Localized myxedema histologically mimicking spindle cell lipoma

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Abstract

In this report, a 55-year-old woman with Graves disease and exophthalmos had a recurrent nodule on the foot. Her initial biopsy and excision specimens were believed to be consistent with spindle cell lipoma, which aligned with her early tumor-like clinical morphology. Her tumor recurred after excision, which is not consistent with spindle cell lipoma. As her condition progressed, her clinical morphology became more consistent with localized myxedema and her biopsies were congruent, securing clinicopathologic correlation. With standard treatment for localized myxedema, she improved significantly. This case emphasizes how clinicians need to have high suspicion for localized myxedema in patients with history of Graves disease and exophthalmos. It also emphasizes how localized myxedema should be included in the histologic differential diagnosis for spindle cell lipoma with prominent myxoid stroma, particularly in those not responding to treatment as anticipated.

Keywords: Graves disease, lipoma, pretibial myxedema, recurrent nodule, spindle cell, thyroid disease

Introduction

Localized myxedema (LM) is a rare manifestation of Graves disease and can histologically resemble spindle cell lipoma (SCL). This case exhibits localized myxedema initially diagnosed as SCL and highlights the importance of clinicopathologic correlation.

Case Synopsis

In spring 2020, a 55-year-old woman presented to our clinic for a second opinion regarding a mass on her left foot of eight years' duration. Her past medical history included Graves disease, (treated with radioiodine ablation two decades prior to presentation), tobacco use, hypertension, hyperlipidemia, chronic obstructive pulmonary disease, and depression. In 2012, an initial biopsy of the mass showed subacute to chronic spongiotic dermatitis, but treatment with topical corticosteroids was not helpful. In fall 2019, the mass had enlarged to 10cm in diameter, at which time a general surgeon excised the growth **(Figure 1**).

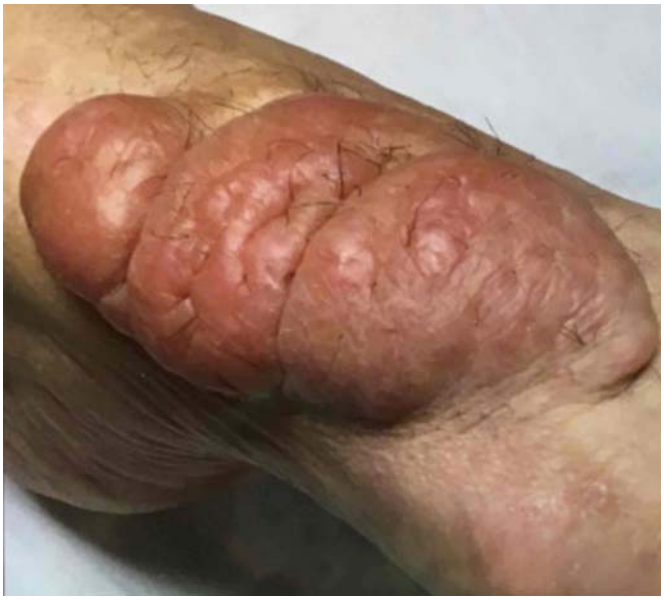

Figure 1. *Localized myxedema, enlarged 10cm mass of left dorsal foot in fall 2019.*

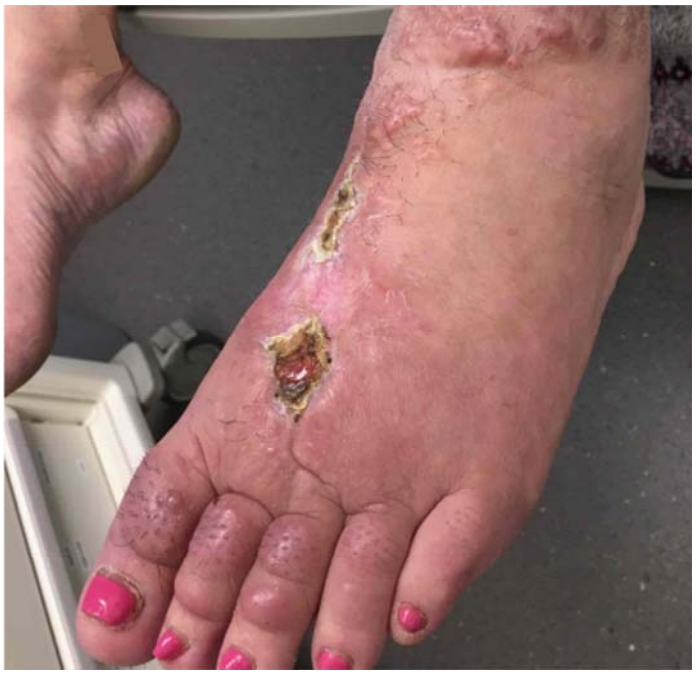

Figure 2. *Localized myxedema, new nodules left dorsal foot and distal shin in early 2020.*

Pathology examination demonstrated a bland spindle cell proliferation with abundant myxoid stroma and marked bundles of ropey collagen, considered to be consistent with intradermal myxoid spindle cell lipoma. The neoplasm stained positive for CD34. It had negative staining for S100, desmin, MDM2, and CDK1, and by report showed equivocal loss of Rb. Pathologists from two separate academic medical centers were consulted and they concurred with this diagnosis. After two months, the patient underwent re-excision for positive margins and pathology showed residual myxoid lipoma with positive margins. Her course was complicated by surgical site pain, wound dehiscence, and worsening of the swelling of her lower leg.

In early 2020, she developed multiple new nodules on the left dorsal foot, which extended to her distal shin **(Figure 2**). Biopsies were performed and interpreted as spindle cell lipoma. The nodules grew larger following biopsy. She was referred to our institution's Multidisciplinary Cutaneous Oncology Clinic. Her physical examination showed edema and scattered dermal papules coalescing into plaques over the left dorsal foot and left shin. She had marked proptosis of both eyes **(Figure 3**). The course and behavior of the left dorsal foot nodules was deemed unusual for spindle cell lipoma, thus a dermatologist was consulted and found her presentation clinically suspicious for pretibial myxedema, also known as localized myxedema. Biopsy of a nodule on the patient's left shin was sent to dermatopathology at our institution. Histology showed dermal mucin and rare adipocytes, supportive of cutaneous mucinosis (**Figure 4**). Our soft tissue pathologist concurred with a diagnosis of cutaneous mucinosis, with the more specific etiology of localized myxedema.

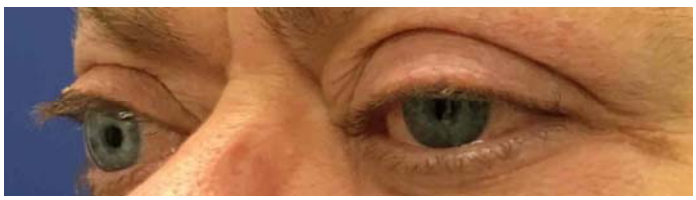

Figure 3. *Exophthalmos secondary to Graves ophthalmopathy.*

Given the clinicopathologic correlation for localized myxedema, treatment was initiated with clobetasol ointment twice daily and smoking cessation was encouraged. She was instructed to compress and elevate her leg to reduce her lower extremity edema. At follow-up two months later, the patient felt that her foot and ankle were 90% improved. Her dermal papules and plaques had resolved, with scattered brown patches of post inflammatory hyperpigmentation. Six months after noting 90% improvement, she started an insulin-like growth factor 1 receptor antibody for ophthalmopathy which can also improve skin disease.

Case Discussion

This case reports localized myxedema histologically mimicking SCL. We hope to raise awareness of and highlight the atypical presentations of localized myxedema, the histologic similarities between LM and SCL, and the importance of clinical context for diagnosis.

Localized myxedema, also known as pretibial myxedema or Graves dermopathy, is an extrathyroidal autoimmune manifestations of Graves disease. It occurs in 1.5% of patients with Graves disease, and nearly always occurs in patients who already have Graves ophthalmopathy [1]. Localized myxedema manifests as raised waxy

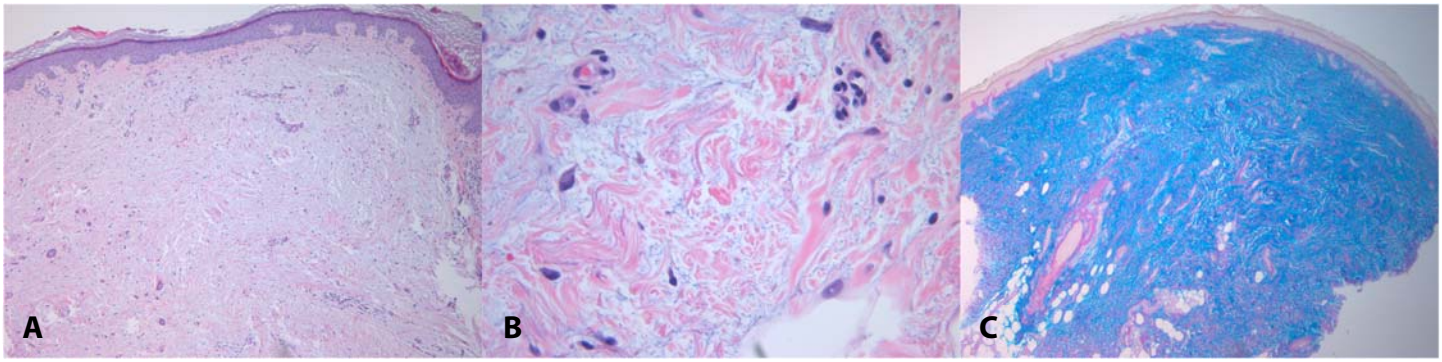

Figure 4. *Histology of localized myxedema. There is increased mucin evenly distributed throughout the dermis, with rare adipocytes. No prominent ropey collagen fibers are present.* ***A)*** *H&E, 5×;* ***B)*** *H&E, 40×;* ***C)*** *colloidal iron stain, 2.5×.*

papules and plaques, which range from light-to-yellowish brown. Lesions are often symmetrical over the pretibial area or feet, but can occur in many different areas, making localized myxedema the preferrable terminology. There are multiple morphologic presentations, which can complicate diagnosis [2]. Forty-three percent of patients have diffuse, nonpitting edema. Twenty-seven percent of cases present with plaques, 18% of patients have tumors or nodules, and 5% of cases present with severe lymphedema and nodules mimicking elephantiasis [3]. Our patient had a tumor-like initial morphology on the dorsal foot. She also had an isomorphic response, with further growth of her LM following surgical excisions. This adds to the small body of reports describing worsening of LM in response to surgical or mechanical trauma, some relatively remote [4]. First-line treatment is application of topical corticosteroids and our patient responded well to clobetasol ointment. Her initial lack of response to topical corticosteroids years prior likely clouded her clinical picture. For refractory cases, treatment options include glucocorticoid and hyaluronidase injection. For severe symptomatic cases, systemic corticosteroids, plasmapheresis, intravenous immune globulin, and rituximab can be tried [1,2].

Our patient's initial biopsy and excision specimens were believed to be consistent with spindle cell lipoma, given her early tumor-like morphology and the pathologic similarities between the two conditions. Spindle cell lipoma is a rare variant of lipoma and is a benign tumor typically found on the posterior trunk, shoulder, and neck. It generally occurs in men ages 40-60 and can be treated with wide local excision. Histologically, SCL consists of mature adipocytes, uniform spindle cells, and bundles of collagen. The proportion of each component is highly variable, complicating diagnosis. Notably, a prominent myxoid stroma can be seen. Other entities in the differential diagnosis include other lipomatous tumors, other spindle cell tumors, and myxoid lesions [5,6]. The pathology of LM consists of mucin, lymphocytic infiltrate, and large stellate fibroblasts [7]. In the context of a nodule on the foot, a biopsy of LM with mucin and fibroblasts could thus easily be interpreted as SCL with prominent myxoid stroma. Lack of response to wide local excision should prompt re-evaluation of the diagnosis, as in this case. With later evaluation, her morphology had advanced to become more consistent with typical LM on the shin and her diagnosis became more clear.

Conclusion

With this case, we hope to emphasize several key points. Clinicians should have high suspicion for LM in patients with a history of Graves disease and exophthalmos, particularly if they present with masses on the lower extremities or areas of chronic pressure. Lack of response of a suspected SCL to wide local excision should prompt re-consideration of this diagnosis. Localized myxedema can have isomorphic response, with regrowth after surgery. Localized myxedema should be included on the histologic differential for SCL with prominent myxoid stroma, particularly in those cases not responding to treatment as anticipated.

Potential conflicts of interest

The authors declare no conflicts of interest/[the following potential conflicts].

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