

Mid-dermal Elastolysis: Another Dermatological Clue to Autoimmunity?

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Mid-dermal elastolysis (MDE) is a rare acquired skin disorder of the elastic tissue, which was first described by Shelley & Wood in 1977 (1). Since the original description, approximately 80 additional cases have been reported in the literature (2). MDE is clinically manifested by skin plaques with fine wrinkling, and histopathologically by a focal band loss of elastic fibres along the mid-dermis. Two main clinical variants have been described: well-defined patches of fine wrinkling (MDE type I) and perifollicular papular protrusions (MDE type II). A third type, consisting of a reticulate erythema on sun-exposed areas, has also been reported (MDE type III) (3).

The pathogenesis of MDE remains obscure. An enhanced extracellular matrix degradation secondary either to an increased synthesis of elastases or to an imbalance between activated matrix metalloproteinases (MMP) and their natural inhibitor molecules has been postulated. Similar to anetoderma, another elastolytic skin disorder involving the whole thickness of the dermis, MDE has been reported in association with several autoimmune disorders (4–8).

We report here a case of a middle-aged woman with a history of several organ-specific autoimmune diseases, who developed typical lesions of MDE. In addition, positive antinuclear, anti-pancreatic islets and anti-phospholipid antibodies were detected.

CASE REPORT

A 40-year-old Caucasian woman, with a medical history of type 1 diabetes mellitus that started at the age of 19 years, and dermatitis herpetiformis diagnosed when she was 25 years old, was referred to our department for evaluation of slowly progressive asymptomatic plaques on the trunk and limbs, which started 2 years before consultation. She did not complain about any other local (itch, redness or blistering) or systemic symptoms, except for a 15 kg weight loss in the context of a hypo-caloric diet. She did not report having taken any new medication in the past few years. The patient followed a gluten-free diet and had remained free from dermatitis herpetiformis symptoms for the last 14 years.

Physical examination revealed multiple small and soft, symmetrically distributed skin-coloured patches of flaccid wrinkled skin, mainly on the upper abdominal anterior wall (Fig. 1) and proximal upper extremities.

A 4-mm punch-biopsy was obtained from a wrinkled area. Histopathological examination disclosed a mild superficial perivascular lymphocytic infiltrate with scattered histiocytes and multinucleated giant cells on the upper and mid-dermis. Occasional elastic fibres engulfed within the cytoplasm of histiocytic and multinucleated cells (elastophagocytosis) were noted. Verhoeff van Gieson stain demonstrated the complete absence of elastic fibres along the mid-dermis (Fig. 2). Based on these data, the diagnosis of mid-dermal elastolysis was

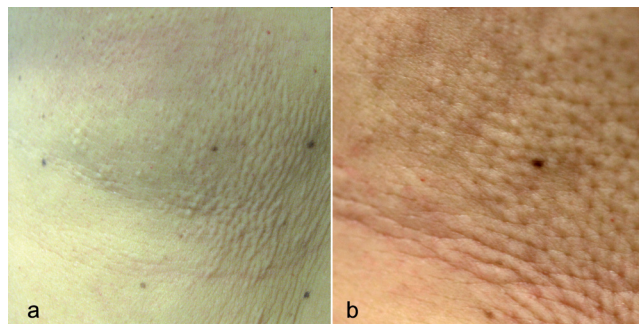


Fig. 1. Well-defined plaques with fine wrinkled skin on (a) the upper abdomen and (b) limbs.

achieved. No histological finding suggestive of dermatitis herpetiformis was observed.

An indirect immunofluorescence study of the patient's serum on normal human skin and salt-split skin failed to detect circulating immunoglobulin (Ig)G or IgA against any skin compartment. Further laboratory studies were performed; pathological findings consisted of polyclonal hypergammaglobulinaemia (21.4%; normal 11.1–18.8%) and positive antinuclear (titre 1/320, speckled pattern), anti-pancreatic islets (specifically, anti-glutamic acid decarboxylase (GAD) 65: 30.6 U/ml; 0–4.9 U/ml) and anti- β 2-glycoprotein-I IgM antibodies (anti- β 2GPI: 2.39 IU; 0–1 IU). Six months later, anti- β 2GPI IgM antibodies remained positive (2.18 IU) and anti-cardiolipin antibodies, which were previously negative, were also detected (15.3 MPL; 0–12.5 MPL). The patient did not mention any previous event of vascular thrombosis or spontaneous foetal loss; therefore, she did not meet the Sapporo diagnostic criteria for antiphospholipid syndrome. The patient carried the coeliac disease-susceptibility haplotypes DQ2A1 and B1. Anti-transglutaminase and anti-endothelial IgA antibodies, as well as other parameters evaluating a possible prothrombotic diathesis

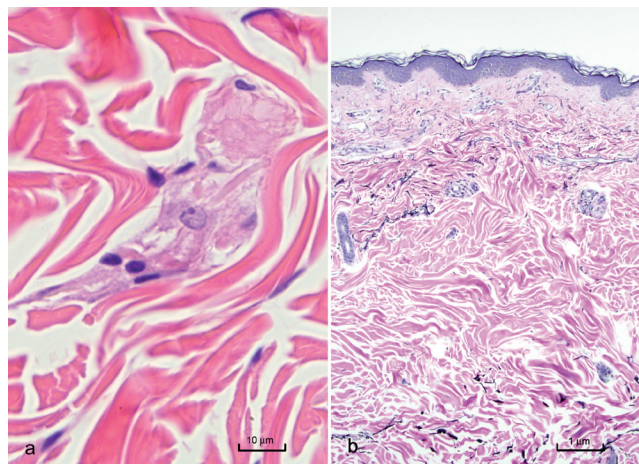


Fig. 2. (a) Multinucleated giant cells in the mid-dermis, with occasional elastophagocytosis (haematoxylin and eosin (H&E) \times 500). (b) Verhoeff van Gieson stain: complete absence of elastic fibres along the mid-dermis (H&E \times 500).

(fibrinogen, D-dimer, lupus anticoagulant, anti-thrombin III, factor II polymorphisms, studies of protein C and protein C-activator resistance, free protein S) were all within normal limits.

Oral hydroxychloroquine (200 mg/day) was prescribed. After 4 months, the patient reported cessation in the progression of the skin lesions, which otherwise remained unaltered on physical examination. After 10 months, plaques on the upper extremities have surprisingly disappeared, with persistence of the trunk lesions.

DISCUSSION

The eruption in MDE follows a symmetrical distribution, typically involving the trunk and upper proximal extremities, with the face and hands usually spared. Inflammatory urticarial papules and plaques have been occasionally reported to precede the development of MDE lesions.

A band-like focal loss of elastic fibres along the mid-dermis is the characteristic histopathological diagnostic feature of MDE. In early lesions, a perivascular infiltrate basically composed of lymphocytes is usually observed. Scattered interstitial histiocytes, multinucleated giant cells and occasional figures of elastophagocytosis may also be present. Older lesions are characterized by slightly thickened dermal collagen fibres parallel to the epidermis in the absence of inflammatory infiltrate. The papillary and deeper reticular dermis are usually spared and no prominent dermal actinic damage (elastosis) is observed. Ultrastructural studies have demonstrated phagocytosis of degenerated abnormal elastic fibres by macrophages, a loose assembly of skeleton fibrils and irregular aggregations of dense substance.

Elastic stains (e.g. orcein, van Gieson) exhibit a band-like loss of elastic fibres along the mid-dermis. With regard to the specific loss of elastic fibres' components in MDE, elastin is markedly reduced, whereas fibrillin is preserved. Immunohistochemical studies have demonstrated enhanced expression of CD34⁺ and CD68⁺ histiocytes and CD4⁺ lymphocytes in lesional skin (9, 10).

MDE has been associated with different autoimmune disorders (Table SI; available from <http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1292>), ranging from isolated serological findings (antinuclear antibodies, positive circulating immunocomplexes and false-positive serology for *Borrelia burgdorferi*) to well-defined diseases, such as lupus erythematosus (8), rheumatoid arthritis (5), Graves' disease (2) and Hashimoto's thyroiditis (6, 7).

An immune-mediated destruction of elastic fibres has also been postulated in anetoderma. For instance, anetoderma has been reported previously together with antiphospholipid antibodies (Table SII; available from: <http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1292>).

Taking the previous observations into account, and according to Witebsky's postulates (11), there is circumstantial evidence (presence of a lesional inflammatory infiltrate, frequent association with autoimmune disor-

ders) to support the hypothesis of an autoimmune origin of MDE. However, indirect immunofluorescence study failed to detect circulating IgG or IgA antibodies against the dermal-epidermal junction or any dermal structure, including elastic fibres or collagen bundles.

The management of MDE remains challenging. Multiple agents have been used with no clear benefits, including topical (steroids and tretinoin) and systemic drugs (chloroquine, clofazimine, colchicine, dapsone, systemic steroids and vitamin E) (2, 12). Sunscreen is considered essential. We treated our patient with oral hydroxychloroquine due to the constant development of new skin lesions. After 10 months, the patient reported cessation of disease progression and remission of the plaques on the upper extremities. However, the follow-up time is too short to allow us draw a definite conclusion.

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