

# Nonscaly Red-Brown Macules on the Feet and Ankles

Jordan E. Lamb, MD; Lauryn M. Falcone, MD, PhD; Katherine Burke, MD; Mehreen Elahee, MD; Magdalena H. Harasimowicz, MD; Tissa Bijoy George, MD; Jonhan Ho, MD, MS; Alaina J. James, MD, PhD



A 59-year-old man presented with a nontender nonpruritic rash on the feet of 2 days' duration. The patient had a several-year history of granulomatosis with polyangiitis (GPA) and was taking methotrexate and prednisone. The rash appeared suddenly—first on the right foot and then on the left foot—and was preceded by 1 week of worsening polyarthralgia, most notably in the ankles. He denied any fever, chills, sore throat, or weight loss. His typical GPA symptoms included inflammatory arthritis, scleritis, leukocytoclastic vasculitis, and sinonasal and renal involvement. He recently experienced exacerbation of inflammatory arthritis that required an increase in the prednisone dosage (from 40 mg to 60 mg daily), but there were no other GPA symptoms. He had a history of multiple female sexual partners but no known history of HIV and no recent testing for

sexually transmitted infections. Hepatitis C antibody testing performed 5 years earlier was nonreactive. He denied any illicit drug use, recent travel, sick contacts, or new medications.

Dermatologic examination revealed nonscaly, clustered, red-brown macules, some with central clearing, on the medial and lateral aspects of the feet and ankles with a few faint copper-colored macules on the palms and soles. The ankles had full range of motion with no edema or effusion. There were no oral or genital lesions. The remainder of the skin examination was normal. Punch biopsies of skin on the left foot were obtained for histopathology and direct immunofluorescence.

## WHAT'S YOUR DIAGNOSIS?

- annular lichen planus
- leukocytoclastic vasculitis
- progressive pigmentary purpura (Schamberg disease)
- purpura annularis telangiectodes (Majocchi disease)
- secondary syphilis

PLEASE TURN TO **PAGE E15** FOR THE DIAGNOSIS

Jordan E. Lamb is from the University of Pittsburgh School of Medicine, Pennsylvania. Drs. Falcone, Burke, Elahee, Harasimowicz, Ho, and James are from the University of Pittsburgh Medical Center, Pennsylvania. Drs. Falcone and James are from the Department of Dermatology; Drs. Burke and Ho are from the Department of Dermatology, Division of Dermatopathology; and Drs. Elahee and Harasimowicz are from the Department of Medicine, Division of Rheumatology and Clinical Immunology. Dr. George is from the Department of Internal Medicine, University of Pittsburgh Medical Center, McKeesport, Pennsylvania.

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Correspondence: Jordan E. Lamb, MD, University of Pittsburgh School of Medicine, 3550 Terrace St, Pittsburgh, PA 15213 (jel199@pitt.edu). *Cutis*. 2024 September;114(2):E14-E16. doi:10.12788/cutis.1102

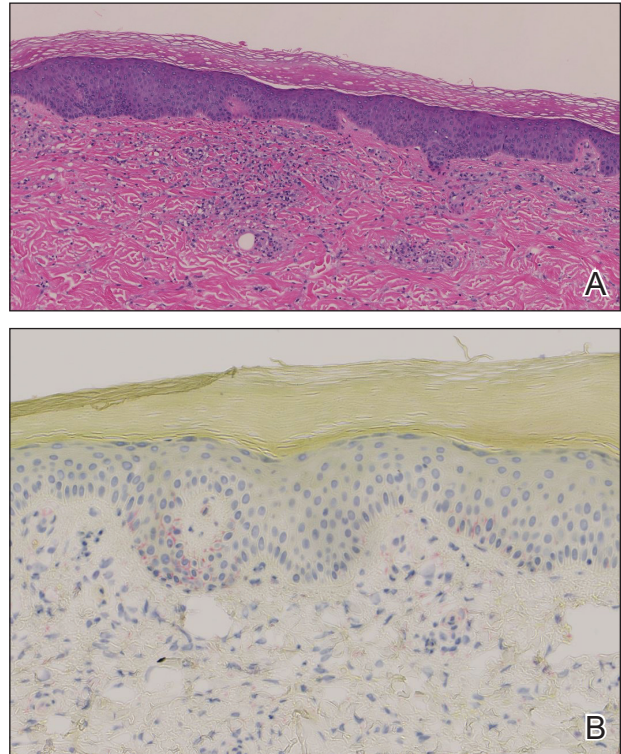
## THE DIAGNOSIS: Secondary Syphilis

Histopathology demonstrated a mild superficial perivascular and interstitial infiltrate composed of lymphocytes, histiocytes, and rare plasma cells with a background of extravasated erythrocytes (Figure, A). *Treponema pallidum* staining highlighted multiple spirochetes along the dermoepidermal junction and in the superficial dermis (Figure, B). Direct immunofluorescence was negative. Laboratory workup revealed a reactive rapid plasma reagin screen with a titer of 1:16 and positive IgG and IgM treponemal antibodies. The patient was diagnosed with secondary syphilis and was treated with a single dose of 2.4 million U of intramuscular benzathine penicillin G, with notable improvement of the rash and arthritis symptoms at 2-week follow-up.

Syphilis is a sexually transmitted infection caused by the spirochete *T pallidum* that progresses through active and latent stages. The incidence of both the primary and secondary stages of syphilis was at a historic low in the year 2000 and has increased annually since then.<sup>1</sup> Syphilis is more common in men, and men who have sex with men (MSM) are disproportionately affected. Although the incidence of syphilis in MSM has increased since 2000, rates have slowed, with slight decreases in this population between 2019 and 2020.<sup>1</sup> Conversely, rates among women have increased substantially in recent years, suggesting a more recent epidemic affecting heterosexual men and women.<sup>2</sup>

Classically, the primary stage of syphilis manifests as an asymptomatic papule followed by a painless ulcer (chancre) that heals spontaneously. The secondary stage of syphilis results from dissemination of *T pallidum* and is characterized by a wide range of mucocutaneous manifestations and prodromal symptoms. The most common cutaneous manifestation is a diffuse, nonpruritic, papulosquamous rash with red-brown scaly macules or papules on the trunk and extremities.<sup>3</sup> The palms and soles commonly are involved. Mucosal patches, “snail-track” ulcers in the mouth, and condylomata lata are the characteristic mucosal lesions of secondary syphilis. Mucocutaneous findings typically are preceded by systemic signs including fever, malaise, myalgia, and generalized lymphadenopathy. However, syphilis is considered “the great mimicker,” with new reports of unusual presentations of the disease. In addition to papulosquamous morphologies, pustular, targetoid, psoriasiform, and noduloulcerative (also known as lues maligna) forms of syphilis have been reported.<sup>3-5</sup>

The histopathologic features of secondary syphilis also are variable. Classically, secondary syphilis demonstrates vacuolar interface dermatitis and acanthosis with slender elongated rete ridges. Other well-known features include endothelial swelling and the presence of plasma cells in most cases.<sup>6</sup> However, the histopathologic



A, A punch biopsy of a lesion on the left foot revealed subtle superficial perivascular and interstitial inflammation as well as extravasated erythrocytes (H&E, original magnification  $\times 100$ ). B, *Treponema pallidum* staining highlighted multiple spirochetes along the dermoepidermal junction and in the superficial dermis, confirming the diagnosis of secondary syphilis (original magnification  $\times 400$ ).

features of secondary syphilis may vary depending on the morphology of the skin eruption and when the biopsy is taken. Our patient lacked the classic histopathologic features of secondary syphilis. However, because syphilis was in the clinical differential diagnosis, a treponemal stain was ordered and confirmed the diagnosis. Immunohistochemical stains using antibodies to treponemal antigens have a reported sensitivity of 71% to 100% and are highly specific.<sup>7</sup> Although the combination of endothelial swelling, interstitial inflammation, irregular acanthosis, and elongated rete ridges should raise the possibility of syphilis, a treponemal stain may be useful to identify spirochetes if clinical suspicion exists.<sup>8</sup>

Given our patient's known history of GPA, leukocytoclastic vasculitis was high on the list of differential diagnoses. However, leukocytoclastic vasculitis most classically manifests as petechiae and palpable purpura, and unlike in secondary syphilis, the palms and soles are less commonly involved. Because our patient's rash was mainly localized to the lower limbs, the differential also included

2 pigmented purpuric dermatoses (PPDs): progressive pigmentary purpura (Schamberg disease) and purpura annularis telangiectodes (Majocchi disease). Progressive pigmentary purpura is the most common manifestation of PPD and appears as cayenne pepper-colored macules that coalesce into golden brown-pigmented patches on the legs.<sup>9</sup> Purpura annularis telangiectodes is another variant of PPD that manifests as pinpoint telangiectatic macules that progress to annular hyperpigmented patches with central clearing. Although PPDs frequently occur on the lower extremities, reports of plantar involvement are rare.<sup>10</sup> Annular lichen planus manifests as violaceous papules with a clear center; however, it would be atypical for these lesions to be restricted to the feet and ankles. Palmoplantar lichen planus can mimic secondary syphilis clinically, but these cases manifest as hyperkeratotic pruritic papules on the palms and soles in contrast to the faint brown asymptomatic macules noted in our case.<sup>11</sup>

Our case highlights an unusual presentation of secondary syphilis and demonstrates the challenge of diagnosing this entity on clinical presentation alone. Because this patient lacked the classic clinical and histopathologic features of secondary syphilis, a skin biopsy with positive immunohistochemical staining for treponemal antigens was necessary to make the diagnosis. Given the variability in presentation of secondary syphilis, a biopsy or serologic testing may be necessary to make a proper diagnosis.

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