Case in Point

Morphea: From a Rash to Atrophy

Aaron C. Garza, MD; and Suresh Kumar, MD

A 30-year-old man presented with a rash on the left lower extremity. Several months later, he developed diffuse skin hypopigmentation associated with bilateral lower extremity myalgia. Two years later, he was prescribed steroids to improve the myalgia. One year later, a musculoskeletal examination showed significant muscle atrophy, and a punch biopsy showed focal atrophic epidermal changes, dense dermal collagen, few pigmented dermal macrophages, and mild chronic inflammation.

Morphea, or localized scleroderma, is a rare, idiopathic, self-limiting inflammatory condition, which causes fibrotic changes that are localized to the skin.[1] Evidence shows an incidence of 0.4 to 2.7 per 100,000, with a female and white predominance.[2] Depending on the clinical presentation, morphea can be classified as circumscribed (with superficial and deep variants), linear, generalized, pansclerotic, and mixed. Regardless of subtype, the natural history of the disease is inflammation, sclerosis, and atrophy. Diagnosis is based on clinical findings, with histopathology, laboratory, and imaging studies for confirmation. Management depends on disease activity, extent and depth of lesions (dermal or subcutaneous), area of involvement, and disease course.

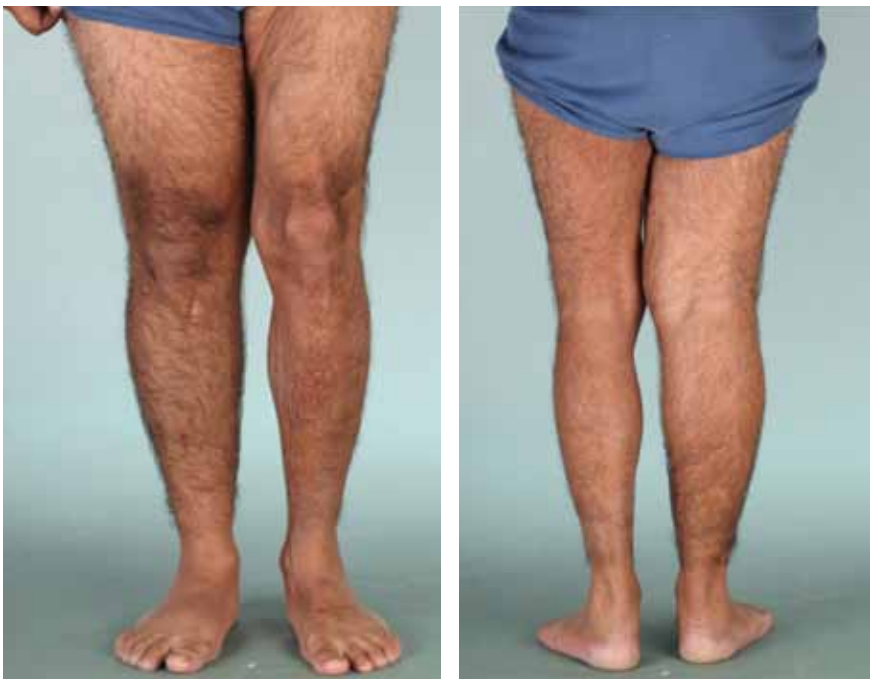

Figure 1. Anterior and posterior views show left lower extremity atrophy.

CASE REPORT

A 30-year-old man presented with a pruritic rash on the left lower extremity (LLE). It was located on the medial aspect of the leg and was erythematous and refractory to topical hydrocortisone. After several months, he developed diffuse skin hypopigmentation without facial involvement associated with bilateral lower extremity myalgia. Two years later, he visited a dermatologist. He was prescribed oral steroids with improvement of myalgia, and he regained most of his pigmentation. At that time, he had a skin biopsy of the anterior chest wall, which showed normal findings.

During the patient's initial rheumatologic evaluation, an electromyography was negative. Magnetic

Dr. Garza is a PGY-3 resident of internal medicine and **Dr. Kumar** is an affiliated associate professor of medicine, both at the University of Miami Miller School of Medicine in Florida. Dr. Kumar is also the chief of rheumatology at the West Palm Beach VAMC in Florida.

resonance imaging (MRI) of the left thigh showed muscle atrophy and diminished left subcutaneous fat. A more extensive evaluation was ordered, but the patient did not follow up and was not seen for about 1 year. Then, he presented with myalgia in the LLE.

There were no other pertinent past medical, surgical, or family histories. The patient worked as a pest control technician, drank alcohol occasionally, and did not report tobacco or illicit drug use. He took tramadol as needed and reported no allergies.

The patient did not report fever, weight loss, or fatigue. There was no Raynaud's phenomenon or sclerodactyly present—no chest pain, shortness of breath, dry eyes or dry mouth, oral or genital ulcers, and no gastrointestinal, urinary, or neurologic symptoms.

On physical examination, the patient's vital signs were normal. He had no oral mucositis or ulcers. The heart, lung, and abdominal examinations were normal.

The patient's musculoskeletal examination showed significant muscle atrophy in the quadriceps and calf of the LLE (Figure 1). There were no synovitis or joint effusions. No sclerodactyly was appreciated. The patient was able to lift his arms over his shoulders and make a complete fist. His overall range of motion and strength were within normal limits.

The skin of the patient's anterior chest wall showed a small area of ice pick sprinkling of hypopigmentation without evidence of skin tightness (Figure 2). Areas of shiny skin with depigmentation were seen, most pronounced in the distal aspect below the knee, with some sprinkling of hypopigmentation on the upper thigh. There was no involvement of the buttocks. There were no nailfold capillary changes. There were no signs of genital lesions or abnormalities.

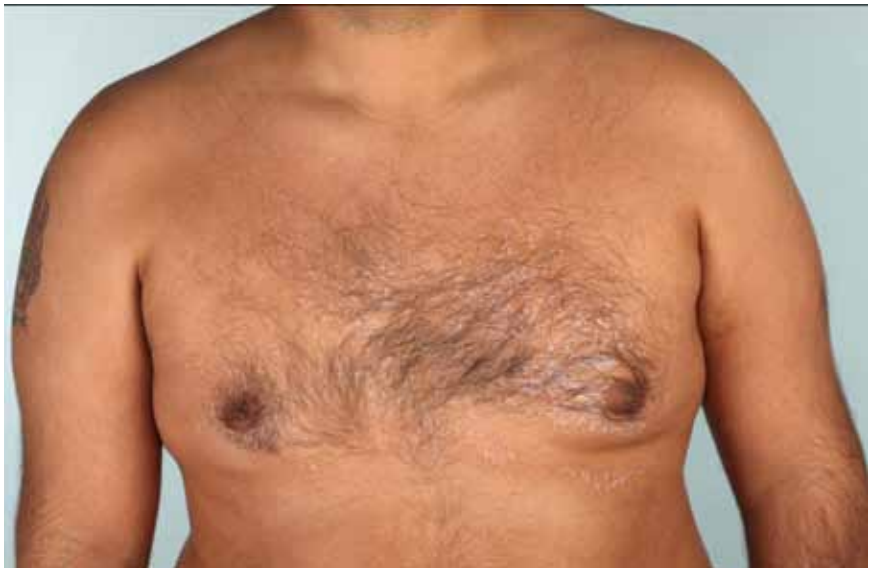

Figure 2. Anterior chest wall with ice pick sprinkling of hypopigmentation.

The complete blood count, complete metabolic panel, thyroid stimulating hormone, and C-reactive protein laboratory results were within normal limits. Urine analysis was negative for any abnormalities. The patient tested negative for hepatitis B, hepatitis C, and enzyme-linked immunosorbent assay for human immunodeficiency virus. The serum antinuclear antibody was positive with a titer of 1:320 (normal range, 1:40). Serum antibodies for scleroderma, anticentromere, ribonucleoprotein, double-stranded DNA, anti-Ro, and anti-La were negative.

A high-resolution computed tomography chest scan, echocardiogram, and pulmonary function tests showed no abnormalities.

Regarding the lesion on the anterior chest, the patient underwent a punch biopsy that showed focal atrophic epidermal changes, dense dermal collagen, few pigmented dermal macrophages, and mild chronic inflammation; the changes were compatible with morphea. Clinically, the lesion had no evidence of induration. The patient was started on topical treatment with tacrolimus twice daily with occlusion for 12 weeks.

Due to advanced atrophy and inactivity of disease with no functional impairment in the LLE, the patient was referred for physical therapy. He was counseled about the importance of the therapy to avoid contracture.

DISCUSSION

The differential diagnosis included systemic sclerosis, lipodermatosclerosis, and morphea. In systemic sclerosis, sclerodactyly, Raynaud's phenomenon, nailfold capillary changes, and internal organ involvement are frequently seen. Lipodermatosclerosis can be excluded, as the patient did not show signs and symptoms suggestive of chronic venous insufficiency.

This case illustrates the classic presentation of a rare disease: linear morphea. An estimated 50% of cases undergo spontaneous remission or skin softening on average 2.7 years after onset.[2] The etiology of morphea is a multifactorial process involving environmental factors and host sus-

ceptibility. For example, trauma, radiation, medications, infections, and autoimmune diseases may cause vascular injury that leads to a decrease in capillary density in the involved skin and increased capillary dermis vascular bed in the basal lamina, as well as death of microvascular endothelial cells. This endothelial injury releases cytokines, which increase molecular adhesion products, and T cells that produce profibrotic cytokines, such as tumor growth factor beta.[3,4] Upregulation of the latter increases collagen and decreases production of proteases, causing the imbalance of collagen production and destruction, leading to fibrosis.[5]

Histologic findings depend on the clinical course of the disease: inflammatory cell infiltrate, advancing to thickened collagen bundles with loss of appendageal structures and finally loss of inflammatory infiltrate and sclerosis. Up to 80% of cases may show elevated antinuclear antibodies. An MRI is used to evaluate the extent of the disease, lesion depth, and involvement of subcutaneous tissues.

Treatment depends on disease activity, extent and depth of lesions (dermal or subcutaneous), area of involvement, and disease course.[6] Subcutaneous involvement, rapid progression, and involvement of functionally or cosmetically sensitive areas or large body surface area are indications for systemic treatment. Superficial involvement is defined by histology with evidence of papillary dermal involvement. Deep involvement is defined as sclerosis or inflammation of reticular dermis, subcutis, fascia, or muscle.

In general, active disease duration of < 3 months or disease in the inflammatory phase is the most responsive. Sclerotic lesions are less likely to improve, and atrophic lesions rarely respond to therapy. For active, superficial, limited, and inflammatory lesions, topical medications are usually used, including tacrolimus, calcipotriene, high-potency corticosteroids, and imiquimod. Topical tacrolimus 0.1% ointment is used under occlusion. For active, superficial, and generalized disease, phototherapy can be used.[7,8] Phototherapy should not be considered if there is deep involvement.[9] Should the lesions continue to progress, systemic therapy (methotrexate and glucocorticoids) is usually the treatment used.[10] For inactive lesions or advanced disease (such as atrophy), an assessment of functional and cosmetic defects should be done with referral to physical therapy, plastic surgery, and orthopedics as appropriate.[6] ●

Author disclosures

The authors report no actual or potential conflicts of interest with regard to this article.

Disclaimer

The opinions expressed herein are those of the authors and do not necessarily reflect those of Federal Practitioner, *Quadrant HealthCom Inc., a division of Frontline Medical Communications, Inc., the U.S. Government, or any of its agencies. This article may discuss unlabeled or investigational use of certain drugs. Please review complete prescribing information for specific drugs or drug combinations—including indications, contraindications, warnings, and adverse effects—before administering pharmacologic therapy to patients.*

REFERENCES

1. Laxer RM, Zulian F. Localized scleroderma. *Curr Opin Rheumatol.* 2006;18(6):606-613.
2. Peterson LS, Nelson AM, Su WP, Mason T, O'Fallon WM, Gabriel SE. The epidemiology of morphea (localized scleroderma) in Olmsted County 1960-1993. *J Rheumatol.* 1997;24(1):73-80.
3. Yamamoto T. Chemokines and chemokine receptors in scleroderma. *Int Arch Allergy Immunol.* 2006;140(4):345-356.
4. Asano Y, Ihn H, Jinnin M, Mimura Y, Tamaki K. Involvement of alphavbeta5 integrin in the establishment of autocrine TGF-beta signaling in dermal fibroblasts derived from localized scleroderma. *J Invest Dermatol.* 2006;126(8):1761-1769.
5. Badea I, Taylor M, Rosenberg A, Foldvari M. Pathogenesis and therapeutic approaches for improved topical treatment in localized scleroderma and systemic sclerosis. *Rheumatology* (Oxford). 2009;48(3):213-221.
6. Zwischenberger BA, Jacobe HT. A systematic review of morphea treatments and therapeutic algorithm. *J Am Acad Dermatol.* 2011;65(5):925-941.
7. Kroft EB, Groeneveld TJ, Seyger MM, de Jong EM. Efficacy of topical tacrolimus 0.1% in active plaque morphea: Randomized, double-blind, emollient-controlled pilot study. *Am J Clin Dermatol.* 2009;10(3):181-187.
8. Mancuso G, Berdondini RM. Localized scleroderma: Response to occlusive treatment with tacrolimus ointment. *Br J Dermatol.* 2005;152(1):180-182.
9. Vilela FA, Carneiro S, Ramos-e-Silva M. Treatment of morphea or localized scleroderma: Review of the literature. *J Drugs Dermatol.* 2010;9(10):1213-1219.
10. Kroft EB, Berkhof NJ, van de Kerkhof PC, Gerritsen RM, de Jong EM. Ultraviolet A phototherapy for sclerotic skin diseases: A systematic review. *J Am Acad Dermatol.* 2008;59(6):1017-1030.