Although an uncommon location, cutaneous mucinoses may present in the pretibial area in distinct clinical circumstances. The terms pretibial myxedema and pretibial mucinosis often are used interchangeably, but pretibial myxedema should be regarded as a type of pretibial mucinosis. We present a case of cutaneous mucinosis localized to the pretibial area of a patient without Graves disease.

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Case Report
A 46-year-old black man presented with enlarging edematous plaques on bilateral pretibial areas of 6 months’ duration. The lesions occasionally caused mild pruritus but had no effect on daily activities and primarily were of cosmetic concern. His medical history was remarkable for type 2 diabetes mellitus, hypertension, and inverse psoriasis. Inverse psoriasis was well-controlled on topical tacrolimus. He denied history of thyroid disease or myeloma. He had no history of lower extremity swelling or trauma.

Physical examination revealed well-demarcated, thick, hyperpigmented plaques and nodules located symmetrically on the pretibial areas (Figure 1). The lesions were edematous with a peau d’orange appearance. There was posterolateral extension on the left leg. No lower extremity edema, varicose veins, or eczematous changes were noted. Exophthalmos and lid lag were not apparent. There were no abnormalities of the fingertips or nails. No thyromegaly or thyroid nodules were palpable upon examination.

Punch biopsy results from the left pretibial skin stained with hematoxylin and eosin showed hyperkeratosis of the epidermis, effacement of rete ridge pattern, and dermal pallor extending to the upper reticular dermis. Higher-power magnification showed a thin layer of normal-appearing collagen in the superficial papillary dermis and extensive mid dermal deposition of mucinous material causing separation of collagen bundles (Figure 2). There was no fibroplasia or fibrosis and vessels were vertically oriented. Mild angioplasia was observed, but there was no hemosiderin deposition. Mucin accumulation was confirmed with Alcian blue staining (Figure 3).

Laboratory studies showed thyrotropin and free thyroxine levels within reference range. Thyroid-stimulating immunoglobulin, antithyroglobulin, and antithyroid peroxidase antibodies were all negative. Serum and urine protein electrophoresis studies were within reference range.

Given the pruritus and cosmetic concern, the patient was treated with triamcinolone acetonide ointment under occlusion. At the 3-month follow-up visit, he had moderate improvement of pruritus and slight improvement in appearance. Repeat thyroid

Figure 1. Erythematous, edematous, and hyperpigmented plaques and nodules on the pretibial areas bilaterally with a peau d’orange appearance (A and B).
function studies were performed and results were within reference range.

Comment
Cutaneous mucinoses uncommonly occur in the pretibial area. Although the terms pretibial myxedema and pretibial mucinosis often are used interchangeably, pretibial myxedema is a type of pretibial mucinosis associated with autoimmune thyroid disease. Lichen myxedematosus, venous insufficiency, lymphedema, obesity, and trauma also are conditions that can lead to pretibial mucin deposition. Clinical, histologic, and laboratory examination is needed to determine the cause of mucin accumulation and exclude underlying systemic disease.

Pretibial myxedema is a rare cutaneous manifestation of autoimmune thyroid disease, occurring in less than 4% of patients with Graves disease and in even fewer patients with Hashimoto thyroiditis. Because skin lesions have been reported to occur on the face, shoulders, and arms, the alternative names thyroid dermopathy or localized myxedema have been suggested. Although typically a late manifestation of Graves-associated hyperthyroidism with preceding ophthalmopathy, the mucinosis rarely has occurred in euthyroid or hypothyroid patients and preceded the ophthalmopathy. Regardless of thyroid function, all patients with pretibial myxedema have elevated levels of autoimmune thyroid antibodies. Thyroid dermopathy may present as nonpitting patches, plaques, nodules, or a rare elephantiasic form, all with a flesh or erythematous color and a peau d’orange appearance. Thyrotropin receptors in the connective tissue initiate both humoral and cellular immune responses, which increase mucin production by fibroblasts. Dependent position and trauma likely contribute to localization on the shins.

Venous insufficiency, lymphedema, obesity, and trauma can lead to pretibial mucin accumulation. Kim et al reported a case of pretibial mucinosis mimicking thyroid dermopathy in a patient with no laboratory evidence of autoimmune thyroid disease. The patient had leg trauma during a motor vehicle accident, leading to venous insufficiency, lymphedema, and recurrent cellulitis before presentation. Tokuda et al reported 3 cases of pretibial mucinosis in patients with morbid obesity and chronic pitting edema, naming the entity chronic obesity lymphoedematous mucinosis. Rongioletti et al reported 5 patients with obesity and chronic edema of the legs presenting with pretibial mucinoses identical to the...
patients described by Tokuda et al. Venous insufficiency leads to decreased oxygen levels and leakage of plasma proteins, such as albumin and coagulation factors. Microthrombi formation worsens ischemia and promotes angioplasia, while albumin and other plasma proteins are thought to cause increased mucopolysaccharide production. The stasis of protein-rich lymphatic fluid in chronic lymphedema may stimulate mucin production in a similar manner.

Somach et al reviewed biopsies of patients with pretibial mucinosis to determine if histologic characteristics can differentiate cases with and without thyroid disease. Distinguishing features included normal-appearing collagen in the papillary dermis (12/12 with Graves disease and 0/6 without), mucin deposition in the reticular dermis (12/12 with Graves disease and 0/6 without), lack of mucin deposition in the superficial papillary dermis (11/12 with Graves disease and 1/6 without), angioplasia (2/12 with Graves disease and 6/6 without), and the presence of hemosiderin (2/12 with Graves disease and 6/6 without). Ten biopsies of stasis dermatitis were evaluated for the presence of mucin, with 6 of 10 having deposition in the papillary dermis and none in the reticular dermis. This study demonstrated reliable criteria to differentiate between stasis and thyroid-associated pretibial mucinoses.

Localized myxedematosus, which includes discrete, acral persistent, nodular, and papular mucinosis of infancy, is distinguished from scleromyxedema (generalized lichen myxedematosus) by absence of systemic involvement and gammopathy. These mucinoses can present at any site, and a case of the discrete subtype presenting as pretibial plaques has been reported. Lichen myxedematosus also is histologically discernable from pretibial myxedema. Scleromyxedema displays diffuse mucin deposition in the upper and mid dermis, fibroblast proliferation, and fibrosis. The localized subtypes have variable fibroplasia and fibrosis, making the pattern of mucin accumulation vital to the diagnosis.

The nonthyroid-associated cases reported by Somach et al histologically displayed angioplasia (6/6) and hemosiderin deposition (6/6), and no papillary dermal sparing or reticular dermal mucin deposition (0/6 for both), findings consistent with venous insufficiency. All cases reported by Tokuda et al and Rongioletti et al had thickened vessels, vertical vessels, stellate fibroblasts, dermal mucin deposition ending at the upper reticular dermis, and lack of hemosiderin, distinguishing lymphedematous mucinoses in obese patients.

Although our case shared many histologic features with the aforementioned obesity-associated cases, fibrosis and stellate fibroblasts were not present on histology. Clinically, our patient had no lymphedema, venous insufficiency, or repeated trauma, and his body mass index (33 kg/m²) was lower than those cases with obesity-associated lymphedematous mucinosis (36, 42, and 51 kg/cm² reported by Tokuda et al, and 40, 43, 35, 43, and 47 kg/cm² reported by Rongioletti et al).

We suggest that pretibial mucinoses not associated with autoimmune thyroid disease may develop in patients lacking chronic lymphedema, venous insufficiency, trauma, or lichen myxedematosus, as previously reported. Pretibial mucinoses can be debilitating and disfiguring; therefore, further evaluation of this rare entity is needed to elucidate more about its etiology.

REFERENCES