

Shiny Indurated Plaques on the Legs

Ashley N. Gray, MD; Stephanie K. Fabbro, MD; Abraham M. Korman, MD



A 70-year-old woman presented with pain and swelling in both legs of many years' duration. She had no history of skin disease. Physical examination revealed shiny indurated plaques on the legs, ankles, and toes with limited range of motion in the ankles (top). Marked thickening of the hands and index fingers also was noted (bottom). A punch biopsy of the distal pretibial region was performed.

WHAT'S YOUR DIAGNOSIS?

- a. hypertrophic lichen planus
- b. lipodermatosclerosis
- c. necrobiosis lipoidica
- d. pretibial myxedema
- e. stasis dermatitis



PLEASE TURN TO **PAGE E8** FOR THE DIAGNOSIS

Drs. Gray and Korman are from the Department of Dermatology, The Ohio State University Wexner Medical Center, Columbus. Dr. Fabbro is from the Division of Dermatology, Department of Internal Medicine, Ohio Health Riverside Methodist Hospital, Columbus.

The authors report no conflict of interest.

Correspondence: Abraham M. Korman, MD, 540 Officenter Center Pl, Ste 240, Columbus, OH 43230 (Abraham.Korman@osumc.edu).

doi:10.12788/cutis.0841

THE DIAGNOSIS: Pretibial Myxedema

Histopathology showed superficial and deep mucin deposition with proliferation of fibroblasts and thin wiry collagen bundles that were consistent with a diagnosis of pretibial myxedema. The patient was treated with clobetasol ointment 0.05% twice daily for 3 months, followed by a trial of pentoxifylline 400 mg 3 times daily for 3 months. After this treatment failed, she was started on rituximab infusions of 1 g biweekly for 1 month, followed by 500 mg at 6 months, with marked improvement after the first 2 doses of 1 g.

Pretibial myxedema is an uncommon cutaneous manifestation of autoimmune thyroid disease, occurring in 1% to 5% of patients with Graves disease. It usually occurs in older adult women on the pretibial regions and less commonly on the upper extremities, face, and areas of prior trauma.¹⁻³ Although typically asymptomatic, it can be painful and ulcerate.³ The clinical presentation consists of bilateral nonpitting edema with overlying indurated skin as well as flesh-colored, yellow-brown, violaceous, or peau d'orange papules and plaques.^{2,3} Lesions develop over months and often have been associated with hyperhidrosis and hypertrichosis.² Many variants have been identified including nodular, plaquelike, diffuse swelling (ie, nonpitting edema), tumor, mixture, polypoid, and elephantiasis; severe cases with acral involvement are termed *thyroid acropachy*.¹⁻³ Pathogenesis likely involves the activation of thyrotropin receptors on fibroblasts by the circulating thyrotropin autoantibodies found in Graves disease. Activated fibroblasts upregulate glycosaminoglycan production, which osmotically drives the accumulation of dermal and subdermal fluid.^{1,3}

This diagnosis should be considered in any patient with pretibial edema or edema in areas of trauma. Graves disease most commonly is diagnosed 1 to 2 years prior to the development of pretibial myxedema; other extrathyroidal manifestations, most commonly ophthalmopathies, almost always are found in patients with pretibial myxedema. If a diagnosis of Graves disease has not been established, thyroid studies, including thyrotropin receptor antibody serum levels, should be obtained. Histopathology showing increased mucin in the dermis and increased fibroblasts can aid in diagnosis.^{2,3}

The differential diagnosis includes inflammatory dermatoses, such as stasis dermatitis and lipodermatosclerosis.

Stasis dermatitis is characterized by lichenified yellow-brown plaques that present on the lower extremities; lipodermatosclerosis then can develop and present as atrophic sclerotic plaques with a champagne bottle-like appearance. *Necrobiosis lipoidica* demonstrates atrophic, shiny, yellow plaques with telangiectases and ulcerations. Hypertrophic lichen planus presents with hyperkeratotic hyperpigmented plaques on the shins.^{1,2} Other diseases of cutaneous mucin deposition, namely scleromyxedema, demonstrate similar physical findings but more commonly are located on the trunk, face, and dorsal hands rather than the lower extremities.¹⁻³

Treatment of pretibial myxedema is difficult; normalization of thyroid function, weight reduction, and compression stockings can help reduce edema. Medical therapies aim to decrease glycosaminoglycan production by fibroblasts. First-line treatment includes topical steroids under occlusion, and second-line therapies include intralesional steroids, systemic corticosteroids, pentoxifylline, and octreotide.^{2,3} Therapies for refractory disease include plasmapheresis, surgical excision, radiotherapy, and intravenous immunoglobulin; more recent studies also endorse the use of isotretinoin, intralesional hyaluronidase, and rituximab.^{2,4} Success also has been observed with the insulin growth factor 1 receptor inhibitor teprotumumab in active thyroid eye disease, in which insulin growth factor 1 receptor is overexpressed by fibroblasts. Given the similar pathogenesis of thyroid ophthalmopathy with other extrathyroidal manifestations, teprotumumab is a promising option for refractory cases of pretibial myxedema and has led to disease resolution in several patients.⁴

REFERENCES

1. Fatourehchi V, Pajouhi M, Fransway AF. Dermopathy of Graves disease (pretibial myxedema): review of 150 cases. *Medicine (Baltimore)*. 1994;73:1-7. doi:10.1097/00005792-199401000-00001
2. Ai J, Leonhardt JM, Heymann WR. Autoimmune thyroid diseases: etiology, pathogenesis, and dermatologic manifestations. *J Am Acad Dermatol*. 2003;48:641-662. doi:10.1067/mjd.2003.257
3. Schwartz KM, Fatourehchi V, Ahmed DDF, et al. Dermopathy of Graves' disease (pretibial myxedema): long-term outcome. *J Clin Endocrinol Metab*. 2002;87:438-446. doi:10.1210/jcem.87.2.8220
4. Varma A, Rheeman C, Levitt J. Resolution of pretibial myxedema with teprotumumab in a patient with Graves disease. *JAAD Case Reports*. 2020;6:1281-1282. doi:10.1016/j.jidcr.2020.09.003