

CASE REPORT

Pretibial myxedema exhibiting prominent asymmetrical manifestations

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ABSTRACT

Pretibial myxedema (PTM) is an uncommon cutaneous manifestation of Graves' disease. A 62-year-old obese Japanese man treated for Graves' disease presented with nodular lesions symmetrically on both pretibial areas. Systemic corticosteroid therapy targeted against simultaneously developing severe Graves' ophthalmopathy almost completely cleared his skin symptoms. About ten years later, edema of both lower legs recurred, and the right lower leg showed an elephantiasis-like condition with nodules. However, the left leg had less edema and only a few nodular lesions. The skin lesions gradually improved with oral prednisolone. We speculate that our patient's habit of lying on the right side of the body induced prominent asymmetry of skin lesions by pooling some immune mediators.

Keywords: Pretibial Myxedema; Asymmetry; Graves' Disease; Systemic Corticosteroid Therapy; Recurrence

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1. Introduction

Pretibial myxedema (PTM) is an uncommon cutaneous manifestation of Graves' disease that usually presents as symmetrical thickening and induration of the shins and dorsa of the feet. Here, we report a peculiar case of PTM exhibiting prominent asymmetrical distribution at the time of recurrence and provide a plausible explanation.

2. Case presentation

A 62-year-old obese Japanese man who had been treated with 10 mg of thiamazole for Graves' disease for about 3 years visited our department with asymptomatic skin problems. Physical examination revealed pigmentation and thickening of the skin on both pretibial areas, with various-sized pink nodules (**Figure 1a**). Laboratory data showed normal free T3 level, low thyroid-stimulating hormone (TSH) level, and high TSH receptor antibody (TRAb). The skin biopsy of a nodule revealed hyperkeratotic epidermis, remarkable edematous changes, and perivascular lymphocytic infiltrations in the dermis. Alcian blue stain demonstrated mucin deposition throughout the dermis (**Figure 1b, 1c**). Based on these findings, his skin lesion was diagnosed as PTM. Systemic corticosteroid therapy targeted against simultaneously developing severe Graves' ophthalmopathy almost completely cleared his skin symptoms in 3.5 years. However, 10 years after the first visit, he revisited the hospital complaining of swelling of the skin, especially of

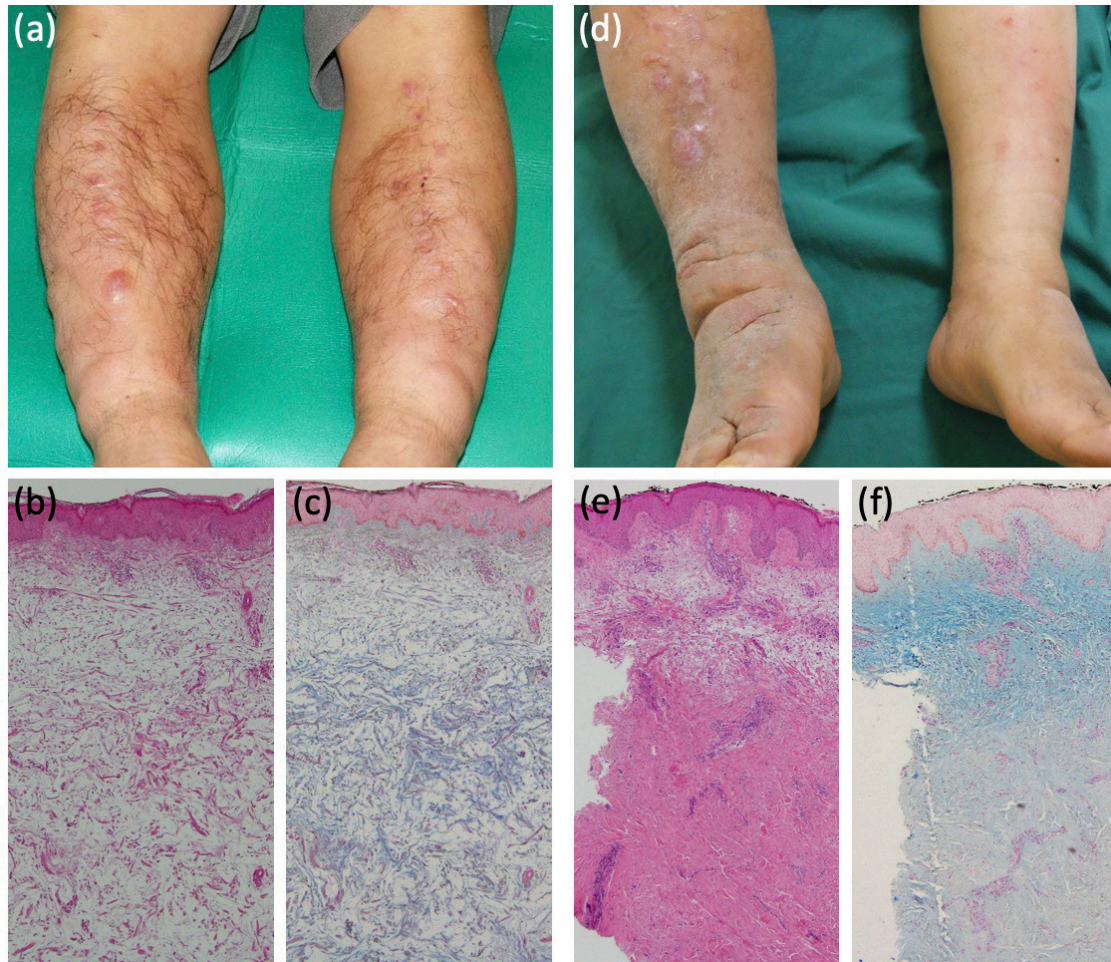


Figure 1. The course of the patient's skin lesions and skin specimen from the nodular lesions from the right lower leg. (a) Picture taken at first visit: pigmented thickening of the skin on both pretibial areas accompanied by various-sized pink nodules. (b) Histopathology of a nodular lesion at the first visit showing hyperkeratotic epidermis and remarkable edematous changes in the dermis (hematoxylin-eosin stain, $\times 40$). (c) Mucin deposition was seen throughout the dermis when (b) was stained (Alcian blue stain, $\times 40$). (d) Picture at the time of recurrence: the right lower leg showing marked coarse thickening of the skin with coalescing nodules and elephantiasis-like changes around the dorsum of the foot in comparison with the left lower leg. (e) Histopathology of the elephantiasic lesion at the time of recurrence showing papillomatous changes in the epidermis, edema confined to the upper dermis, and eminent lymphocytic infiltrations (hematoxylin-eosin stain, $\times 40$). (f) Edematous area in (e) stained blue (Alcian blue stain, $\times 40$).

the right lower leg. He stated that he habitually lay in a right lateral supine position, day and night, for several years. On physical examination, the right lower leg showed marked coarse thickening of the skin with coalescing nodules and elephantiasis-like changes around the dorsum of the foot, compared to the left lower leg showing only few nodules (**Figure 1d**). A venous ultrasonography did not demonstrate varicose veins or intravenous thrombus on the right leg. Serum TRAb level was elevated again. The second skin biopsy from the elephantiasis-like lesion presented findings similar to the first one. We also noticed papillomatous changes in the epidermis,

mucin deposition confined to the upper dermis, and more prominent lymphocytic infiltrations (**Figure 1e, 1f**). As topical corticosteroid treatment did not improve this enough, systemic corticosteroid therapy with prednisolone 10 mg/day was initiated, which resulted in gradual alleviation of skin lesions and a decrease in serum TRAb level.

3. Discussion

PTM is an autoimmune manifestation of Graves' disease. For most patients, therapy is not needed because the lesions are usually not symptomatic or particularly unsightly and may regress

with time^[1]. However, our patient's complaints were so pressing that we tried systemic corticosteroid therapy which was not commonly used but was reported to be effective for elephantiasic PTM by Shirai *et al*^[2]. They stated that low-dose corticosteroid suppressed pretibial fibroblasts and T cells, with a resulting decrease in glycosaminoglycans production in the dermis. Additionally, we consider that systemic corticosteroid therapy brings favorable results by reducing serum TRAb level.

Although TRAb, which stimulates pretibial fibroblasts to produce glycosaminoglycans, might play a role in the development of PTM^[3], mechanical contribution has also been proposed to be involved in its pathogenesis^[1]. Dependent edema may reduce the clearance and prolong the half-life of fibroblast-stimulating cytokines^[4]. Rodia *et al.* reported a case of Graves' dermopathy, which appeared only on the left leg and left hand of a patient who preferentially slept laying on the left side, and suggested that gravitational factors, such as the sleeping position, were responsible for unilateral-ity of the lesions^[5]. Volke's case of unilateral pitting edema of the left leg in a patient with Graves' disease also grabbed our interest^[6]. However, that case demonstrated no mucin deposition in the skin lesions histopathologically, while our case was a definite PTM. We speculate that our patient's habit of lying on the right side of the body induced prominent asymmetry of skin lesions by pooling immune mediators such as TRAb on the dependent side. This might provide modest evidence of the involvement of local and mechanical factors in the pathogenesis of PTM.

Conflict of interest disclosure

None declared.

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