۳۰ درصد تخفیف نوروزی ویژه کارگاه‌ها و فیلم‌های آموزشی

اصول تنظیم قراردادها

پروپوزال نویسی

آموزش مهارت های کاربردی در ندوین و چاب مقاله
Localized Myxedema of the Toe: A Rare Presentation of Graves’ Dermopathy

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Infiltrative dermopathy is an uncommon manifestation of Graves’ disease. The most frequent location of infiltration is the lower extremities, especially the pretibial areas and on the dorsum of the foot. Rarely the hand, elbow, arm, and forearm are affected.

We report a 66-year-old man with Graves’ disease of nine years duration who presented with dermopathy and nonpitting edema of the toe with no involvement of the pretibial portion since four years ago. Radiologic studies of the foot were normal, without subperiosteal bone formation or reaction. Skin biopsy was consistent with pretibial myxedema. This presentation of myxedema and limitation to a localized area for several years is very unusual.

Keywords: Dermopathy • Graves’ disease • myxedema

Introduction

Dermopathy is an uncommon manifestation of Graves’ disease. Little information is available about its natural course and its relation to other manifestations of Graves’ disease. The pretibial area is the most commonly involved (99.4%) region.1,2

We report a case who presented with dermopathy and nonpitting edema of the toe, which had remained limited to this area for four years. The literature on Graves’ dermopathy and pretibial myxedema indicates that this form of dermopathy, limited to the toe with no extension for several years, is unusual.1,3,4

Case Report

A 66-year-old man who had been diagnosed as having Graves’ disease (ophthalmopathy and thyrotoxicosis) since nine years ago presented with toe enlargement. He had suffered from diabetes mellitus (type 2) in the last five years and also from coronary artery disease for which he was recommended to have coronary artery bypass graft surgery.

His drug history was metformin 500 mg/day, captopril 25 mg/day, ASA 80 mg/day, propranolol 40 mg/day, and nitroglycerin 2.6 mg thrice daily.

Nine years ago, he had been treated with methimazole for two years and because of the recurrence of Graves’ disease, he received an ablative dose of 20 mCi (740 MBq) iodine-131. The patient had developed hypothyroidism secondary to iodine ablation of the thyroid, so in the follow-up, levothyroxine 100 µg/day was started and the patient became euthyroid with a maintenance dose of 800 µg/week.

Four years ago, his left big toe began to enlarge gradually. He had no pain or dysesthesia. He was referred to us because of the atypical manifestation and progressive enlargement that had recently extended to his ankle.

On physical examination, he had exophthalmus, proptosis, and staring (Figure 1A) but no lid lag. The thyroid gland was diffusely enlarged, with a firm texture but no nodule. The left big toe was generally enlarged and edematous (Figures 1B and 1C). The edema was firm, nonpitting, and slightly
erythematous. No ulcer, tenderness, scaling, or nail abnormality was detected. The pretibial portion and foot were normal, but the left ankle circumference was increased (one centimeter difference in comparison with the right side). The rest of the systemic examination was unremarkable.

Plain radiograph of the toe was normal and no subperiosteal bone formation was seen. Because of this unusual lesion, a skin biopsy was taken. One piece of skin measuring 1×0.5×0.5 cm with a rubbery consistency was examined microscopically, which revealed hyperkeratotic epidermis covering the dermis, and empty spaces splitting collagen fibers with some mucin-like material between them. The final diagnosis according to the pathology report was consistent with pretibial myxedema. To treat the local discomfort, topical glucocorticoid ointment covered by an occlusive dressing (fluocinolone 0.02%) was applied. The patient was followed for five months and a relative response to the local treatment without any disease progression was achieved. An informed consent was obtained from the patient.

Discussion

This patient had dermopathy, which is an uncommon manifestation of Graves’ disease. Moreover, he had the unusual presentation of localized myxedema of a single toe for several years. In a case series of 178 patients with thyroid dermopathy visited at an institution between 1967

Figure 1. Graves’ ophthalmopathy (staring and proptosis) of the patient (A). Chronic Graves’ dermopathy of the toe. The lesion is firm, nonpitting, and limited to the toe (B and C).
Graves' dermopathy

Graves' disease is characterized by diffuse goiter, thyrotoxicosis, infiltrative orbitopathy and ophthalmopathy, and occasionally, infiltrative dermopathy.  

Infiltrative dermopathy (localized myxedema) is the least common manifestation of Graves' disease. It occurs in up to 4 to 5% of patients with Graves' disease. The characteristic abnormality—skin thickening—is usually limited to the pretibial area (99.4%). Thus, the disorder has been called pretibial myxedema. However, because it occasionally occurs in other areas, localized myxedema is a more appropriate term. 

Pretibial myxedema is an autoimmune manifestation of Graves' disease and this localization relates to mechanical factors and dependent position. Rarely the fingers, hands, elbows, arms, or face are affected. In acropathy, another presentation of Graves' dermopathy, subperiosteal new bone formation is also present.

The antigen for T-cell reaction is the TSH receptor, and TSH receptor antibodies are important in the pathogenesis of Graves' dermopathy. This etiologic role for TSH receptor antibodies and TSH receptor-specific T-lymphocytes could also explain the occasional worsening of dermopathy after trauma, surgery, and radioiodine therapy for hyperthyroidism.

Clinical features of infiltrative dermopathy are nonpitting scaly thickening and induration of the skin, papules, nodules, pigmentation, plaque, and rarely elephantiasic form. The content of hyaluronic acid and chondroitin sulfates in the dermis is increased, causing compression of the dermal lymphatics and nonpitting edema.

Differential diagnoses of infiltrative dermopathy are chronic lymphatic and venous obstruction of the lower extremities, chronic dermatitis, and cutaneous mucinosis. Skin biopsy may be necessary to establish the correct diagnosis.

In this case, history of ophthalmopathy was positive but dermopathy had developed five years later. In a recent review, the most common time of onset of dermopathy was one to two years after the diagnosis of thyrotoxicosis. Iodine ablation was a risk factor for myxedema dermopathy in this patient, but history of trauma was negative.

His left big toe had gradually become edematous since four years ago and extended to the ankle in the recent two months. The typical lesions usually appear over a period of several months and then stabilize, or in some patients, regress spontaneously.

The diagnosis of infiltrative dermopathy is usually confirmed by the location, nonpitting nature, and distinct borders of the lesions in a patient who has longstanding hyperthyroidism, has suffered from the disease for several years, or has ophthalmopathy. In this case, both the location and nature of the lesion were atypical and biopsy was necessary to establish the correct diagnosis and differentiate it from chronic dermatitis, cutaneous mucinosis, and chronic venous and lymphatic obstruction, although the latter is unusual in a localized lesion. The histopathologic features of the skin were typical and diagnostic.

Will this lesion progress to involve the whole foot? We do not know the answer, but considering this probability and the local discomfort, treatment with topical glucocorticoid ointment covered by an occlusive dressing (fluocinolone 0.02%) was started.

Dermopathy may be quite resistant to this treatment and response will be determined in the follow-up. Resistant lesions may require systemic glucocorticoid therapy.

A new drug in refractory pretibial myxedema is octreotide (insulin-like growth factor 1 antagonist), which was administered in a case as intraleisional injection and improved the tumoral lesions. But in another report of three cases, lack of long-term effects of octreotide has been reported.

This case showed that Graves' dermopathy may present as an edematous toe and be localized for several years. As we know, myxedema relates to mechanical factors and occurs in dependent areas, but in a patient with no obvious history of trauma, involvement of one toe is very unusual and other factors must be considered.

In spite of euthyroidism, we believe that autoimmune processes are still on track. Hence, ophthalmopathy and dermopathy could be related to this active trend.

References

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