and celecoxib. Dermatologic examination revealed a purpuric plaque with an overlying bulla on the right ventral wrist and a targetoid plaque on the right palm. Pink, edematous papules and plaques, some targetoid in appearance, were present diffusely (Fig 1, *A*–*C*). The surgical incision site showed no signs of infection. No mucosal lesions were noted. Labs revealed a leukocyte count of 13,800/μL (86% neutrophils). Histopathology showed marked papillary dermal edema with dense neutrophilic infiltrate (Fig 2, *A* and *B*).

Question 1: Which of the following is the mostly likely diagnosis?

A. Linear IgA bullous dermatosis (LABD)

B. Morbilliform drug eruption

C. Acute urticaria

D. Sweet syndrome

E. Stevens-Johnson syndrome (SJS)

Answers:

A. LABD — Incorrect. LABD typically presents with tense vesicles and bullae and may be intensely pruritic. However, fever and leukocytosis would be unusual.

B. Morbilliform drug eruption — Incorrect. Morbilliform drug eruptions may be pruritic but are not typically edematous and do not blister.

C. Acute urticaria — Incorrect. Pink, pruritic, edematous papules and plaques may raise concern for acute urticaria. However, wheals of urticaria are evanescent, lasting less than 24 hours, and do not blister or become purpuric as occurred on this patient's wrist.

D. Sweet syndrome — Correct. Sweet syndrome, or acute febrile neutrophilic dermatosis, is an inflammatory skin disorder characterized by the abrupt eruption of painful and edematous papules, plaques, and nodules. Lesions are typically erythematous or violaceous and accompanied by fever and leukocytosis. Bullous or targetoid lesions may be present. Three etiologic subtypes have been described: classical (idiopathic), malignancy-associated, and drug-induced. Our patient met all criteria for drug-induced Sweet syndrome: abrupt onset of characteristic lesions, histopathologic evidence of a dense neutrophilic infiltrate with minimal to no evidence of vasculitis, pyrexia >38 °C, temporal relationship between drug exposure and onset, and temporal relationship between treatment and resolution.[1] This case is remarkable in that the patient's primary complaint was pruritus rather than tenderness or a burning sensation. Notably, 1 retrospective study of 77 patients with Sweet syndrome reported pruritus in 18% of cases.[2]

E. SJS — Incorrect. The emergency physician initially raised concern for SJS. However, the majority of this patient's lesions were pink, edematous papules and plaques with notable involvement of the head and upper extremities, typical of Sweet syndrome. There was no mucosal involvement as is typical of SJS.

Question 2: What is the best next step in the management of this patient?

A. Oral prednisone

B. Supportive care

C. Oral antihistamines and reassurance

D. Topical antibiotics

E. Methotrexate

Answers:

A. Oral prednisone — Correct. Corticosteroids are the first-line therapeutic option in the management of Sweet syndrome, with most patients showing rapid clinical response. In fact, improvement with systemic corticosteroids is included in the diagnostic criteria for Sweet syndrome.[1] Topical or intralesional corticosteroids may be considered in patients with localized disease. Alternative first-line therapeutic options include colchicine, dapsone, and potassium iodide. Our patient showed rapid improvement with 60 mg daily of oral prednisone, with near-complete resolution of her rash and pruritus at 2-week follow-up.

B. Supportive care — Incorrect. Supportive care is the mainstay of management for Stevens-Johnson syndrome, but pharmacologic therapy is indicated in the treatment of Sweet syndrome.

C. Oral antihistamines and reassurance — Incorrect. Although drug-induced Sweet syndrome may improve following discontinuation of the offending medication, antihistamines and reassurance alone would not be appropriate. Oral antihistamines may be used for symptomatic relief, but further pharmacologic therapy is indicated.

D. Topical antibiotics — Incorrect. Postoperative infection and bacterial sepsis are important initial considerations in the differential diagnosis of this patient with fever, rash, and leukocytosis following surgery. Empiric intravenous vancomycin and cefepime were administered until the correct diagnosis of Sweet syndrome was established. In this situation of a systemic illness, topical antibiotic therapy is not indicated.

E. Methotrexate — Incorrect. Methotrexate has been used with success in refractory cases of Sweet syndrome. However, it is not a first-line treatment option.

Question 3: Which medication is most commonly associated with drug-induced Sweet syndrome?

A. Hydrocodone

B. Granulocyte colony-stimulating factor

C. Trimethoprim-sulfamethoxazole

D. Ipilimumab

E. Celecoxib

Answers:

A. Hydrocodone — Incorrect. Based on timing, hydrocodone/acetaminophen was initially considered as a potential offending agent in this case. However, literature review identified only 1 case of a narcotic/acetaminophen combination, specifically codeine/acetaminophen, triggering Sweet syndrome. Hydrocodone has not been reported to cause Sweet syndrome. For this reason and because our patient had tolerated hydrocodone/acetaminophen on multiple occasions in the past, celecoxib was the suspected trigger in this case. The patient did receive a one-time intraoperative dose of cefazolin, which was deemed a highly unlikely trigger given that the patient had previously tolerated cephalosporins on multiple occasions, the eruption occurred 9 days following cessation of the drug, and cephalosporins have not been implicated in drug-induced Sweet syndrome. Finally, the patient's daily medication regimen consisted of diclofenac, diphenhydramine, montelukast, and tramadol. Given their chronicity, these were less likely than a newly initiated medication to be the perpetrator.

B. Granulocyte colony-stimulating factor — Correct. Granulocyte colony-stimulating factor has been reported to cause cutaneous vasculitis and neutrophilic dermatoses, and it is the most widely reported trigger of drug-induced Sweet syndrome.

C. Trimethoprim-sulfamethoxazole — Incorrect. Trimethoprim-sulfamethoxazole has been implicated in drug-induced Sweet syndrome, but it is not the leading cause.

D. Ipilimumab — Incorrect. Checkpoint inhibitors such as ipilimumab have been associated with various adverse cutaneous reactions including Sweet syndrome, but they are not the most common cause of drug-induced Sweet syndrome.

E. Celecoxib — Incorrect. Though this patient was diagnosed with celecoxib-induced Sweet syndrome, celecoxib has only rarely been implicated in drug-induced Sweet syndrome.[2-5]

Abbreviations used:

LABD: linear IgA bullous dermatosis
SJS: Stevens-Johnson syndrome

Conflicts of interest

None disclosed.

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