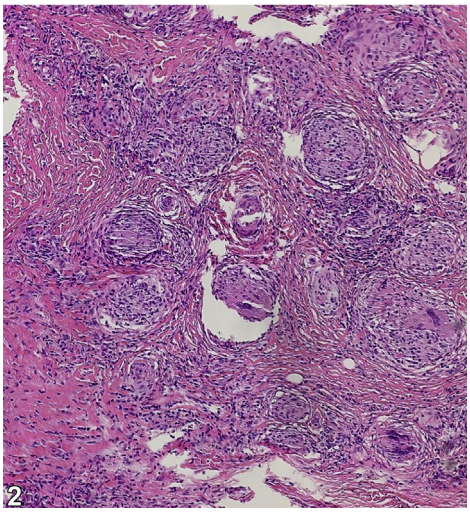
# Ichthyosiform red-brown plaques on bilateral shins

Ali Duffens, BS,[a] Christina N. Kraus, MD,[b] Ashley N. Elsensohn, MD, MPH,[c] Jessica Shiu, MD, PhD,[b] and Janellen Smith, MD[b]
*Irvine, California and Danville, Pennsylvania*


A 58-year old African-American woman presented with a 3-year history of scaly plaques on her legs. Prior treatment consisted of triamcinolone cream and compression stockings. Examination found thin, red-brown rhomboidal plaques with adherent scale on anterior legs bilaterally (Fig 1) and no other skin involvement. Review of systems was positive for chronic dyspnea on exertion. Tuberculin test was negative. A punch biopsy found numerous deep dermal noncaseating granulomas composed of epithelioid cells and giant cells surrounded by a pauci-cellular cuff of lymphocytes (Fig 2). Fite and periodic acid–Schiff stains were negative, and foreign body was not seen on birefringence.

**Question 1. What is your diagnosis?**

**A.** Granulomatous cutaneous T cell lymphoma

**B.** Ichthyosis vulgaris

**C.** Ichthyosiform sarcoidosis

From the School of Medicine[a] and the Department of Dermatology,[b] University of California and the Section of Dermatopathology, Geisinger Medical Center.[c]

Funding sources: None.
Conflicts of interest: None disclosed.

Correspondence to: Christina N. Kraus, MD, Department of Dermatology, University of California, Irvine, 118 Med Surge I, Irvine, CA 92697. E-mail: ckraus@hs.uci.edu.

JAAD Case Reports 2020;6:838-40.
2352-5126



https://doi.org/10.1016/j.jdcr.2020.07.010

**D.** Leprosy

**E.** Secondary syphilis

**Answers:**

**A.** Granulomatous cutaneous T cell lymphoma — Incorrect. Granulomatous mycosis fungoides has not been reported with ichthyosis features. Although histopathology finds multinucleated giant cells and/or sarcoidal granulomas, these are often accompanied by atypical lymphocytes and epidermotropism in about half of cases.[1] Granulomatous slack skin is another entity with overlapping histologic features with granulomatous mycosis fungoides but is rare. Granulomatous slack skin differs clinically by the development of bulky skin folds.

**B.** Ichthyosis vulgaris — Incorrect. Ichthyosis vulgaris presents with these clinical findings, but histopathology would find mild hyperkeratosis and a diminished granular layer. Granulomas would not be present.

**C.** Ichthyosiform sarcoidosis — Correct. Ichthyosiform sarcoidosis is a rare cutaneous form of sarcoid that presents with polygonal, adherent scales on the lower extremities. Histologically, sarcoidal granulomas are found in the dermis with epidermal changes consistent with ichythosis.[2]

**D.** Leprosy — Incorrect. Leprosy is a chronic granulomatous condition caused by *Mycobacterium leprae*, an acid-fast mycobacterium. Sarcoid and leprosy have overlapping clinical and histopathologic findings, and ichthyosis can be seen in both. In tuberculoid leprosy, skin biopsy would find epithelioid granulomas traveling with neurovascular bundles, with absent or few acid-fast bacilli. The most common presentation of tuberculoid leprosy is a single anesthetic lesion. Lepromatous leprosy would lack epithelioid granulomas, and acid-fast bacilli would be numerous.[3]

**E.** Secondary syphilis — Incorrect. Syphilis is caused by the spirochete *Treponema pallidum*. Although secondary syphilis can present with a granulomatous pattern, it is uncommon. Most granulomatous cases have papules or nodules clinically.[4] Spirochetes would be identified by *Treponema pallidum* immunohistochemistry.

**Question 2. Which of the following is the next *best* step in management?**

**A.** Administer intramuscular (IM) penicillin

**B.** Check serum angiotensin-converting enzyme (ACE) level

**C.** Order chest radiograph and pulmonary function tests

**D.** Refer to infectious disease department to start multidrug therapy

**E.** Start topical triamcinolone

**Answers:**

**A.** Administer IM penicillin — Incorrect. A single IM injection of benzathine penicillin G is US Food and Drug Administration approved for treatment of primary, secondary, or early latent syphilis.

**B.** Check serum ACE level — Incorrect. Studies found that serum ACE levels have limited utility as a diagnostic test and may be more appropriately used for monitoring disease progression. This is not the next best step in management.

**C.** Order chest radiograph and pulmonary function tests — Correct. Chest radiography and pulmonary function tests should be ordered in any patient with cutaneous findings that are clinically and histopathologically consistent with sarcoidosis to evaluate for lung involvement, particularly in the case of ichthyosiform sarcoidosis, where one study found 95% of patients have systemic involvement at the time of diagnosis.[2] Chronic lung disease caused by sarcoidosis can progress to pulmonary fibrosis, leading to increased morbidity and mortality. Electrocardiogram and ophthalmologic examination should also be performed in the workup for systemic disease.

**D.** Referral to infectious disease to start multidrug therapy — Incorrect. Infectious disease referral would be appropriate in the case of leprosy. Treatment typically requires multidrug therapy including rifampicin, dapsone, and, in some cases, clofazimine.

**E.** Start topical triamcinolone — Incorrect. Although the first-line treatment for skin-limited disease includes topical or intralesional corticosteroids, this patient should first undergo thorough evaluation for systemic involvement.

**Question 3. Which of the following agents has been reported to cause cutaneous sarcoid?**

**A.** Cytotoxic T-lymphocyte-associated antigen-4 (CTLA)-4 inhibitors

**B.** Programmed cell death-1 receptor (PD-1) inhibitors

**C.** Interleukin (IL)-17 inhibitors

**D.** Janus kinase (JAK) inhibitors

**E.** A and B

**Answers:**

**A.** CTLA-4 inhibitors — Incorrect. Both CTLA-4 and PD-1 inhibitors are reported to cause cutaneous sarcoid.

**B.** PD-1 inhibitors — Incorrect. Both CTLA-4 and PD-1 inhibitors are reported to cause cutaneous sarcoid.

**C.** IL-17 inhibitors — Incorrect. IL-17 inhibitors (eg, secukinumab, brodalumab, and ixekizumab) target the IL-23/T helper cell 17 pathway and are used for the treatment of psoriasis, psoriatic arthritis, and ankylosing spondylitis. They have not been reported to cause cutaneous sarcoidosis.

**D.** JAK inhibitor — Incorrect. JAK inhibitors, such as tofacitinib, block cytokine signaling through the JAK-STAT signaling pathway and are used to treat autoimmune diseases like psoriasis, ulcerative colitis, and rheumatoid arthritis. Recent evidence suggests that JAK inhibitors may be used for the treatment of sarcoidosis. They have not been reported to cause cutaneous sarcoidosis.

**E.** A and B — Correct. Both CTLA-4 inhibitors and PD-1 inhibitors are immune checkpoint inhibitors used to treat various malignancies. They act to enhance the immune response against tumor cells; thus, immune-related adverse events are consequences of therapy. Both ipilimumab (anti—CTLA-4) and nivolumab (anti—PD-1) have been reported individually (and in combination) to cause cutaneous sarcoidosis.[5] Clinicians should maintain a high index of suspicion for medication-induced cutaneous sarcoidosis in patients on immune checkpoint inhibitor therapy who present with sarcoidal lesions.

## Abbreviations used:

ACE: angiotensin-converting enzyme
CTLA-4: cytotoxic T-lymphocyte-associated antigen-4
IL: interleukin
IM: intramuscular
JAK: janus kinase
PD-1: programmed cell death-1 receptor

## REFERENCES

1. Kempf W, Ostheeren-michaelis S, Paulli M, et al. Granulomatous mycosis fungoides and granulomatous slack skin: a multicenter study of the Cutaneous Lymphoma Histopathology Task Force Group of the European Organization For Research and Treatment of Cancer (EORTC). *Arch Dermatol*. 2008;144(12):1609-1617.
2. Haimovic A, Sanchez M, Judson MA, Prystowsky S. Sarcoidosis: a comprehensive review and update for the dermatologist: part I and II. *J Am Acad Dermatol*. 2012;66(5):699.e1-699.e18.
3. Massone C, Belachew WA, Schettini A. Histopathology of the lepromatous skin biopsy. *Clin Dermatol*. 2015;33(1):38-45.
4. Rysgaard C, Alexander E, Swick BL. Nodular secondary syphilis with associated granulomatous inflammation: case report and literature review. *J Cutan Pathol*. 2014;41(4):370-379.
5. Mobini N, Dhillon R, Dickey J, Spoon J, Sadrolashrafi K. Exclusive cutaneous and subcutaneous sarcoidal granulomatous inflammation due to immune checkpoint inhibitors: report of two cases with unusual manifestations and review of the literature. *Case Rep Dermatol Med*. 2019;2019:6702870.