Answer to Dermacase continued from page 357

4. Pretibial myxedema

Pretibial myxedema (PM), often referred to as localized myxedema or thyroid dermopathy, is an autoimmune manifestation of Graves disease (GD). It affects approximately 4% of patients with GD and has also been described in euthyroid and hypothyroid patients.1,2 The classic triad of ophthalmopathy, thyroid acropathy, and PM occurs in less than 1% of patients with GD.1 With Graves ophthalmopathy (GO) preceding PM in approximately 78% of cases, most patients with PM have underlying ocular disease.1 Pretibial myxedema has a gradual onset and typically develops 12 to 24 months after the diagnosis of thyrotoxicosis. It tends to affect older adults (peak incidence in the sixth decade of life); women are more frequently affected than men (female-to-male ratio 3.5:1).2

There are 4 main clinical variants of PM: diffuse, non-pitting edema (43%); plaque (27%); nodular (18%); and elephantiasis (5%).2 The plaque and nodular forms usually occur on a background of nonpitting edema. The elephantiasic form is the most symptomatic and debilitating, consisting of nodular, polypoid, or fungating lesions with marked lymphedema. Lesions are commonly located in the pretibial regions and, less often, on the toes and feet.2,4 Involvement of the face, ears, chest, back, and upper extremities has rarely been described and has been associated with preceding trauma.2,4 The lesions can vary in colour and may exhibit a characteristic pea d’orange (orange peel) appearance and texture due to prominent hair follicles. Typically asymptomatic, they are rarely pruritic or painful. In severe cases associated with thyroid acropathy, bone pain can result from an underlying periostea reaction.2 Hyperhidrosis, hypertrichosis, and entrapment neuropathies have also been reported.2,3

All patients with active PM have antibodies against the thyroid-stimulating hormone receptor.2 Both humoral and cellular immune-mediated processes are involved in the stimulation of fibroblasts, resulting in the overproduction and accumulation of glycosaminoglycans (especially hyaluronic acid) in the dermis.2

Diagnosis

In most cases, diagnosis of PM is based on characteristic pretibial lesions, the presence of GO (especially exophthalmos), and a history of thyrotoxicosis. The diagnosis should be considered doubtful in the absence of GO. In select cases, a biopsy can be beneficial. Histopathologic findings include large amounts of glycosaminoglycans in the reticular dermis, fragmentation of collagen fibres, and marked edema.2 Stellate fibroblasts and a scant, perivascular lymphocytic infiltrate might also be observed.2 Serologic evidence of thyroid autoimmunity could be required in some cases. Patients with active PM typically have high levels of serum thyroid-stimulating hormone receptor antibodies.2 Imaging studies (eg, bone radiography) can also help in diagnosing associated thyroid acropathy.

Differential diagnoses include simple edema resulting from chronic lymphatic obstruction or venous insufficiency, generalized myxedema, scleromyxedema, fibrosing dermopathy, diabetic dermopathy, cutaneous mucinosis, lichen amyloidosis, hypertrophic lichen planus, and chronic or lichenified dermatitis, such as lichen simplex chronicus.

Treatment

Usually PM is asymptomatic and can partially or completely resolve itself with time.6 Treatment is reserved for patients with cosmetic concerns, local discomfort, or functional impairment. As tobacco is associated with the autoimmune manifestations of GD, patients should be advised to stop smoking.2 Management of other risk factors, such as obesity, should be optimized. Although not yet proven, it has been suggested that the normalization of thyroid function has beneficial effects on PM.2

The mainstay of treatment remains topical corticosteroids under an occlusive dressing (eg, 0.05% fluocinonide cream under a plastic film) every night or every other night for about 4 to 6 weeks.2 Frequency of application can gradually be reduced as the condition improves. In severe cases, a more potent topical steroid (eg, 0.05% clobetasol propionate cream) should be considered.2 In some cases, intralesional corticosteroid or hyaluronidase injections can be administered with caution.2 Systemic immunomodulation is rarely indicated in patients with localized PM. In those with associated GO, however, systemic corticosteroids (eg, prednisone at 1-2 mg/kg daily) can prove beneficial. Case reports document mixed efficacy for octreotide, plasmapheresis, and intravenous immunoglobulin in the treatment of PM.5

To minimize fluid accumulation in the lower extremities, compression bandages or stockings are valuable adjuvants for more severe forms of PM. Complete decompensatory physiotherapy can help manage chronic lymphedema.2 Local excision of pseudotumorous lesions has been reported; however, surgical excision is not recommended, as PM is known to occur at sites of recent or previous trauma.2 Current therapies for PM are supportive at best; safer and more effective treatments are required.

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Competing interests

None declared

References