

Elephantiasic Pretibial Myxoedema in a Patient with Graves' Disease

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Abstract

Pretibial myxoedema (PM) is a late and rare manifestation of autoimmune thyroiditis, particularly in patients with Graves' disease. It occurs in 0.5% to 4.3% of patients [1], and is usually associated with high levels of thyroid hormones. The classification of PM includes four forms: non-pitting edema; plaque; nodular; or elephantiasis [1]. Mild PM often regresses spontaneously, but the severe, elephantiasic variant is typically progressive and refractory to treatment. Elephantiasic pretibial myxoedema (EPM) is characterized by massive edema, skin fibrosis and verrucous nodule formation, and it clinically resembles lymphedema. Herein, we describe a man with Graves' disease presenting with EPM for nearly 2 years. Although advanced cases have been described in the literature, to our knowledge, none have reached this level of severity.

Keywords

Pretibial Myxoedema (PM), Graves' Disease

1. Introduction

A 57-year-old Chinese man came to our clinic for advice on the cause and management of a severe skin condition of his legs. His lesions had occurred and progressed relentlessly over the past year. There was no obvious pain, but there was occasional pruritus. Once local skin was injured, it needed more than a month to heal. Physical examination revealed nonpitting edema, flesh-colored to erythematous, firm, confluent, polypoid nodules and fissured plaques extending from the shins to the heels of the feet, the dorsa of the left foot and the large toe (**Figure 1**). Initially, the disorder was thought to be the result of chronic lymphedema. However, his proptosis with eyelid retraction bilaterally reminded us to consider another diagnosis. Questioning the patient revealed that

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Figure 1. Nonpitting edema, flesh-colored to erythematous, firm, confluent, polypoid nodules and fissured plaques extending from the shins to the heels of the feet, the dorsum of the left foot and large toe.

he had been diagnosed with hyperthyroidism 15 years ago and treated with oral therapy for 6 months (he did not remember the details). A laboratory evaluation revealed: thyrotropin (TSH), <0.01 IU/mL (0.30 - 5.56); free thyroxine (T4), 31.01 pmol/L (11.46 - 23.17); free triiodothyronine (T3), 11.95 pmol/L (2.80 - 7.10); thyroglobulin (TG), 150 mg/ml (0.00 - 85.00); anti-thyroid peroxidase antibody (A-TPO), and 39.60 IU/ml (≤ 34). The patient looked healthy without evidence of other malignancy or systemic disease. He refused our request for a biopsy. Based on the clinical and laboratory results, EPM in Graves' disease was diagnosed. The patient was referred to the Department of Endocrinology to treat his hyperthyroidism, and then he was lost to follow-up.

2. Discussion

The most common presentation of dermatopathy in Graves' disease is PM. The time delay from treatment of hyperthyroidism to presentation with localized myxoedema varies from 1 month to 16 years (mean 5.13 years). Clinical features are nonpitting scaly thickening and induration of the skin. In a previous report, among 150 patients with PM, 58% had nonpitting edema, 20% had the nodular variant, 21% had the plaque type, and less than 1% had either the polypoid or the elephantiasic morphologies [2]. Although several theories have been suggested, the exact pathogenesis of PM remains to be clarified [3]. It was speculated that pretibial fibroblasts may

react with T cell lymphocytes via their thyrotropin receptors and then they may overproduce glycosaminoglycans. The content of hyaluronic acid and chondroitin sulfates in the dermis is increased, causing compression of the dermal lymphatics and nonpitting edema. The predilection for localization to the pretibial area may result from trauma with the release of inflammatory cytokines and inflammatory cells or local hypoxia resulting from arterial or venous insufficiency.

The diagnosis of EPM is easily made by clinical findings and histological investigation. Our patient refused a skin biopsy. Thus differential diagnoses, including secondary edema resulting from chronic lymphatic obstruction or venous insufficiency, diabetic dermopathy, lichen amyloidosis and hypertrophic lichen planus were considered. The history of hyperthyroidism and abnormal levels of T3, T4, TG and A-TPO supported the diagnosis. Other systemic examinations excluded diabetes and vascular diseases. Therefore, the final diagnosis was made.

EPM is typically progressive and refractory to treatment. Some therapeutics are effective but are not curative. A potent topical glucocorticoid applied under occlusion is the primary treatment although intralesional steroids are sometimes used. However, local and systemic steroids very rarely give improvement. Other therapeutics have been reported. A 44-year-old woman with Graves' disease and EPM was treated in a trial of multiple recognized therapies, but had a rapid response to rituximab and plasmapheresis [4]. Another patient with PM improved significantly after treatment with I¹³¹ for his Graves' disease [5]. Some authors have reported using complete decongestive physiotherapy [6] or low-dose intravenous immunoglobulins [7] to treat EPM, and have obtained satisfactory results.

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