Euthyroid pretibial myxedema and EMO syndrome

E. Şenel and A.T. Güleç

SUMMARY

EMO syndrome is a rare extrathyroid syndrome, seen in only 1% of patients affected by extrathyroid complications of Graves' disease. A 73-year-old woman presented with a 1-year history of asymptomatic local swellings on her legs and feet. Physical examination revealed moderate proptosis and multiple, firm subcutaneous nodules of 1 to 5 cm in diameter located on the anterior and medial aspects of the shins and on feet. The patient had a history of bilateral knee arthroplasty 5 years ago. Histopathologic examination showed deposition of mucin and perivascular lymphocytic infiltration in the dermis. Dermatologic and pathologic findings were consistent with pretibial myxedema. Laboratory tests showed normal thyroid stimulating hormone (TSH) and serum free T_3 and T_4 levels. The TSH receptor antibody titer was elevated. Thus, with all these findings she was diagnosed with exophthalmia, myxedema, and hypertrophic osteoarthropathy (EMO) syndrome. The lesions were completely treated with three monthly intralesional corticosteroid injections and at the 4-month follow-up no recurrence was observed. Only three euthyroid cases with pretibial myxedema have been reported in the literature. Patients that have asymptomatic pretibial nodular or plaque lesions should be investigated with an ophthalmologic examination and laboratory workup to clarify a possible underlying thyroid gland disease and EMO syndrome.

KEY WORDS

extrathyroid syndrome, pretibial myxedema, EMO syndrome

Introduction

Pretibial myxedema (PM) is a late and rare manifestation of autoimmune thyroiditis, particularly of Graves' disease. It is usually associated with high levels of thyroid hormones. EMO syndrome, a rare (< 1%) disease, has a triad of exophthalmia, myxedema, and osteoarthropathy (1).

Case Report

A 73-year-old woman presented with a 1-year history of asymptomatic nodules on her legs and feet. The patient had a history of bilateral knee arthroplasty. Dermatological examination revealed bilateral moderate proptosis, multiple, firm, subcutaneous nodules of both lower legs and feet (Figure 1), and fusiform swelling of

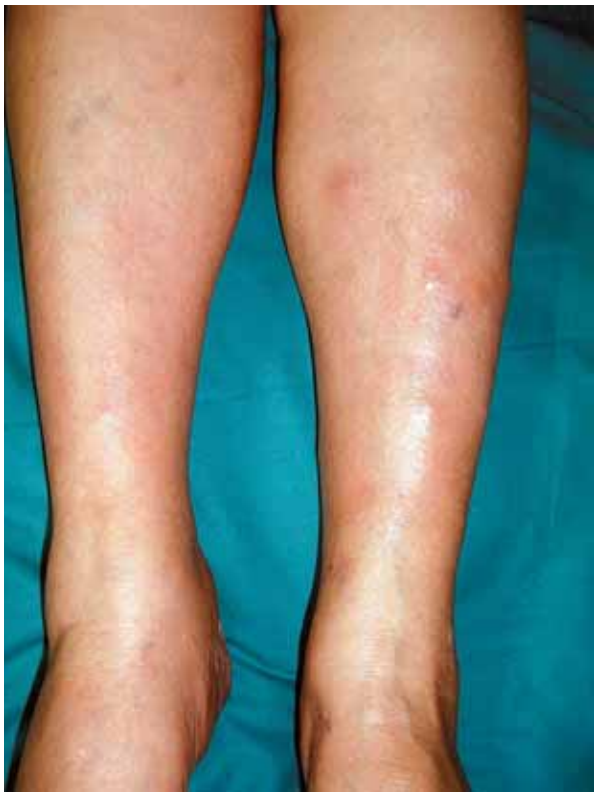

Figure 1. Multiple, firm subcutaneous nodules on both legs.

all digits with clubbing. Laboratory tests showed a normal thyroid-stimulating hormone (TSH) level at 2.34 mIU/mL (normal range, 0.35–4.0 mIU/mL), free triiodothyronine (T3) level at 2.67 pg/mL (normal range, 1.71–3.7 pg/ml), free thyroxine (T_4) level at 1.13 pg/ml (normal range, 0.8–1.9 pg/mL), and elevated TSH receptor antibody at 65.4% (normal <15%). Anti-TPO and antithyroglobulin antibodies were negative. Histopathologic examination disclosed deposition of mucin and perivascular lymphocytic infiltration in the dermis (Figure 2). The patient was diagnosed with exophthalmia, myxedema, and osteoarthropathy (EMO) syndrome. The lesions were completely treated with monthly intralesional triamcinolone injections, 5 mg/mL, 0.5 to 1.0 mL per nodule. Treatment was stopped at the third cycle and at the 9-month follow-up no recurrence was observed.

Discussion

Thyroid dermopathy, which is characterized by localized thickening of the skin, is a late and rare (1–4% of patients) manifestation of autoimmune thyroiditis, particularly of Graves' disease. It is occasionally related to Hashimoto's thyroiditis (2). It most commonly affects

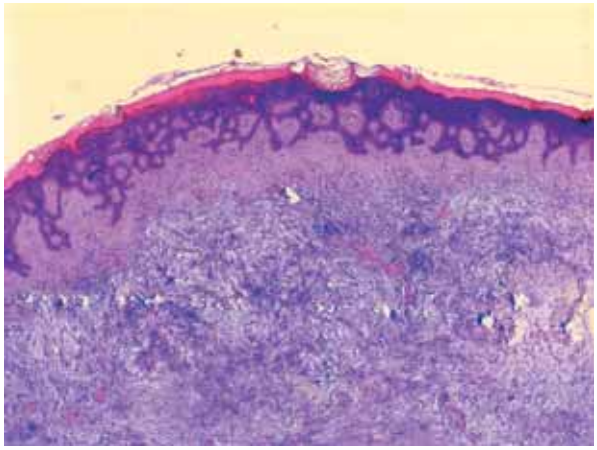

Figure 2. Mucin deposition in the dermis (Alcian blue, magnification ×4).

middle-aged females. Its onset usually follows ophthalmopathy, another extrathyroidal manifestation of Graves' disease (71.9%). It occurs in the pretibial region (93.3%), pretibial area and feet (3.9%), and pretibial area and upper extremities (1.1%). Therefore it is often referred to as PM. The clinical forms of lesions are nonpitting edema (43.3%), plaque (27%), nodule (18.5%) and elephantiasis (2.8%) (3). PM is usually asymptomatic; however, hyperhidrosis limited to the affected region has been described in the literature (4). Histopathologic examination of PM reveals typical mucin deposition and separation of normal collagen bundles by mucin.

Although several theories have been suggested, the exact pathogenesis of PM remains to be clarified. Autoantibodies against thyroid antigens and reactive T lymphocytes are thought to cross-react with connective tissue and muscle antigens. TSH receptor antibodies binding to the receptors in the connective tissue may stimulate fibroblasts to produce a large amount of glycosaminoglycans (5). It was speculated that pretibial fibroblast may react with T cell lymphocytes on their thyrotrophin receptors and then they may overproduce glycosaminoglycans (6). The predilection of localization to the pretibial area may result from trauma with the release of inflammatory cytokines and inflammatory cells or local hypoxia that results from arterial or venous insufficiency. Although PM does not seem to be related to the levels of T3 and T4, only three euthyroid cases with PM have been reported in the literature (7–9).

Treatment of PM is difficult. Topical corticosteroids under occlusion and intralesional corticosteroid injections are the therapy choices most often used. Octreotide (an insulin-like growth factor 1 antagonist) injections have been found to be beneficial for treating refractory PM in some recent reports (5, 10, 11).

Ophthalmopathy occurs in 30% to 40% of patients with Graves' disease (1, 3, 12). Exophthalmia, myxe-

dema, hypertrophic osteoarthropathy (EMO) syndrome is a rare extrathyroid syndrome, seen in less than 1% of the patients affected by extrathyroid complications of Graves' disease (1).

Although it is rare, PM should be kept in mind when subcutaneous nodular lesions are observed in a euthyroid patient. The patient should be investigated for the other extrathyroid complications of Graves' disease. Levels of TSH receptor antibody titer should be measured to clarify the exact diagnosis.

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AUTHORS' ADDRESSES

Engin Şenel, MD, Baskent University Faculty of Medicine, Department of Dermatology, 5. sokak No: 48 Bahcelievler, Ankara, Turkey 06490, e-mail: enginsenel@enginsenel.com
Ayşe Tülin Güleç, MD, same address