CASE REPORT

THE PATIENT
40-year-old woman

SIGNS & SYMPTOMS
– Fever
– Rash
– Arthralgia

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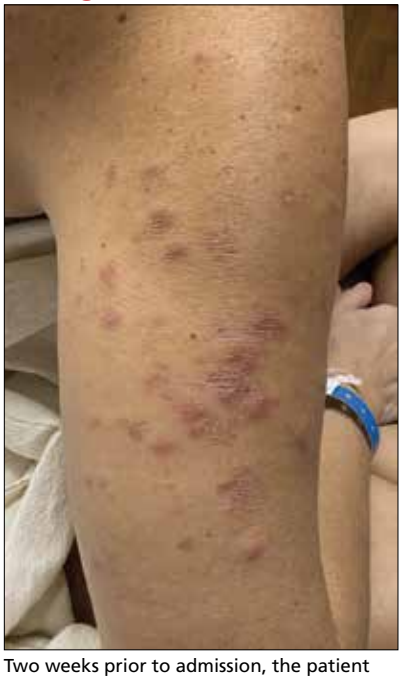
THE CASE

A 40-year-old woman with no significant medical history sought care at the emergency department for a fever, rash, and arthralgia. On admission, she had worsening bilateral ankle pain and was having difficulty walking. During the previous 3 months, she'd had 3 episodes of tonsillitis, all of which were presumed to be caused by *Streptococcus,* although no swabs were obtained. Her primary care physician treated her with antibiotics each time: 1 round of amoxicillin 500 mg twice daily for 10 days and 2 rounds of amoxicillin/clavulanate 875 mg twice daily for 7 to 10 days. During the previous month, she'd experienced intermittent fevers ranging from 100.2 °F to 100.8 °F, with no distinct pattern.

The patient said that 2 weeks prior to her admission to the hospital, she'd developed a rash on her right arm, which was papular, nondraining, nonpruritic, and not painful (**FIGURE 1**). Six days later, the rash spread to her left arm, chest, and back, with a few lesions on her legs (**FIGURE 2**). A few days later, she developed arthralgias in her hips, knees, and ankles. These were associated with the appearance of large, flat, erythematous lesions on her anterior lower extremities (**FIGURE 2**). About 5 days before she was admitted to our hospital, the patient was seen at another hospital and treated for possible cellulitis with cephalexin (500 mg 4 times daily for 5-7 days), but her symptoms persisted.

At this point, she sought care at our hospital for her worsening lower extremity arthralgia, difficulty walking, and the persistent rash. An initial lab report showed a white blood cell (WBC) count of 12.6 × 10^3/μL (normal range, 4.0-10.0 × 10^3/μL) with an absolute neutrophil count of 9.7 × 10^3/μL (normal, 1.7-7.0 × 10^3/μL). Her C-reactive protein (CRP) level was elevated (194.7 mg/L; normal, 0.0-5.0 mg/L), as was her erythrocyte sedimentation rate (ESR) (102.0 mm/h; normal, 0.0-20.0 mm/h). A rapid pharyngeal strep test was negative. Her anti-streptolysin O (ASO) titer was elevated (2092.0 IU/mL; normal, < 250.0 IU/mL), and her rheumatic factor was mildly elevated (19.0 IU/mL; normal, 0.0-14.0 IU/mL). An antinuclear antibody panel was positive at 1:80. Further testing was performed, and the patient was found to be negative for Sjögren syndrome A, Sjögren syndrome B, anti-Smith, scleroderma-70, double-stranded DNA, and chromatin AB—making an autoimmune disease unlikely.

FIGURE 1
Initial lesions on right arm



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Two weeks prior to admission, the patient developed a papular, nondraining, nonpruritic rash that was not painful.

THE DIAGNOSIS

The patient met the American Heart Association's revised Jones criteria for the diagnosis of rheumatic fever: She had a positive ASO titer; polyarthritis and subcutaneous nodules (2 major criteria); and ESR > 60 mm/h and CRP > 3 mg/L (1 minor criterion).[1] She started taking naproxen 500 mg twice per day and was given a penicillin G 1.5-million-unit injection. A transthoracic echocardiogram also was performed during her admission to rule out endocarditis; no abnormalities were found.

A few days after starting treatment for rheumatic fever, the patient's WBC count returned to within normal limits and her joint swelling and pain improved; however, her rash did not go away, leading us to wonder if there was a second disease at work. Dermatology was consulted, and a punch biopsy was obtained. The results showed acute febrile neutrophilic dermatosis, or *Sweet syndrome*.

DISCUSSION

Sweet syndrome is considered rare, and incidence numbers are elusive.[2] It has a worldwide distribution and no racial bias.[3] Sweet syndrome usually occurs in women ages 30 to 50 years, although it may also occur in younger adults and children.[3] The differential diagnosis for Sweet syndrome is broad and includes infectious and inflammatory disorders, neoplastic conditions, reactive erythemas, vasculitis, other cutaneous conditions, and other systemic diseases.[3]

Three subtypes have been defined based on etiology: (1) classical (or idiopathic) Sweet syndrome; (2) malignancy-associated Sweet syndrome, which is most often related to acute myelogenous leukemia; and (3) drug-induced Sweet syndrome, which is usually associated with granulocyte colony–stimulating factor treatment.[4] Our patient had the most common subtype: classical Sweet syndrome.

What you'll see. Classical Sweet syndrome usually develops approximately 1 to 3 weeks after an infection—usually an upper respiratory tract or gastrointestinal infection.[5] It may also be associated with inflammatory bowel disease or pregnancy.[5] Potential symptoms include pyrexia; elevated neutrophil count; papules, nodules, or plaques; and a diffuse infiltrate of predominantly mature neutrophils located in the upper dermis.[1,5]

FIGURE 2
Rash spread to the patient's left arm, back, and ankle

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Corticosteroid therapy is the gold standard for treatment of classical Sweet syndrome. Dosing usually starts with prednisone 1 mg/kg/d, which can be tapered to 10 mg/d within 4 to 6 weeks.[5] If steroid treatment is contraindicated in the patient, alternative treatments are colchicine 0.5 mg 3 times daily for 10 to 21 days or enteric-coated potassium iodide 300 mg 3 times daily until the rash subsides.[5] Without treatment, symptoms may resolve within weeks to months; with treatment, the rash usually resolves within 2 to 5 days. Some resistant forms may require 2 to 3 months of treatment.

There is a risk of recurrence in approximately one-third of patients after successful treatment of classical Sweet syndrome.[5] Recurrence can be caused by another inciting factor (ie, irritable bowel disease, upper respiratory tract infection, malignancy, or a new medication), making a new investigation necessary. However, treatment would entail the same medications.[5]

CONTINUED

The patient was placed on penicillin V 250 mg twice daily for 5 years due to the significant risk of carditis in the setting of rheumatic fever. She started an oral steroid regimen of a prednisone weekly taper, starting with 60 mg/d, for 4 to 6 weeks. Her papular rash improved soon after initiation of steroid therapy.

THE TAKEAWAY

On presentation, this patient's symptoms met the Jones criteria for rheumatic fever, but she did not respond to treatment. This led us to revisit her case, order additional tests, and identify a second diagnosis—Sweet syndrome—that responded positively to treatment. This case is a reminder that sometimes the signs and symptoms we are looking at are the result of 2 underlying illnesses, with 1 possibly triggering the other. That was likely what occurred in this case. JFP

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REFERENCES

1. Gewitz MH, Baltimore SR, Tani LY, et al. Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of doppler echocardiography: a scientific statement from the American Heart Association. *Circulation*. 2015;131:1806-1818. doi: 10.1161/CIR.0000000000000205
2. Joshi TP, Friske SK, Hsiou DA, Duvic M. New practical aspects of Sweet syndrome. *Am J Clin Dermatol*. 2022;23:301-318. doi: 10.1007/s40257-022-00673-4
3. Cohen PR, Kurzrock R. Sweets syndrome revisited: a review of disease concepts. *Int J Dermatol*. 2003;42:761-778. doi: 10.1046/j.1365-4362.2003.01891.x
4. Merola JF. Sweet syndrome (acute febrile neutrophilic dermatosis): pathogenesis, clinical manifestations, and diagnosis. UpToDate. August 9, 2020. Accessed October 27, 2022. www.uptodate.com/contents/sweet-syndrome-acute-febrile-neutrophilic-dermatosis-pathogenesis-clinical-manifestations-and-diagnosis
5. Cohen PR. Sweets syndrome—a comprehensive review of an acute febrile neutrophilic dermatosis. *Orphanet J Rare Dis*. 2007;2:34. doi: 10.1186/1750-1172-2-34

PRACTICE ALERT

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pression, anxiety, and suicide risk in adults: a systematic evidence review for the US Preventive Services Task Force. Accessed November 22, 2022. www.uspreventiveservicestaskforce.org/home/getfilebytoken/dpG5pjV5yCew8fXvctFJNK
8. Sapra A, Bhandari P, Sharma S, et al. Using Generalized Anxiety Disorder-2 (GAD-2) and GAD-7 in a primary care setting. *Cureus*. 2020;12:e8224. doi: 10.7759/cureus.8224
9. Spitzer RL, Kroenke K, Williams JBW, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166:1092-1097. doi: 10.1001/archinte.166.10.1092
10. Viswanathan M, Wallace IF, Middleton JC, et al. Screening for anxiety in children and adolescents: evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2022;328:1445-1455. doi: 10.1001/jama.2022.16303
11. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care*. 2003;41:1284-1292. doi: 10.1097/01.MLR.0000093487.78664.3C
12. Viswanathan M, Wallace IF, Middleton JC, et al. Screening for depression and suicide risk in children and adolescents: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2022;328:1543-1556. doi:10.1001/jama.2022.16310