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Elephantiasic Graves' Dermopathy in a Patient with Negative Thyroid-Receptor Auto-Antibodies

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Dear Editor:

A 64-year-old man presented with elephantiasic skin changes of the lower extremities evolved over a period of minimum 10 years. He was obese (body mass index, 34.6 kg/m^2) but had no significant co-morbidities.

The skin changes were localized on the dorsal sides of the feet, on the crurae as well as on the left femur (Fig. 1), and consisted of pachydermal hyperkeratosis and a characteristic cobblestone appearance with malodourous scattered impetiginized crusted wounds and fissures. Clinically, the skin changes were compatible with the elephantiasic form of Graves' dermopathy (GD). A deep skin biopsy showed substantial fibrosis, edema, and a slightly increased amount of mucin in both papillary and reticular dermis. However, the mucin was mainly located in reticular dermis (Fig. 2). There were no lymphatic proliferation or other signs of lymphangiomatosis. Histopathologically, a diagnosis of GD was neither rejected, nor confirmed, due to the massive edema and fibrosing tissue. Subclinical hyperthyroidism was present (thyroid-stimulating-hormone $<$ 0.0014 (reference, 0.30 $\sim$ 4.50) 10^{-3} ie/L, thyroxine = 108 (reference, 60 $\sim$ 140) nmol/L, and triiodothyronine = 1.26 (reference, 1.10 $\sim$ 2.50) nmol/L). Thyroid-receptor-antibodies (TRAb) were negative. An ultrasound examination of the thyroid showed a multinodular goiter. A computed tomography-scan of thorax and abdomen rejected internal disease and ve-

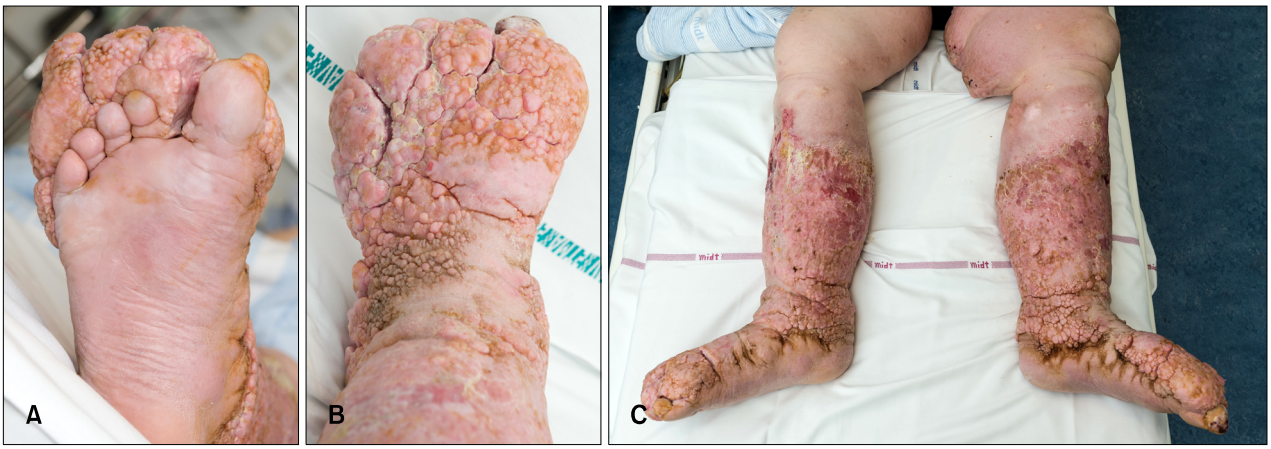

Fig. 1. (A $\sim$ C) Elephantiasic skin changes on the dorsal sides of the feet and legs consisting of pachydermal hyperkeratosis and a papillomatous cobblestone appearance with malodourous scattered impetiginized crusted wounds and fissures.

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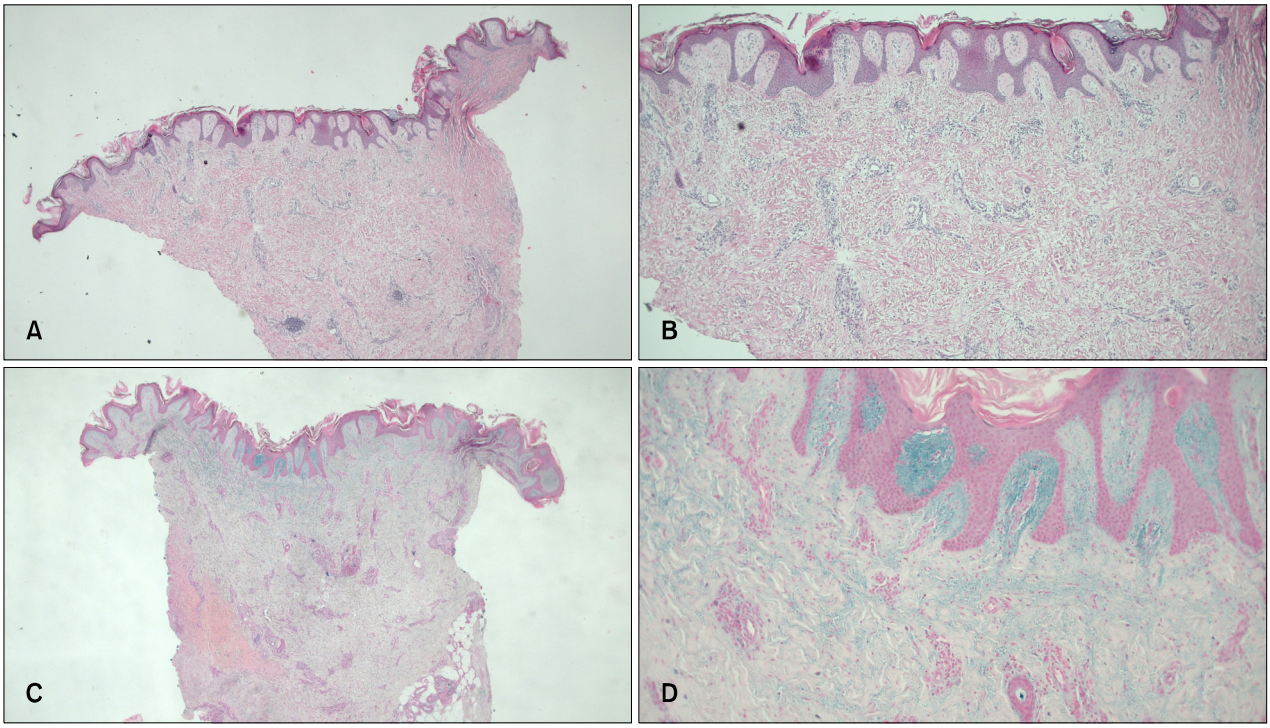

Fig. 2. Histopathology. (A) Punch biopsy from lower leg, showing papillary epidermal hyperplasia, slight inconspicuous vascular proliferation and edema (H&E, ×20). (B) Higher magnification. Inconspicuous vascular pattern (H&E, ×40). (C) Increased amount of mucin in papillary and reticular dermis (Colloidal iron stain, ×20). (D) Higher magnification showing the distribution of mucin in dermis (Colloidal iron stain, ×100).

nous obstruction. There was no history of leg trauma, former thyroid disease, previous risk of lymphatic filariasis infection, nor presence of eosinophilia.

Betamethasone with clioquinol and sodium permanganate water combined with extensive compressive therapy including intermittent pneumatic compression only improved skin changes marginally. Euthyroidism was achieved treating with thiamazole.

GD present in approximately 1,5% of patients with Graves' disease and is characterized by localized thickening of the skin, typically in the pretibial area. The pathogenesis is complex and not fully understood. However, immunologic, cellular, molecular, environmental, and mechanical factors are believed being involved. Among these, an autoimmune process stimulated by TRAb is considered the main factor[1,2]. The skin changes are caused by an increased fibroblast synthesis of mucin accumulating in primarily the papillary and reticular dermis with subsequent edema due to fluid retention. In severe cases, the lymphatic microcirculation may obstruct leading to additional lymphedema and development of elephantiasis[2]. Graves' ophthalmopathy is typically concomitantly present[2].

GD is associated with positive TRAb and must be questioned in the absence hereof[1]. However, cases of TRAb negative GD have been reported[3,4].

Heart failure, nephrotic syndrome, obesity, lymphangiomatosis, cancer or venous obstruction subsequent to surgery can cause lymphedema and skin changes clinically compatible with GD[5]. Except of obesity, none of these were present in this patient and this combined with: 1) the classic clinical skin changes, 2) the histopathological findings compatible with GD, albeit masked by the chronicity of the condition, and 3) the patient's neglect for several years making a previous undiagnosed Graves' disease likely, the clinical picture of this patient was in keeping with elephantiasic GD.

Thus, in conclusion, we present a case of a TRAb negative GD progressed to an extreme elephantiasic form. Clinicians should consider GD as a differential diagnosis in patients with skin changes clinically compatible with GD even though TRAb are undetectable and ophtalmopathy is absent.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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