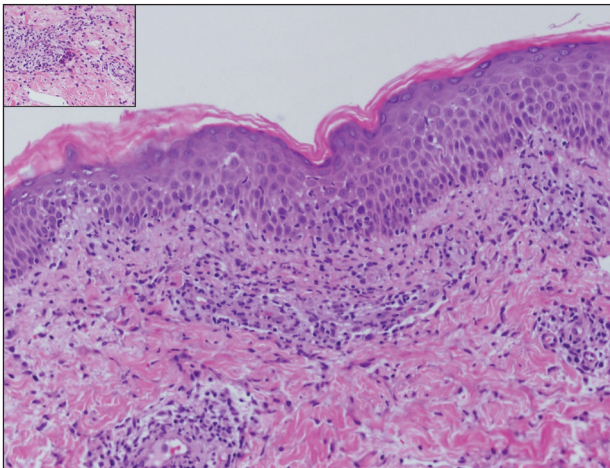


Erythematous Papules on the Scrotum, Trunk, and Extremities

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H&E, original magnification $\times 100$ (inset, original magnification $\times 400$).

A 54-year-old man presented with painful, non-pruritic, erythematous papules that began on the scrotum. The eruption progressed to involve the trunk, arms, and legs.

THE BEST DIAGNOSIS IS:

- discoid lupus erythematosus
- interstitial granuloma annulare
- interstitial granulomatous dermatitis
- postviral granulomatous reaction
- secondary syphilis

PLEASE TURN TO **PAGE 236** FOR THE DIAGNOSIS

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The authors report no conflict of interest.

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THE DIAGNOSIS:

Lichenoid and Granulomatous Dermatitis in the Setting of Secondary Syphilis

Syphilis, an infectious disease that has risen in incidence and is most commonly reported in men who have sex with men, involves a vast array of clinical and histologic presentations.¹ Clinically, secondary syphilis involves an erythematous maculopapular eruption on the face, trunk, palms, soles, or genital area.² The characteristic histologic features for secondary syphilis include endothelial swelling, interstitial inflammatory array, irregular acanthosis, elongated rete ridges, and vacuolar interface dermatitis with lymphocytes and plasma cells.¹ Syphilitic infection has been associated with lichenoid and granulomatous dermatitis, which is an inflammatory skin disease described by Magro and Crowson.³ Lichenoid and granulomatous dermatitis has been linked to various systemic disorders, including chronic hepatitis C, Crohn disease, rheumatoid arthritis, endocrinopathy, subacute cutaneous lupus erythematosus, secondary syphilis, prior herpes infection, tuberculous leprosy, mycobacterial infection, and human immunodeficiency virus infection.³⁻⁷ For this patient, given histopathology findings, clinical presentation, and positive rapid plasma reagin serologies, a diagnosis of lichenoid and granulomatous dermatitis in the setting of a secondary syphilis infection was established. A comprehensive investigation should be conducted to consider secondary syphilis or other systemic diseases in patients with a histologic finding of lichenoid and granulomatous dermatitis.

Histologically, lichenoid and granulomatous dermatitis cases show a bandlike infiltrate of lymphocytes with neighboring histiocytes along the dermoepidermal junction, accompanied by epithelial changes of dyskeratosis, vasculopathy, and colloid body formation, in addition to a dermal histiocytic component.³ Our patient's biopsy showed a lichenoid reaction pattern with vacuolar interface changes, dyskeratosis, plump endothelial cells, and small collections of plasma cells. Additionally, there was a granulomatous component in the dermis with histiocytes admixed with lymphocytes and plasma cells. The presence of spirochetes was confirmed with antitreponemal immunohistochemical stain (Figure 1). Quantitative rapid plasma reagin was 1:64 (reference range, <1:1) and *Treponema pallidum* antibody was reactive.

Interstitial granulomatous dermatitis has a variable clinical presentation, often with red-purple annular plaques, hyperpigmented papules, and nodules frequently in a linear arrangement and predominantly on the trunk, thighs, groin, or buttocks.^{8,9} On histopathology, there are histiocytes in the reticular dermis and/or a macrophage infiltrate in the mid to deep dermis with collections of degenerated collagen (Figure 2).^{8,10} An interstitial infiltrate of eosinophils and neutrophils also may be appreciated, but mucin generally is

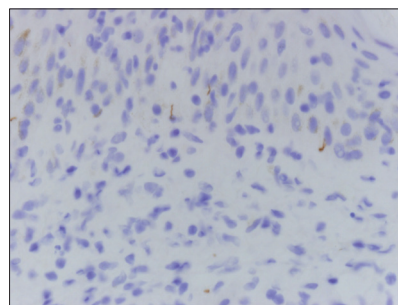


FIGURE 1. Secondary syphilis. *Treponema pallidum* immunohistochemistry showed scattered spirochetes (original magnification $\times 600$).

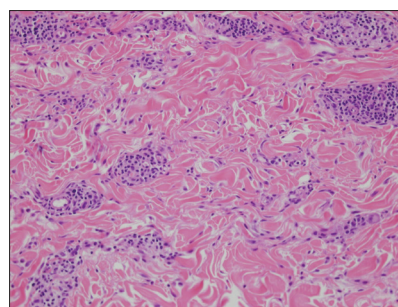


FIGURE 2. Interstitial granulomatous dermatitis. Thickened collagen bundles interlaced with histiocytes and lymphocytes. Little to no mucin is appreciated (H&E, original magnification $\times 200$).

absent.^{8,11} This condition often coexists with rheumatic and systemic autoimmune diseases.⁸⁻¹⁰

Interstitial granuloma annulare is a noninfectious granulomatous skin condition that often presents clinically as asymptomatic annular red-brown patches, usually on the extremities.¹¹⁻¹³ On histopathology, an interstitial or palisaded inflammatory infiltrate with histiocytes and multinucleated giant cells may be seen along with collagen degeneration or collagen bundles without necrosis (Figure 3).⁹ Mucin often is associated with the histiocytes.¹¹ Of note, our patient's skin biopsy shows interface dermatitis, differentiating it from both interstitial granuloma annulare and interstitial granulomatous dermatitis.

Postviral granulomatous reactions are the most frequently reported types of reactions to occur at the location of herpes zoster infection up to years after the initial disease. Wolf isotopic reaction encompasses skin reactions in the body region of formerly resolved skin disease, commonly herpesvirus infection.^{14,15} This manifestation may occur due to a hypersensitivity reaction from enduring viral proteins, resident memory T cells, or local neuroimmune imbalance from herpesvirus-induced injury to dermal sensory nerve fibers.¹⁴⁻¹⁷ Clinically,

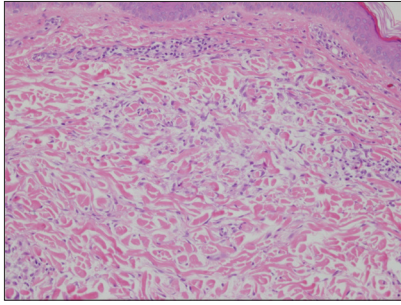


FIGURE 3. Interstitial granuloma annulare. A busy dermis with increased histiocytes and lymphocytes arranged about vessels and between collagen bundles that are separated by increased mucin (H&E, original magnification $\times 200$).

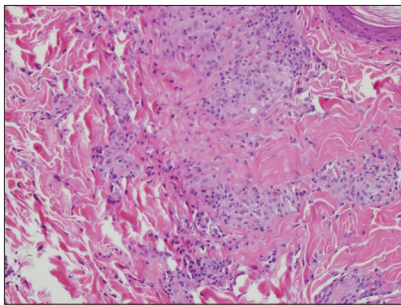


FIGURE 4. Postviral granulomatous reaction. Histiocytes, lymphocytes, and multinucleated giant cells with thickened collagen bundles (H&E, original magnification $\times 200$).

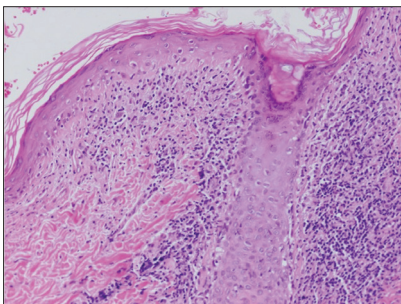


FIGURE 5. Discoid lupus erythematosus. Perifollicular and perivascular inflammatory infiltrate with vacuolization along the dermoepidermal junction and scattered dyskeratotic keratinocytes along the basal layer of the epidermis. There is focal follicular plugging and the basement membrane zone appears thickened (H&E, original magnification $\times 200$).

patients present with red-purple pruritic papules and plaques in a bandlike unilateral pattern, usually in the same region as the prior herpes infection and often accompanied by postherpetic neuralgia.¹⁶⁻¹⁹ Of note, our patient's clinical findings were more diffuse than the frequently localized and often linear distribution seen in postherpetic granulomatous reaction. On histopathology, granulomatous or lichenoid tissue reaction most commonly is appreciated.¹⁵ Specifically, interstitial granulomatous dermatitis with histiocytes, lymphocytes, and multinucleated giant cells showing elastophagocytosis and an inflammatory infiltrate with lymphocytes and plasma cells

around vasculature, eccrine glands, and nerves can be noted (Figure 4).¹⁹

Lupus erythematosus is an autoimmune condition with a wide array of clinical features, including skin manifestations and systemic symptoms. Specifically, discoid lupus erythematosus presents with clearly outlined, red-pink macules or papules with scaling. Histologic features include keratotic follicular plugging, acanthosis, dermal mucin, thickening of the basement membrane zone, and dense lymphocytic infiltrate (Figure 5).²⁰

REFERENCES

- Flamm A, Parikh K, Xie Q, et al. Histologic features of secondary syphilis: a multicenter retrospective review. *J Am Acad Dermatol.* 2015;73:325-330.
- Zeltser R, Kurban AK. Syphilis. *Clin Dermatol.* 2004;22:461-468.
- Magro CM, Crowson AN. Lichenoid and granulomatous dermatitis. *Int J Dermatol.* 2000;39:12-33.
- S Breza T Jr, Magro CM. Lichenoid and granulomatous dermatitis associated with atypical mycobacterium infections. *J Cutan Pathol.* 2006;33:512-515.
- Granel B, Serratrice J, Rey J, et al. Chronic hepatitis C virus infection associated with a generalized granuloma annulare. *J Am Acad Dermatol.* 2000;43(5, pt 2):918-919.
- Jorizzo JL, Gonzalez EB, Apisarnthanarax P, et al. Pigmented purpuric eruption in a patient with rheumatoid arthritis. *Arch Intern Med.* 1982;142:2184-2185.
- Magro CM, Crowson AN, Regauer S. Granuloma annulare and necrobiosis lipoidica tissue reactions as a manifestation of systemic disease. *Hum Pathol.* 1996;27:50-56.
- Błażewicz I, Szczerkowska-Dobosz A, Pęksa R, et al. Interstitial granulomatous dermatitis: a characteristic histological pattern with variable clinical manifestations. *Postepy Dermatol Alergol.* 2015;32:475-477.
- Sezer E, Luzar B, Calonje E. Secondary syphilis with an interstitial granuloma annulare-like histopathologic pattern. *J Cutan Pathol.* 2011;38:439-442.
- Peroni A, Colato C, Schena D, et al. Interstitial granulomatous dermatitis: a distinct entity with characteristic histological and clinical pattern. *Br J Dermatol.* 2012;166:775-783.
- Sakiyama T, Hirai I, Konohana A, et al. Interstitial-type granuloma annulare associated with Sjögren syndrome. *J Dtsch Dermatol Ges.* 2014;12:415-416.
- Spring P, Vernez M, Maniu CM, et al. Localized interstitial granuloma annulare induced by subcutaneous injections for desensitization. *Dermatol Online J.* 2013;19:18572.
- Kluger N, Moguet P, Chaslin-Ferbus D, et al. Generalized interstitial granuloma annulare induced by pegylated interferon-alpha. *Dermatology.* 2006;213:248-249.
- Ruocco E, Baroni A, Cutri FT, et al. Granuloma annulare in a site of healed herpes zoster: Wolf's isotopic response. *J Eur Acad Dermatol Venereol.* 2003;17:686-688.
- Ise M, Tanese K, Adachi T, et al. Postherpetic Wolf's isotopic response: possible contribution of resident memory T cells to the pathogenesis of lichenoid reaction. *Br J Dermatol.* 2015;173:1331-1334.
- Lora V, Cota C, Kanitakis J. Zosteriform lichen planus after herpes zoster: report of a new case of Wolf's isotopic phenomenon and literature review. *Dermatol Online J.* 2014;20. pii:13030/qt5v99178.
- Lin CH, Chen HC, Gao HW, et al. Wolf's post-herpetic isotopic response to tocilizumab for rheumatoid arthritis. *Australas J Dermatol.* 2018;59:E135-E137.
- Melgar E, Henry J, Valois A, et al. Extra-facial Lever granuloma on a herpes zoster scar: Wolf's isotopic response. *Ann Dermatol Venereol.* 2018;145:354-358.
- Ferenczi K, Rosenberg AS, McCalmont TH, et al. Herpes zoster granulomatous dermatitis: histopathologic findings in a case series. *J Cutan Pathol.* 2015;42:739-745.
- Li Q, Wu H, Liao W, et al. A comprehensive review of immune-mediated dermatopathology in systemic lupus erythematosus. *J Autoimmun.* 2018;93:1-15.