Brownish-grey, Papular Scaling Rash on the Trunk and Lower Limbs: A Quiz

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A 30-year-old man with Fitzpatrick skin type III/IV presented to our clinic with a moderately itchy rash on his back, shoulders and lower limbs. The symptoms had started approximately 15 years previously.

Skin examination revealed multiple, 1–2-mm, firm, hyperkeratotic, brownish-grey coloured papules symmetrically located on his trunk, shoulders and shins (**Fig. 1**). The lesions partly coalesced into large plaques on the surface of the shins, while disseminated maculo-papules were scattered on the trunk. Scratch marks were evident near the papules.

The patient reported that the lesions first developed on the pretibial part of the lower limbs, before appearing successively on other areas. The itch first presented together with the lesions on the lower limbs, before decreasing progressively in that area and reappearing in association with the recently-developed lesions on the back.

The patient's medical and family histories were unremarkable. Laboratory testing for complete blood count, IgE levels, renal hepatic and lipid profiles were within normal limits.

What is your diagnosis? See next page for answer.

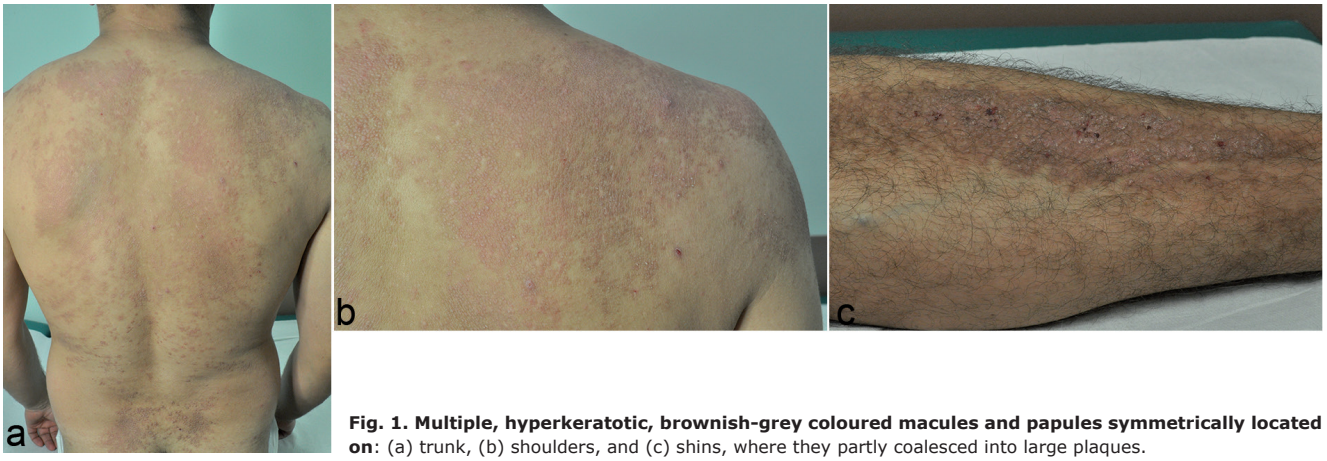

Fig. 1. Multiple, hyperkeratotic, brownish-grey coloured macules and papules symmetrically located on: (a) trunk, (b) shoulders, and (c) shins, where they partly coalesced into large plaques.

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ANSWERS TO QUIZ

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Diagnosis: **Generalized lichen amyloidosus**

Histopathological examination of a 6-mm skin-punch biopsy of a papular lesion on the left anterior surface of the leg revealed hyperkeratosis, acanthosis, hypergranulosis and elongated rete ridges (**Fig. 2**). The basal layer was characterized by vacuolization, ballooned degenerations, and rounded eosinophil bodies (Civatte bodies). The papillary dermis showed globular deposits of eosinophilic, amorphous acellular material, which presented as reddish orange on Congo red staining (**Fig. 3**).

These clinico-histopathological findings were suggestive for generalized lichen amyloidosus (LA).

LA is a subtype of primary localized cutaneous amyloidosis characterized by the deposition of amyloid, an abnormal fibrillar form of soluble autologous protein, in the papillary dermis, not involving the internal organs (1). LA is more common in males with olive or dark skin (2) and is generally sporadic, although up to 10% of patients may have an autosomal dominant family history (3, 4). In most cases the site of involvement is limited to the pretibial region, while generalized LA, with widespread involvement of the arms and trunk, is rarely reported (5–7). Our patient presented generalized LA involving both upper and lower extremities, trunk and lumbosacral area.

Multiple endocrine neoplasia type 2A (MEN2A) is often associated with LA (8). MEN2A is a hereditary syndrome characterized by medullary carcinoma of the thyroid with usual onset in childhood, pheochromocytoma, hyperparathyroidism and, often, cutaneous LA. The overall reported prevalence of LA in patients with MEN2A is approximately 50% (9), which results in LA being the second most frequent manifestation of the syndrome. The gene associated with MEN2 is called *RET*. A *RET* gene mutation leads to increased risk of developing medullary thyroid cancer and other tumours associated with MEN2.

Associations of other diseases, such as atopic dermatitis, lichen planus, mycosis fungoides, chronic urticaria, HIV infection, angiolymphoid hyperplasia with eosinophilia, and, more rarely, ankylosing spondylitis, autoimmune thyroiditis and hyperthyroidism, with LA have also been reported (5).

The precise pathogenesis of LA is unknown. According to the apoptosis theory, amyloid material in the papillary dermis is thought to derive from degenerated keratin peptides of apoptotic keratinocytes in genetically predisposed individuals (5–7). When LA is associated with other pruritic dermatological diseases, such as atopic dermatitis and lichen planus, chronic scratching and rubbing may be responsible for keratinocyte degradation and consequent amyloid formation. On the other hand, cases of LA without accompanying itch have been reported: LA may therefore not necessarily be secondary to chronic scratching. Pruritus could therefore be a possible symptom of this skin disease, not necessarily a causative factor (10, 11). In the case of our patient thyroid and parathyroid profiles were in the normal range, as were urinary and plasma catecholamines, metanephrine and normetanephrine. Because of the unremarkable past medical history of our patient and the absence of thyroid disorders, neck tumours or pheochromocytoma in the family history, a search for a possible mutation of the *RET* gene was, at least temporarily, put off.

Several treatment options have been reported for LA, mostly with unsatisfactory results, in particular concerning generalized LA. Among topical therapies, potent corticosteroids have been used with variable efficacy, but are obviously unfit for long-term use (12). Therapies with intralesional corticosteroid and topical calcipotriol, keratolytics, and dimethylsulphoxide (DMSO) have also been reported, with different outcomes (13, 14). Good results have been described in 2 cases with tacrolimus ointment 0.1%, one in monotherapy (14) and the other in combination with narrow-band UVB (13). Systemic options for treatment include colchicine, cyclosporine, cyclophosphamide, retinoids, UVB-nb and PUVA (6, 13). Given the widespread

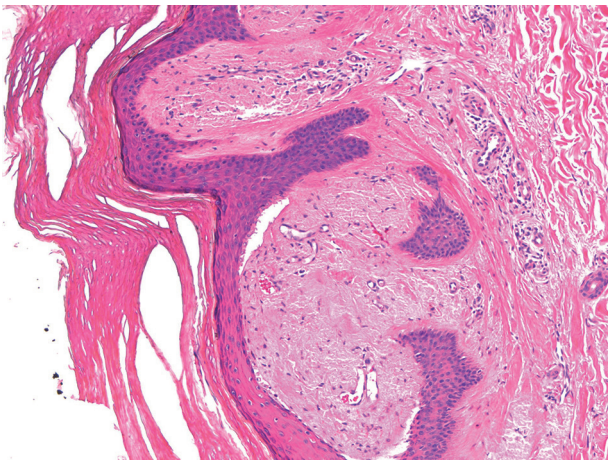

Fig. 2. Hyperkeratosis, acanthosis, hypergranulosis, and elongated rete ridges. Vacuolization, ballooned degenerations, and Civatte bodies in the basal layer (haematoxylin and eosin, ×100).

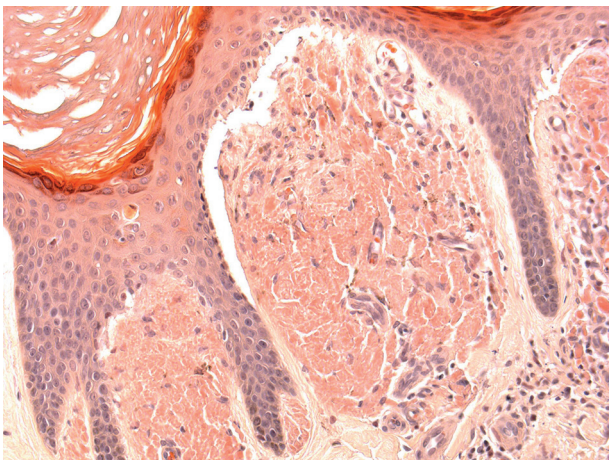

Fig. 3. Amorphous eosinophilic deposits in the papillary dermis (Congo red, ×200).

involvement, we prescribed tacrolimus ointment 0.1% twice daily for a month, which yielded a marked relief of itch, as well as a moderate decrease in the thickness of skin lesions.

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