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Journal
Dermatology Online Journal, 25(2)

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Publication Date
2019

DOI
10.5070/D3252042916

Electrosurgical debulking of pretibial myxedema of the foot

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Abstract

Pretibial myxedema or thyroid dermopathy constitutes dermal deposition of mucin, primarily hyaluronic acid and chondroitin sulfate. It is a manifestation of autoimmune thyroiditis, seen more in Graves disease than in Hashimoto thyroiditis. The time delay from treatment of hyperthyroidism to appearance of localized myxedema varies from one month to 16 years (mean 5.13 years). Despite a variety of therapeutic options, failure and relapse rates are high. Therapeutic options reported in the literature include compression, topical and intralesional corticosteroids, oral pentoxifylline, octreotide, rituximab, plasmapheresis, and high-dose intravenous immunoglobulin. We share our experience in two patients who were treated with electrosurgical debulking of selected longstanding myxedematous lesions, with one positive result and one negative result.

Keywords: pretibial myxedema, elephantiasic pretibial myxedema, electrosurgical debulking, electrosurgery, Graves disease

Introduction

Pretibial myxedema (PTM), also called thyroid dermopathy, localized myxedema, or infiltrative dermopathy, is an infrequent manifestation of autoimmune thyroid disease. It can present as discrete tumors or as a diffusely infiltrative plaque. Therapy of PTM is challenging at best, with no single modality enjoying consistent results. Herein we report two cases of electrosurgical debulking, one with excellent results and another with only a fair outcome.

Case Synopsis

Case 1. A 64-year-old woman, was diagnosed with Graves disease in 1993, with thyrotoxicosis and ophthalmopathy followed 18 months later with PTM. She was treated with radioactive iodine (I^{131}) and is currently on levothyroxine 100mcg daily. Her lower extremities were indurated up to the mid-calves with slowly progressive verrucous hypertrophic vegetations of the dorsal feet (**Figure 1A**). Monthly intralesional triamcinolone (ILTAC) 10-40mg/cc and weekly intralesional hyaluronidase over the course of

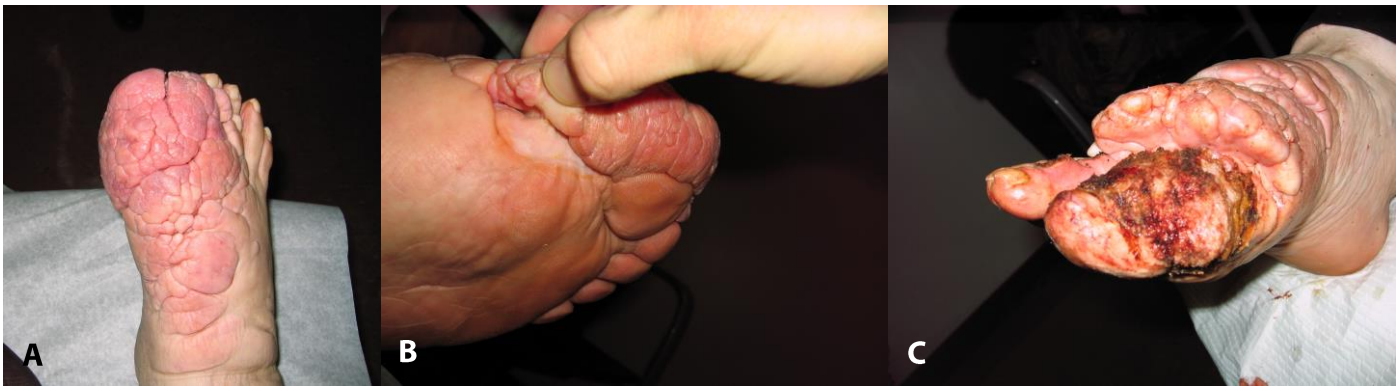

Figure 1. ***A)*** *Verrucous hypertrophic vegetations of the dorsal feet cover the toe before surgical treatment.* ***B)*** *The plantar view clarifies the pedunculated nature of the tumor.* ***C)*** *The char from electrosurgery is shown immediately after surgery.*

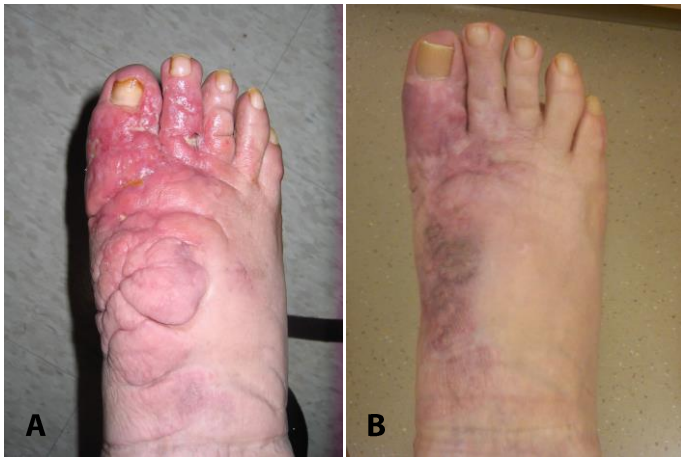

Figure 2. ***A)*** *Two months after treatment the wounds are nearly re-epithelialized.* ***B)*** *Two years after surgery, the foot is free of recurring PTM lesions (status post further debulking proximally using similar electrosurgical methods).*

several years failed to shrink the lesions. The patient was resistant to surgical debulking after experiencing a recurrence from a debulking attempt years prior. The repeated ILTAC injections caused hypertension and osteopenia. Intralesional octreotide injections were added but failed after a 6-month trial. Owing to the upcoming wedding of the patient's daughter, the patient was motivated to try a second attempt at debulking. In three separate sessions, we debulked nodular and pedunculated lesions (**Figure 1B, C**) by electrosurgery under local anesthesia, prescribing post-procedure antibiotics to prevent infection. Durable remission was evident at both two months (**Figure 2A**) and two years (**Figure 2B**). PTM was confirmed histologically (**Figure 3**).

Case Synopsis

Case 2. A 48-year-old woman suffered five years of worsening elephantiasic PTM affecting her toes (**Figure 4A, B**), dorsal feet, and inferior shins that impaired ambulation, and prevented her from wearing regular shoes. Graves disease was diagnosed and treated three years prior to PTM onset with radioactive iodine (I^{131}) and was managed with levothyroxine 175mcg daily. She exhibited moderate exophthalmos but no acropachy. Additional medical problems included migraines, iron-deficiency anemia, irritable bowel syndrome, urinary tract infection, diverticulitis, and multiple surgeries including gastrectomy with gastric bypass for gastroesophageal reflux disease, appendectomy, cholecystectomy, and vulvar surgery for vulvar vestibulitis. Prior failed therapy for the PTM included one year of ILTAC 10-40mg/cc and hyaluronidase 200U/ml, oral pentoxyfylline 400mg three times daily, clobetasol 0.05% ointment, and compression stockings. We treated the nodular lesions of the left great toe, and later the right great toe with electrosurgical excision under local anesthesia (**Figure 4C-E**). PTM was confirmed histologically (**Figure 5A-D**). Recovery was complicated by bilateral lower extremity cellulitis (approximately one month post-debulking). Complete healing took six months (**Figure 6A, B**). The patient received two doses of rituximab 1g IV at three months and 12

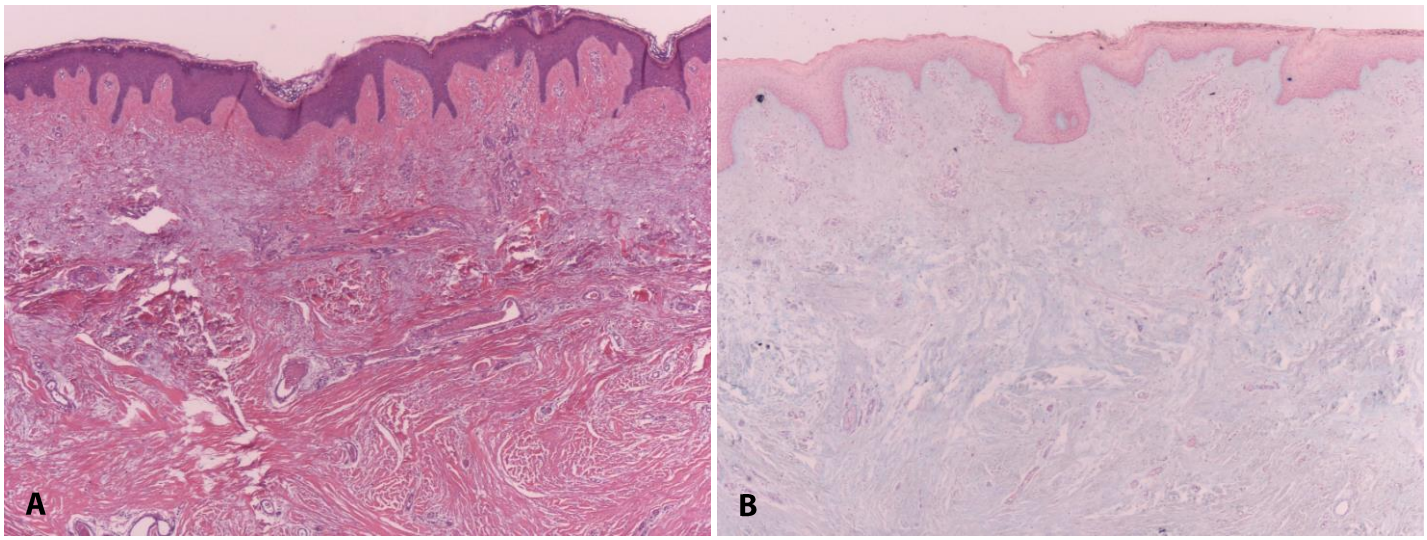

Figure 3. ***A)*** *Right great toe biopsy shows focal cutaneous mucinosis with fibrosis, consistent with PTM. H&E, 4×.* ***B)*** *Increased dermal mucin is evident. Alcian blue, 4×.*

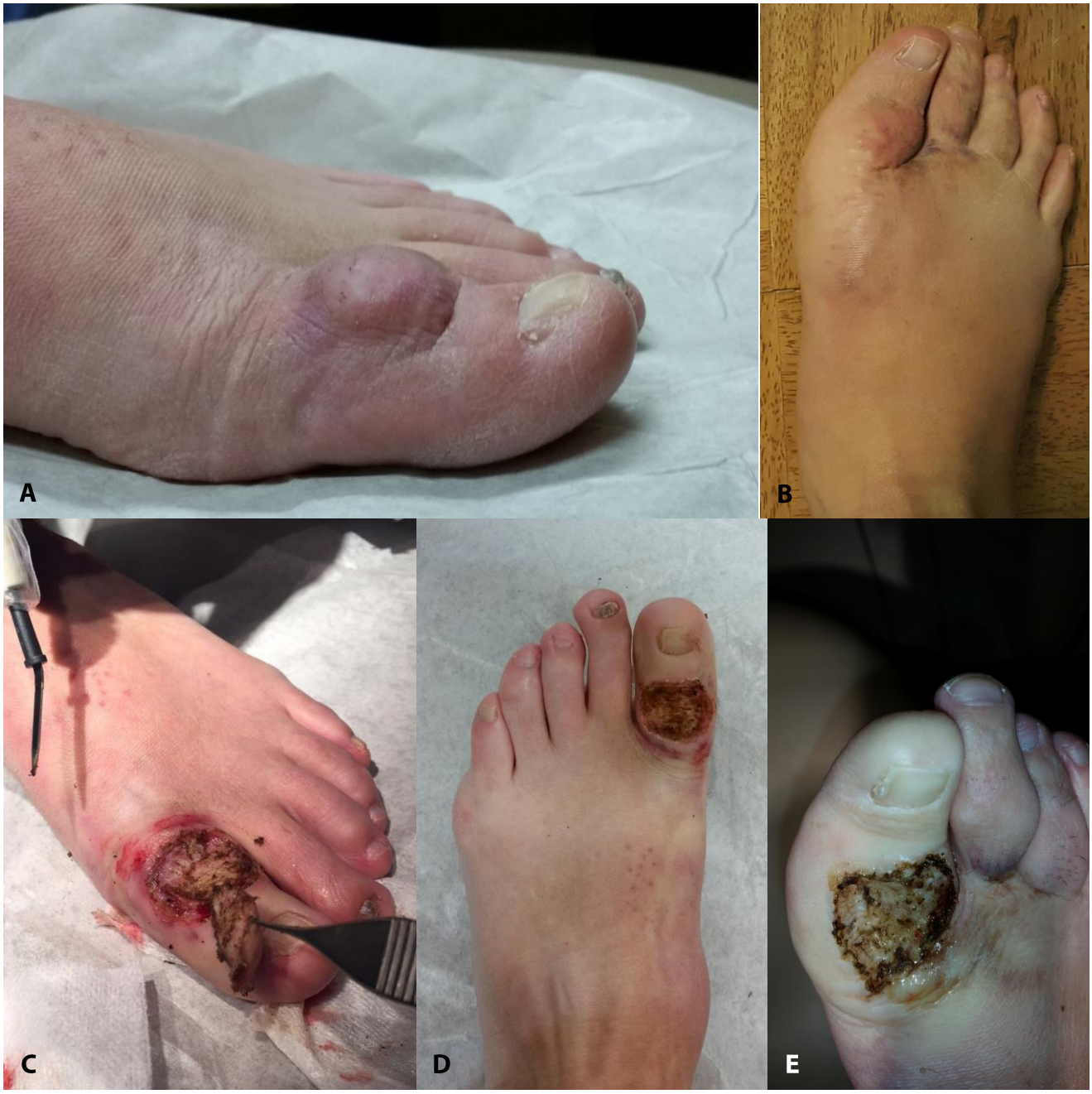

Figure 4. ***A)*** *The nodular myxedematous lesion of left toe is shown.* ***B)*** *The nodular myxedematous lesion of right toe is shown.* ***C)*** *Intraoperative electrosurgical excision of the left toe is shown.* ***D)*** *The left toe is shown immediately after surgical debulking.* ***E)*** *The right toe is shown immediately after surgical debulking.*

months following the debulking procedures. Although the cosmetic outcome was initially promising, the great toes developed indurated plaques with central scarring at 14 months following the procedures (**Figure 6C, D**). Whether the natural course of the PTM caused the appearance of these plaques or the electrosurgery triggered them remains uncertain.

Case Discussion

Pretibial myxedema (PTM) or thyroid dermopathy constitutes dermal deposition of mucin, primarily hyaluronic acid and chondroitin sulfate [1]. It is a manifestation of autoimmune thyroiditis, seen more in Graves disease than in Hashimoto thyroiditis. The time delay from treatment of hyperthyroidism to appearance of localized myxedema varies from one

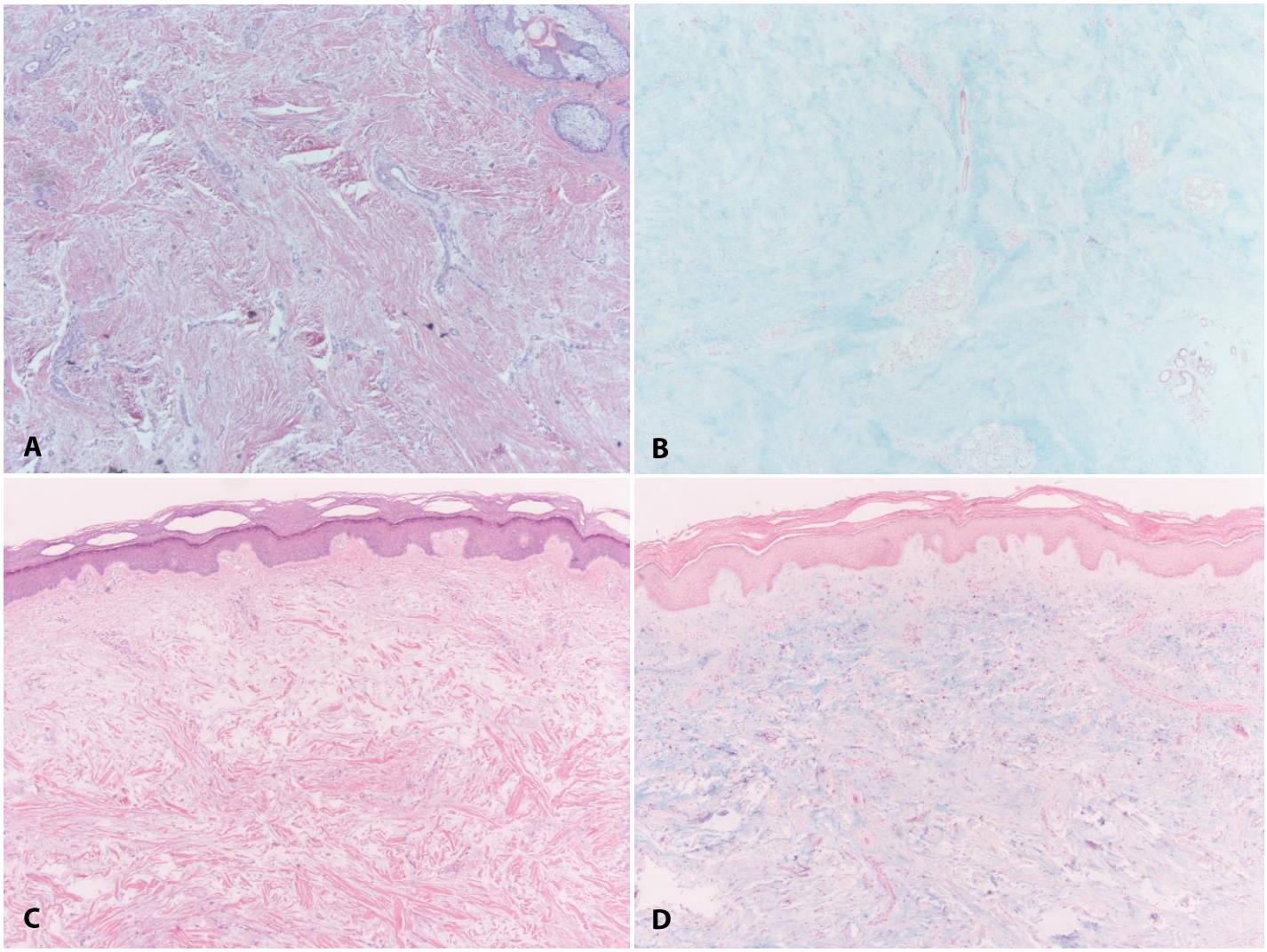

Figure 5. ***A)*** *Left great toe biopsy reveals dermal scar and edema, compatible with PTM. H&E, 4×.* ***B)*** *Colloidal iron stain is strongly positive, confirming the diagnosis of PTM. Colloidal iron, 4×.* ***C)*** *Right great toe biopsy reveals increased dermal mucin, compatible with PTM. H&E, 4×.* ***D)*** *Colloidal iron stain is strongly positive, confirming the diagnosis of PTM. Colloidal iron, 4×.*

month to 16 years (mean 5.13 years). The pretibial area is by far the most common site of involvement (93.3%) in PTM, followed by the dorsal foot. Unusual locations have been reported, including the forearms, shoulders, arms, palms, upper back, neck, pinna, and lower part of the abdomen [2]. Morphologic variants of PTM include nonpitting edema (43.3%), plaques (27%), nodules (18.5%) or elephantiasis (2.8%), [3]. PTM generally occurs in the setting of Graves disease and can coexist with Graves ophthalmopathy and thyroid acropachy (digital clubbing, swelling of digits and toes, and periosteal reaction of extremity bones). PTM lesions contain 6 to 16 times more hyaluronic acid than unaffected skin [1]. The accumulation of these highly hydrophilic compounds produces edema and consequently disrupts dermal collagen and elastic fibers, resulting in malfunction of the subcutaneous lymphatic network [4]. Typically, thyroid dysfunction in Graves disease occurs first, followed by ophthalmopathy in the first year, PTM several months after that, and finally acropachy in the setting of severe thyroid disease [3, 5]. One case of PTM as the initial presentation of Graves disease has been reported [6]. PTM occurs in 0.5-5% of patients with Graves disease but has also been reported less frequently in Hashimoto thyroiditis, primary hypothyroidism, and euthyroidism. Peak incidence occurs in the fifth to sixth decades of life with a female-to-male ratio of 3.5:1 [7].

Although the precise pathophysiology of PTM is complex and still enigmatic, both humoral and cellular immune mechanisms and mechanical factors are involved in the stimulation of fibroblasts and the production of large amounts of glycosaminoglycans (GAGs). PTM arises from a local autoimmune response of the connective tissue, probably caused by TSH receptor autoantibodies (TRAb), formerly known as long-acting thyroid stimulator (LATS), [7]. TRAb is present in the serum of most patients with PTM (80-100%), but it has also been found in the serum of patients without PTM [8].

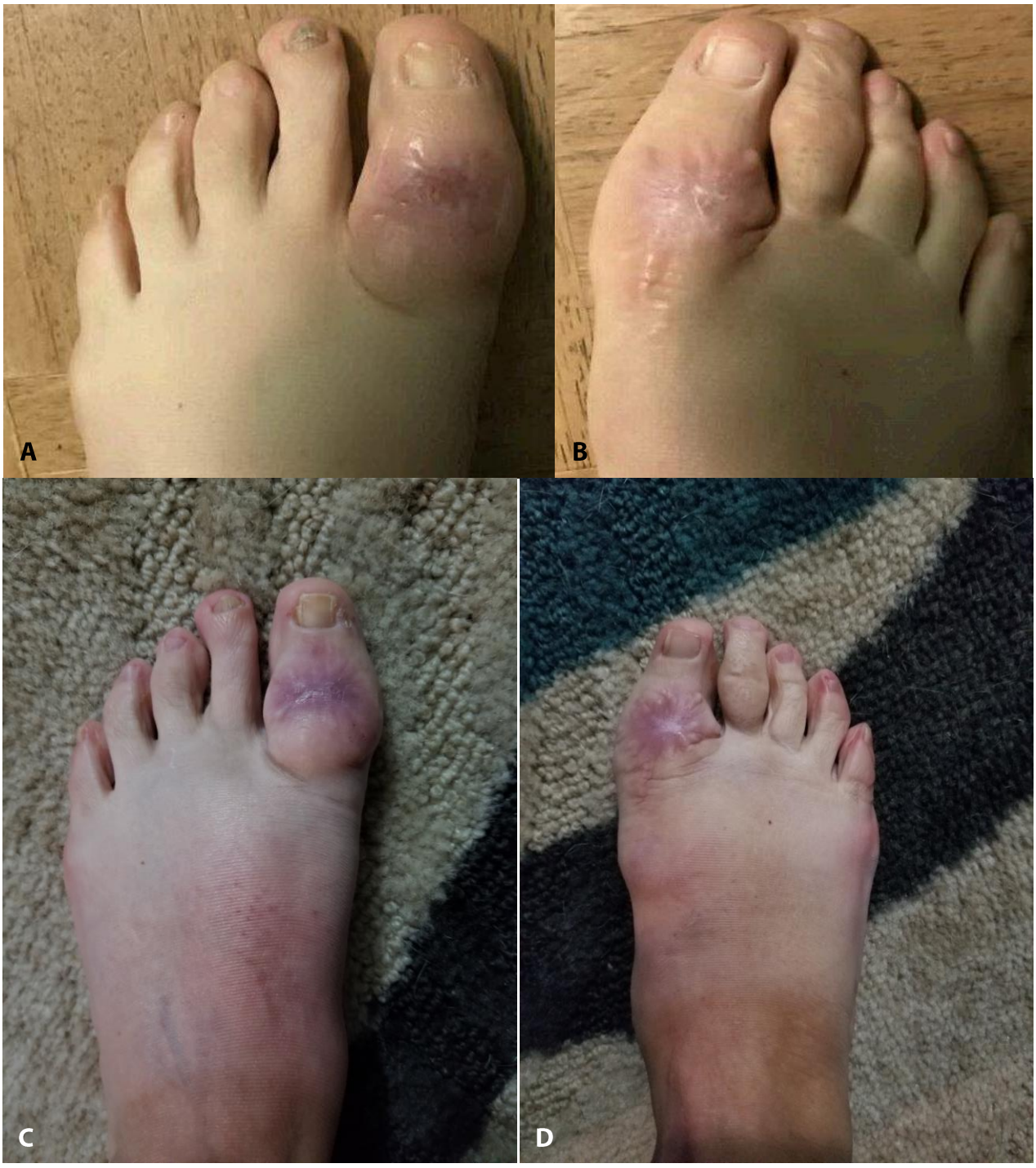

Figure 6. ***A)*** *The left great toe shows recurrence after 6 months.* ***B)*** *The right great toe has good healing after 6 months.* ***C)*** *The indurated plaque of left great toe with central scarring at 14 months is larger than the original tumor.* ***D)*** *The indurated plaque of right great toe with central scarring at 14 months appears more consistent with hypertrophic scarring than with recurrence.*

Trauma and prolonged standing contribute to local fibroblast activation. The local increase in GAGs leads to the accumulation of fluid and the expansion of dermal connective tissue [3].

Treatment of PTM aims to diminish the production of mucin by fibroblasts. Glucocorticoids suppress fibroblasts and T cells, with a resulting decrease in GAG production in the dermis. Success has been reported with topical glucocorticoids, with or without hydrocolloid or plastic wrap occlusion [3, 5, 9]. Weekly intralesional triamcinolone or systemic steroid pulse therapy has also been reported. A novel approach to injecting steroids in the dermis with mesotherapy needles reportedly achieved durable improvement in PTM [10]. Compression bandages or stockings (20-40mm Hg) provide additional benefit, especially in patients with the elephantiasic form [11]. Oral pentoxifylline has been employed in two studies, in association with topical or intralesional steroids [12]. Promising newer approaches that require further investigation include octreotide, rituximab, plasmapheresis, and high-dose intravenous immunoglobulin [13, 14].

Surgical removal is generally ill advised because scarring may worsen dermopathy. However, at least one patient with thick plaques prior to surgical shaving of the lesion and daily octreotide injections for 6 months did not have recurrence after 9 years of surveillance [15, 16]. Our first case supports an adjuvant role for electrosurgical debulking of discrete nodular and pedunculated lesions.

Conclusion

First-line treatment for pretibial myxedema is topical or intralesional corticosteroids. Surgery for pretibial myxedema carries risk of scarring that may aggravate dermopathy. One of our cases supports at least an adjuvant role of surgical debulking for discrete nodules and tumors of pretibial myxedema. If local or mechanical symptoms predominate or if lesions are pedunculated, surgical excision should be considered as a treatment option.

Potential conflicts of interest

The authors declare no conflicts of interest.

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