A 69-year-old female with a past medical history of hypothyroidism presented to dermatology for evaluation of a one-month history of multiple, painful, erythematous plaques on her right dorsal hand and bilateral lower extremities. The patient previously failed oral doxycycline and oral terbinafine, and had multiple inconclusive biopsies suggestive of a neutrophilic dermatosis. In our clinic, the patient denied any history of inflammatory bowel disease, constitutional symptoms, weight loss, abdominal pain, cough, or diarrhea. Laboratory studies revealed an elevated erythrocyte sedimentation rate (ESR) of 47, elevated C-reactive protein (CRP) of 3.2, a positive QuantiFERON gold test, and a mild anemia with a hemoglobin of 11.0. All other labs, including an autoimmune workup, were normal or negative.

Physical exam was significant for a large, annular, erythematous plaque and a few nearby erythematous and edematous papules on the hand (Figure 1A) along with multiple indurated, erythematous plaques and nodules on her bilateral lower legs (Figure 1B-D). The lesions were all extremely tender to the touch.

The patient underwent incisional biop-
sies of one of the erythematous, indurated nodules on her right lower leg. The biopsies were sent for hematoxylin and eosin (H&E) stain, direct immunofluorescence (DIF), and tissue culture. The patient was then started on topical triamcinolone 0.1% ointment twice daily and was referred for the evaluation and treatment of her newly diagnosed latent tuberculosis (TB) and for an age appropriate malignancy screening work-up.

Histopathology revealed a neutrophilic dermatosis and leukocytoclastic vasculitis (LCV) with an uninvolved epidermis and underlying subcutaneous fat containing scattered mononuclear cells. DIF was negative and nonspecific for any immunologic process. Tissue culture was negative for growth of any organisms. The leading differential diagnosis at this time included atypical Sweet syndrome (given the atypical finding of LCV on pathology). The patient was then started on a prednisone taper, which consisted of 60mg/day for one week, followed by 40mg/day for the second week and 20mg/day for the third week, and a slower taper of 10mg/day for 10 days after that, with a very good response. One month later her lesions were almost completely resolved, with only mild to moderate erythema remaining at the previously involved locations.

DISCUSSION

We present this case as an atypical presentation of Sweet syndrome in the context of latent tuberculosis. Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is an inflammatory skin condition that presents with tender, erythematous to violaceous papules, plaques, or nodules with a neutrophilic infiltrate in the upper dermis. These lesions occur most often on the arms in an asymmetrical distribution, but can also occur on the face, neck, trunk, and legs.1 SS most commonly affects middle-aged women and is often associated with fever and neutrophilia.2 Fever is often the most common extra-cutaneous manifestation and can present prior to or during the onset of cutaneous lesions. SS can cause neutrophilic infiltration into almost any part of the body, which can lead to extracutaneous manifestations in any organ system. Aside from fever, the most common extracutaneous manifestations occur in the lungs, causing symptoms ranging from mild dyspnea to respiratory failure and, in the eyes, causing inflammation of various ocular structures.1 Histopathology of the cutaneous lesions demonstrates a dense, mature, neutrophilic infiltrate in the upper dermis, classically without evidence of LCV. Occasionally, the neutrophilic infiltrate can extend into the subcutaneous fat and lead to panniculitis.1,2

The workup for SS starts with a detailed history and physical examination to help elucidate a possible underlying cause such as an infection, a medication, or a malignancy. A comprehensive laboratory evaluation should be performed, including a complete blood count (CBC) with differential, ESR, CRP, comprehensive metabolic panel (CMP), urinalysis, and other laboratory tests, such as thyroid function tests and rheumatoid factor to rule out common autoimmune diseases. If the cutaneous manifestations raise suspicion for SS, a tissue biopsy should be performed with H&E and tissue culture.1,3 It is imperative to carry out proper malignancy

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Minor Criteria</th>
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<tbody>
<tr>
<td>Acute, sudden onset of tender, erythematous plaques, nodules, or papules</td>
<td>Fever &gt;38 degrees Celsius</td>
</tr>
<tr>
<td>Histopathological evidence of a dense neutrophilic infiltrate in the upper dermis without evidence of leukocytoclastic vasculitis</td>
<td>Association with a malignancy, inflammatory bowel disease, infection, vaccination, or pregnancy</td>
</tr>
<tr>
<td>Excellent response to treatment with corticosteroids</td>
<td>Three out of four laboratory abnormalities including ESR &gt;200, elevated CRP, leukocytosis &gt;800, and neutrophilia &gt;70%</td>
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Criteria for Drug-induced SS

<table>
<thead>
<tr>
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<th>Minor Criteria</th>
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<tbody>
<tr>
<td>Acute, sudden onset of tender, erythematous plaques, papules, or nodules</td>
<td>Histopathological evidence of a dense neutrophilic infiltrate in the upper dermis without evidence of leukocytoclastic vasculitis</td>
</tr>
<tr>
<td>Fever &gt;38 degrees Celsius</td>
<td>Temporal relationship between the start of a medication and symptom onset</td>
</tr>
<tr>
<td>Disappearance of cutaneous lesions after discontinuation of offending drug or treatment with corticosteroids.</td>
<td>Excellent response to treatment with corticosteroids</td>
</tr>
</tbody>
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**TABLE 1: DIAGNOSTIC CRITERIA FOR SWEET SYNDROME.**

*Major and Minor Criteria Listed Are for Both Classical and Malignancy-Associated SS*.1,4

screening in any patient suspected to have SS. This starts with a detailed past medical history, as well as physical exam of the thyroid, lymph nodes, oral cavity, breasts, and a digital rectal exam, prostate exam, or pelvic exam if necessary.\(^1,2\)

The importance of a full malignancy workup was emphasized to our patient, especially in the context of her anemia and history of melena.

The diagnostic criteria for Sweet syndrome includes both major and minor criteria (Table 1). To diagnose classical Sweet syndrome, a patient must have both of the major criteria, along with two of the minor criteria to establish a diagnosis. In malignancy-associated Sweet syndrome, the presentation must have a temporal relationship or association with a known malignancy. All five diagnostic criteria must be present in order to make a diagnosis of drug-induced SS.\(^1,2,4\)

Many patients with SS may have spontaneous remission, but oftentimes initiation of treatment is necessary to reduce the chance of relapse. For patients with malignancy-associated or drug-induced SS, treatment of the underlying cause by treating the malignancy or removing the offending drug, respectively, will usually lead to resolution of cutaneous lesions.\(^1\) When treatment is initiated, the gold-standard treatment for SS is systemic corticosteroids.\(^1,3,5,6\) It is recommended to start patients on oral prednisone 0.5-1mg/kg/day, and taper the dose over a four to six week period. Both systemic and cutaneous manifestations tend to show rapid improvement over the first 24-72 hours of

**Table 2: Treatments for Sweet Syndrome Included in Reviews and Case Reports**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing</th>
<th>Duration</th>
<th>Indication</th>
</tr>
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<tbody>
<tr>
<td>Prednisone(^1,3,5,6)</td>
<td>Prednisone 0.5-1mg/kg/day</td>
<td>Four- to six-week taper, may require two to three months of therapy if relapse</td>
<td>First line</td>
</tr>
<tr>
<td>Methylprednisolone IV(^1,3,5,6)</td>
<td>1000mg/day pulse dosing over a 1-hour time frame</td>
<td>Three to five days, often requiring an oral prednisone taper afterwards(^1)</td>
<td>Lesions refractory to oral prednisone. Patients who receive this treatment will need oral steroid taper following IV treatment.</td>
</tr>
</tbody>
</table>
| Local corticosteroids\(^1,3,5,6\) | Topical clobetasol propionate 0.05% cream, ointment, gel\(^1\)  
Intralesional triamcinolone acetate 3mg/ml-10mg/ml\(^1\) | Adjunct therapy as needed                                   | Localized Sweet syndrome or an adjunct to systemic corticosteroids |
| Colchicine\(^1,6\)     | 0.5mg orally TID\(^1\)  
1-2mg orally TID\(^2,5,6\) | 10-21 days\(^1\)                                   | First-line steroid-sparing therapy or combination with steroids |
| Potassium Iodide\(^1,5,6\) | 300mg enteric-coated tablet TID (900mg total)\(^2,6\)  
1g/ml solution three drops TID\(^1\) | 10-14 days                                            | First-line steroid-sparing therapy |
| Dapsone\(^1,3,6\)      | 100mg/day-200mg/day orally                  | 10-21 days                                           | Second-line, monotherapy or combination therapy |
| Indomethacin\(^1,3,6\) | 100-150mg/day\(^12\)  
50-100mg/day\(^2,6\) | 150mg for 7 days, followed by 100mg for 14 days\(^1,5,6\) | Second-line therapy |
| Cyclosporine\(^1,3,6\) | 2-10mg/kg/day                                | 21 days\(^1\)                                         | Second-line therapy: used as monotherapy or steroid-sparing agent. Patients with underlying autoimmune disease including rheumatoid arthritis or IBD\(^1\) |
| Clofazimine\(^1,2,6\)  | 100-200mg oral daily                         | 200mg for four weeks followed by 100mg for four weeks | Second-line therapy |
| TNF-alpha inhibitors: Etanercept, infliximab, adalimumab\(^1\) | 100-200mg oral daily | 200mg for four weeks followed by 100mg for four weeks | Can be considered in patients with underlying autoimmune conditions |
The patient was given topical isoniazid due to experiencing nausea, 3.75% isoniazid ointment BID, 300mg TID. Ten patients with erythema induratum were treated with potassium iodide. Duration Three patients with refractory idiopathic erythema induratum were treated with potassium iodide 300mg TID for 10-14 days. Seven out of 10 of these patients achieved complete remission in 14 days.

Topical isoniazid was given to one patient due to experiencing nausea, vomiting, and thrombocytopenia with oral isoniazid and rifampicin. This treatment resulted in complete resolution of symptoms in six months with no relapses.

Several studies have shown colchicine and potassium iodide (KI) to be effective first-line steroid-sparing agents in the treatment of SS. Colchicine has been shown to be effective at 1-2mg/day, often given for a total of 10-21 days, and can lead to improvement of cutaneous lesions and systemic symptoms in just one to two days. High potency topical or intralesional corticosteroids can also be used for localized lesions or as an adjunct treatment to systemic corticosteroid therapy.

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Severe cases are refractory to first-line medications and include dapsone, indomethacin, cyclosporine, clofazimine, and tumor necrosis factor (TNF)-alpha inhibitors. This regimen can lead to systemic symptom resolution in one to two days, and resolution of cutaneous lesions within one week. Table 2 includes other second-line therapies for SS refractory to first-line medications and includes dapsone, indomethacin, cyclosporine, clofazimine, and tumor necrosis factor (TNF)-alpha inhibitors. This regimen can lead to systemic symptom resolution in one to two days, and resolution of cutaneous lesions within one week. Table 2 includes other second-line therapies for SS refractory to first-line medications and includes dapsone, indomethacin, cyclosporine, clofazimine, and tumor necrosis factor (TNF)-alpha inhibitors.

Because of the patient’s diagnosis of latent tuberculosis, prior to the availability of the pathology results, erythema induratum (EI) was also high on our differential diagnosis. Erythema induratum is believed to be cutaneous hypersensitivity reaction to mycobacterium tuberculosis (MTB). EI usually presents as tender, erythematous to violaceous nodules or plaques on the posterior or anterolateral lower legs and can appear on other parts of the body, such as the hands, feet, arms, and buttocks. As the lesions progress, they can eventually ulcerate, desquamate, and form an overlying crust, which will often heal with scarring and post-inflammatory hyperpigmentation. Histopathology of these cutaneous lesions will show diffuse lobular panniculitis, often with neutrophilic vasculitis of the nearby vessels. Coagulative or caseous necrosis can also be present with associated granuloma formation. Lobular panniculitis is considered to be the main diagnostic finding, and other histological findings can be present to varying degrees and are not necessary to make a diagnosis of EI.

Although EI has a strong association with TB, mycobacteria cannot be cultured from cutaneous lesions. However, it is possible to detect mycobacterium tuberculosis within cutaneous lesions via DNA polymerase chain reaction (PCR). While this can be helpful in pointing towards a diagnosis of EI, DNA PCR is not always successful in revealing mycobacterium tuberculosis DNA, suggesting that TB may not be the only cause. Other suggested infectious causes include Nocardia and Pseudomonas species, and Hepatitis B and C. EI may also have an association with non-infectious diseases such as hypothyroidism, rheumatoid arthritis, leukemia, and Crohn’s disease.

Similar to SS, the workup for EI starts with a comprehensive history and physical examination. For suspicious lesions, an excisional biopsy should be performed down to the subcutaneous fat and be sent for H&E stain, fungal, bacterial, and mycobacteria cultures, as well as PCR for MTB DNA. A full workup should be performed to evaluate the patient for an underlying TB infection including obtaining a QuantiFERON gold test or purified protein derivative test, and if positive, a chest x-ray or other imaging. The treatment of erythema induratum is aimed at treating the underlying cause, which is often an underlying TB infection. Table 3 includes other reported treatments for EI that can be used as adjuncts to systemic anti-tuberculosis treatment.

Although erythema induratum was a diagnostic consider-
(Continued from page 32) 

ation in our patient in the setting of a positive QuantiFERON gold test, our patient’s histopathology findings did not fit the criteria for diagnosis. Based on the diagnostic criteria for both SS and EI, our patient more closely fits the picture for SS. While she did have the classic cutaneous manifestations and neutrophilic dermal infiltrate seen in SS, her histopathology demonstrated a presence of LCV, which prevents her from fulfilling both major criteria. While the current criteria call for the absence of LCV, others have proposed that one should not rule out SS solely based on the presence of LCV. Amouri et al. performed a retrospective case study in 90 patients with SS and found that 8.8 percent of these patients had the presence of LCV on histopathology. It is thought that the presence of vasculitis on histology in conjunction with SS is secondary to toxic products released from the dense neutrophilic infiltrate, leading to vascular endothelial damage. This has been supported by the lack of immune complex deposition in these damaged vessels, indicating the lack of a primary vasculitis process, and rather suggesting a secondary process due to toxin-mediated damage. Considering this patient’s pathology and laboratory data, we diagnosed her with atypical SS with an incidental finding of latent TB. Our case highlights the complexity of this diagnosis, including its management and workup, especially when pathology findings are atypical and demonstrate LCV.

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