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Case Report

Eruptive mid-dermal elastolysis: report of a case and brief review of the literature

發疹性真皮中部彈性組織溶解：一例報告及簡要文獻回顧

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Mid-dermal elastolysis (MDE) is a rare, acquired, idiopathic disorder of elastic tissue, characterised clinically by macules and plaques with superficial fine wrinkling and histologically by focal loss of elastic tissue in the reticular dermis. Herein we present a 26-year-old female patient with eruptive MDE and briefly review the current literature. Except for stressful life events recently, no causative factor could be elicited from personal history. A trial of topical medications was ineffective both in reducing the unsightly appearance and in halting MDE progression. Awareness of the condition and reporting of successful therapeutic experiences might enable appropriate management of affected patients.

真皮中部彈性組織溶解是一種罕見的後天特發性的彈性組織疾病，其特徵是臨床上表現為表面有細微皺紋斑點和斑塊，組織學上表現則為網狀真皮中彈性組織的局部損失。本文闡述了一名 26 歲的女性患者的發疹性真皮中部彈性組織溶解病例，並簡要回顧當前文獻。除了最近的生活壓力外，問診中未能找到因果關係因素。外用藥物的試驗，均未能改善患者因此病導致的外觀影響或阻止病情繼續。對此病的認識及成功治療經驗的報告可以有效提高受影響患者得到適切治療的機會。

Keywords: Anetoderma, elastic tissue disorders, elastolytic disorders, mid-dermal elastolysis

關鍵詞：皮膚鬆弛症、彈性組織疾病、彈性溶解疾病、真皮中部彈性組織溶解

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Introduction

Mid-dermal elastolysis (MDE) is a rare, acquired, idiopathic disorder of elastic tissue, characterised clinically by macules and plaques with superficial fine wrinkling and histologically by focal loss of elastic tissue in the reticular dermis.[1] Up to now, less than a hundred cases have been reported.[2,3]

Case report

A 26-year-old female patient presented to

Dermatology Outpatient Clinic with a 1-month history of asymptomatic wrinkling on the back, arms and chest. The lesions had been rapidly spreading, and each day she noticed new areas of involvement. Prior to admission, she was diagnosed to have pityriasis versicolor and she received oral and topical antifungals, without obvious benefit. She could not recall an erythematous stage before the development of these lesions. Personal medical history was unremarkable, except for recent stress. There was no history of atopy, smoking, UV exposure, sunbed use, intake of oral contraceptive pills or other medications. There was no family history with a similar condition.

Dermatological examination revealed flesh-coloured, discrete and confluent macules and plaques with overlying fine wrinkling and *peau d'orange* appearance, located on the back, chest, in the abdomen and shoulders (Figure 1). Histopathological examination showed minimal superficial perivascular dermatitis in H&E stained sections. Elastic stain revealed loss of elastic fibres in the mid-reticular dermis, whereas those in the papillary and deep reticular dermis were preserved (Figure 2). A detailed laboratory analysis consisting of complete blood count, fasting blood glucose, renal and liver function tests, thyroid stimulating hormone, anti-nuclear antibodies and rheumatoid factor yielded normal or negative findings.

As treatment with potent topical steroid (clobetasol propionate) cream and then tacrolimus 0.1% ointment for three months was ineffective within 3 months, no further treatment was attempted. The patient still has progressive disease six months after the initial diagnosis.

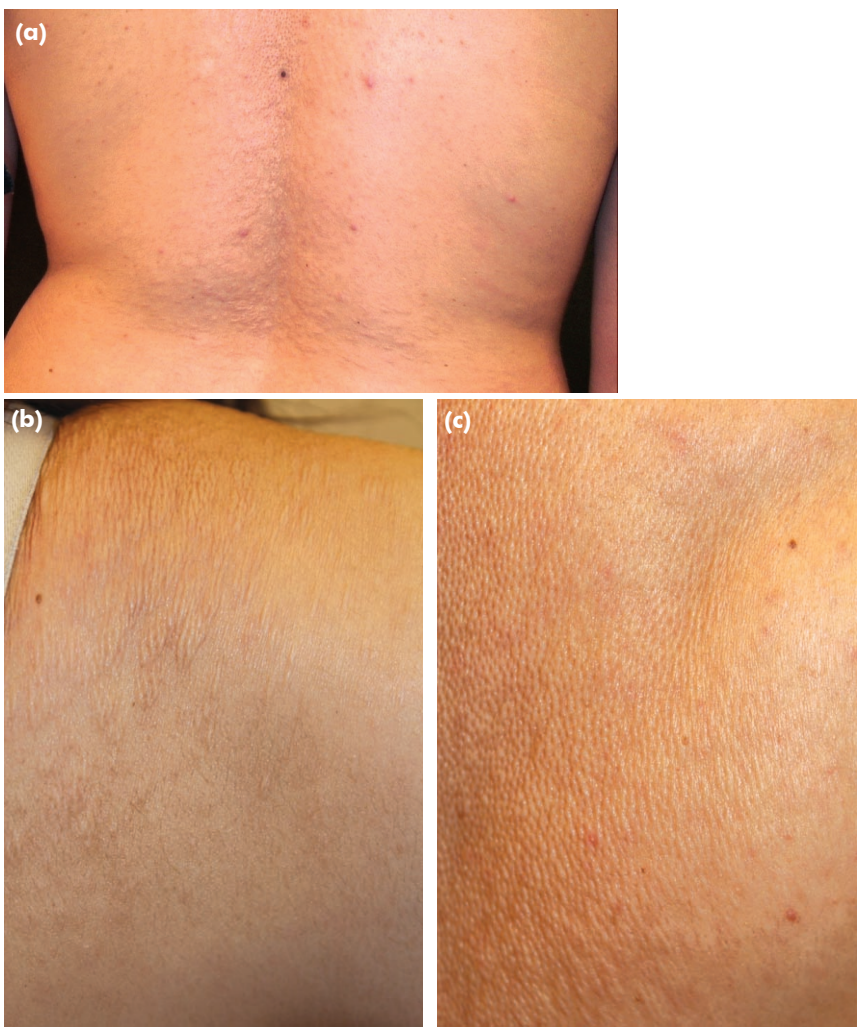

Figure 1. Flesh-coloured, discrete and confluent papules and plaques with overlying fine wrinkling and *peau d'orange* appearance, on the midline of the back and shoulders.

Discussion

Mid-dermal elastolysis was first described by Shelley And Wood in 1977.[4] Although it was initially defined as a non-inflammatory disorder, current evidence points to inflammatory/immunological events as potential inciting factors.[1,5] Supporting this hypothesis is the fact that MDE may be a consequence of or be associated with some dermatoses, conditions or comorbidities as follows: urticaria, solar urticaria, atopic dermatitis, granuloma annulare, Sweet syndrome, phototoxic dermatitis, pityriasis rosea, mycosis fungoides, HIV infection, nephrogenic fibrosing dermopathy, haemodialysis, asthma, protein S deficiency, uterine cancer, false-positive Borrelia serology, Keutel syndrome, pacemaker implantation, augmentation mammoplasty and silicone implants.[1,6-9] However, preceding inflammation is not the rule, since many patients develop MDE without a clinically apparent inflammatory prodrome.[10]

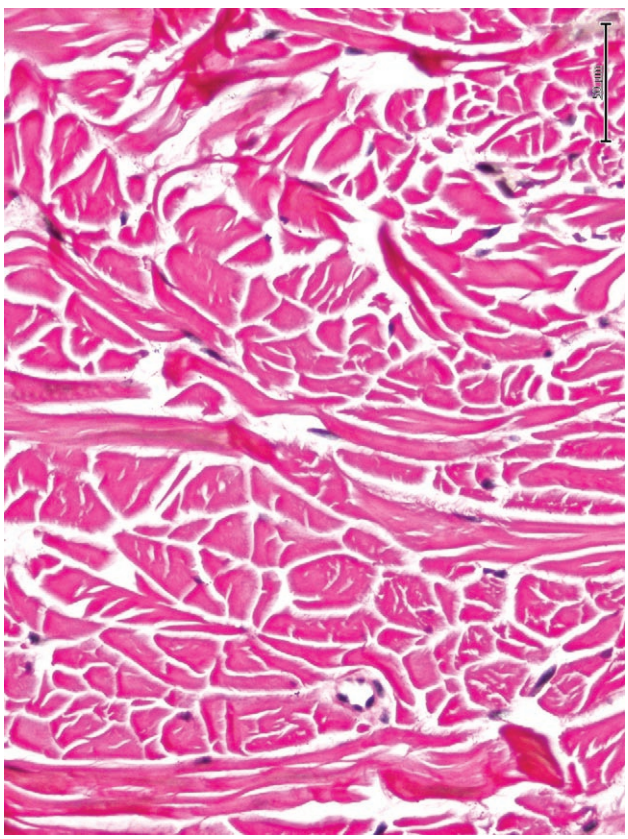

Figure 2. Loss of elastic fibres in mid-reticular dermis (Verhoeff-van Gieson stain X 400).

Mid-dermal elastolysis has been assumed to represent an idiosyncratic photo-induced or photo-aggravated disorder. This hypothesis was based on preferential involvement of females with fair skin, the development of lesions at skin sites exposed to solar radiation or tanning devices and the proven ability of UVA exposure to upsurge the synthesis of elastolytic enzymes, such as elastase, cathepsin G and MMP.[1,6] However, the lack of typical UV-associated histological changes (actinic elastosis) and the lack of predilection for chronically UV-exposed sites (e.g. face and back of hands) speak against this hypothesis.[3,7,11]

Mid-dermal elastolysis is more commonly encountered in middle-aged (30-50 years) white females.[1,3,9,10] Hormonal factors have been implicated in the disorder based on this striking female predominance.[3] Remarkably, a quarter of MDE cases are associated with prior use of contraceptives or pregnancy.[3,11] Although MDE has itself been proposed as an autoimmune disorder, there has been no evidence of circulating autoantibodies directed against the dermoepidermal junction or dermal elastic tissue components.[2] However, MDE may accompany autoimmune disorders such as SLE, Hashimoto's thyroiditis, Graves' disease, type I diabetes, dermatitis herpetiformis and rheumatoid arthritis.[1-3,6,9] Laboratory tests may reveal positive autoantibodies such as ANA and anti-phospholipid antibodies.[2,3] Smoking has also been incriminated in the pathogenesis of MDE.[11] Since MDE is extremely rare as compared with the number of smokers or ex-smokers within the population, smoking *per se* is not enough to explain the occurrence of MDE. There may be an underlying inherent genetic susceptibility in affected patients.

Fibroblasts cultured from lesional skin of MDE demonstrate an 80% reduction in elastin mRNA levels and a twofold increase in elastolytic activity.[1] Thus, both augmented elastolytic activity and impaired elastin renewal are presumed to contribute to the pathogenesis of MDE. Impaired

elastin renewal might stem from altered lysyl oxidase-like 2 (LOXL2) enzyme expression.[12] On the other hand, increased elastolytic activity might be attributed to an imbalance between MMPs and MMP inhibitors. Lesional skin in MDE is reported to harbour increased expression of MMP 1, MMP 9 and MMP 12 and reduced expression of TIMP 1 (tissue inhibitor of metalloproteinases 1). Finally, CD34 (+) dendritic fibroblasts or CD68 (+) histiocytes are held responsible for elastophagocytosis.[2,3,6,12]

Clinically, MDE usually involves the neck, trunk and upper extremities in a symmetrical pattern.[1,2,6,7,10] Generalised variants and involvement of the face and extremities have rarely been documented.[3,7,9] In half of the cases, a prelesional prodromal phase is encountered, consisting of burning erythematous papules and plaques, urticaria, persistent reticular erythema and telangiectasia.[1-3] During healing, these lesions leave circumscribed asymptomatic macules with overlying fine wrinkling following lines of cleavage (type I).[1,2,6,12] Perifollicular umbilicated protrusions (type II) may impart the skin an orange peel appearance.[1,2,12] As in our case, both type I and II manifestations may coexist in the same patient.[5,9] A type III variant showing a male predominance and consisting of reticular erythema and wrinkling on sun-exposed sites has been reported in less than 10 patients up to date.[2,3,9,12] Another distinctive clinical variant comprising multiple, asymptomatic, flesh-coloured, raised, firm, linear, cord-like bands on the lumbar area has been designated as 'linear lumbar localised elastolysis'.[9]

Histologically, there are no specific abnormalities in H&E stained slides. Elastic stains reveal a band-like loss of elastic fibres in the mid-reticular dermis, while those in papillary and lower reticular dermis are retained.[1,2] Perifollicular elastic fibres are preserved even in type II variant of the disorder.[1,3,8] Inflammatory lesions display perivascular lymphocyte, monocyte or neutrophil infiltration and elastic tissue phagocytosis by multinuclear giant cells.[1,2,6] EM studies demonstrate phagocytosis of degenerated elastic fibers by macrophages, disordered elastic fibre structure, irregular accumulation of dense material.[1,3] Immunohistochemical studies identify damage to elastin fibres, sparing of fibrillin fibres and enhanced expression of CD34+ and CD68+ histiocytes and CD3+ and CD4+ lymphocytes.[1,3,6]

Mid dermal elastolysis shows no extracutaneous involvement.[1] The lesions may be stable or as in the present case, spread and enlarge over months.[1,10] Lesions may progress to anetoderma, suggesting that MDE is positioned within a continuous spectrum of elastolytic disorders with anetoderma at the extreme end.[8] In addition to anetoderma, the list of differential diagnostic considerations include perifollicular elastolysis, postinflammatory elastolysis and cutis laxa.

Although the lesions in MDE are asymptomatic, they may be cosmetically disfiguring.[3,12] Unfortunately, response to standard therapeutic options is limited. Colchicine, topical tretinoin, oral and topical steroids, chloroquine, clofazimine, dapsone and vitamin E do not significantly alter the course of the disorder.[1,2] Surgical intervention is usually futile.[10] Although it may be difficult, if not impossible, to reverse the disfiguring skin changes, agents that prevent spread of the condition are required. Until now, only hydroxychloroquine has been observed to halt progression of disease and provide partial benefit.[2] Novel natural therapies include soybean extract and eicosapentanoic acid.[3]

Conclusion

Eruptive MDE is a devastating disorder. We are curious about its cause and its optimum treatment. We believe that MDE represents the end-stage (wreckage) of a preceding clinical/subclinical inflammation, perhaps in subjects with an inherent genetic predisposition. Therapeutic agents or modalities should aim not only at minimising the disfiguring changes, but also at suppressing MDE progression.

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