Mid-dermal Elastolysis in a Patient Undergoing Chronic Hemodialysis

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GOAL

To understand mid-dermal elastolysis (MDE) to better manage patients with the condition

LEARNING OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Recognize the inciting events for MDE.
2. Assess the role of matrix metalloproteinases in the pathogenesis of MDE.
3. Discuss the role of mast cells in MDE.

INTENDED AUDIENCE

This CME activity is designed for dermatologists and generalists.

CME Test on page 130.

This article has been peer reviewed and approved by Michael Fisher, MD, Professor of Medicine, Albert Einstein College of Medicine. Review date: February 2009.

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Mid-dermal elastolysis (MDE) is a rare acquired disorder of unknown etiology that typically presents as discrete patches of wrinkling over the trunk and arms or as perifollicular papules in the same distribution. The histopathologic finding of a bandlike loss of elastic tissue localized to the mid dermis is diagnostic. Our patient presented with atypical clinical features of urticarial papules and plaques that were histopathologically diagnostic of MDE. To our knowledge, the atypical presentation of MDE and association with hemodialysis have not been described. Furthermore, we believe matrix metalloproteinase (MMP)

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dysfunction to be involved in the pathogenesis of the disease.

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In 1977, Shelley and Wood[1] first described mid-dermal elastolysis (MDE), a rare acquired disorder characterized by the selective loss of elastic tissue in the mid dermis. This condition typically presents as either patches of finely wrinkled skin following cleavage lines or perifollicular papules.[1,2] The pathogenesis of the disease currently is unknown, though one theory attributes the loss of elastic tissue to actinic damage, postinflammatory change, or autoimmune processes.[3] We report an atypical presentation of MDE in a patient with chronic renal failure (CRF), with disease appearing after the onset of hemodialysis.

Case Report

A 51-year-old man with CRF secondary to hypertension presented with intensely pruritic, erythematous papules and plaques over his arms and chest that developed after the onset of hemodialysis. Although symptoms initially abated several hours after completion of dialysis, they eventually became persistent. The patient denied a recent history of intense UV light exposure, but he did report a substantial amount of sun exposure in the past. He denied personal or family history of similar skin disease. Varying dosages of oral diphenhydramine hydrochloride as monotherapy and in combination with oral cetirizine hydrochloride, oral doxepin hydrochloride, oral ranitidine hydrochloride, and high-potency topical corticosteroids were used with little relief of his symptoms. Additional medications at the time of presentation included inhaled albuterol sulfate–ipratropium bromide, as well as oral alprazolam, aluminum hydroxide, clonidine hydrochloride, doxazosin mesylate, gabapentin, lansoprazole, lorazepam, metoprolol tartrate, multivitamin, sertraline hydrochloride, and sevelamer hydrochloride.

Physical examination demonstrated multiple coalescing, soft, urticarial, erythematous papules and plaques distributed over the upper chest and extensor surfaces of the upper extremities with distal extension as far as the proximal dorsal hands. The papules were not perifollicular and did not display central umbilication (Figure 1). Additionally, there was a large hemodialysis shunt in the left forearm. There was no involvement of the face or lower extremities, and there was an absence of dermatographism. Follow-up examination approximately 2 hours postdialysis revealed similar findings with slight edema of papules and increased erythema, with continued absence of dermatographism.

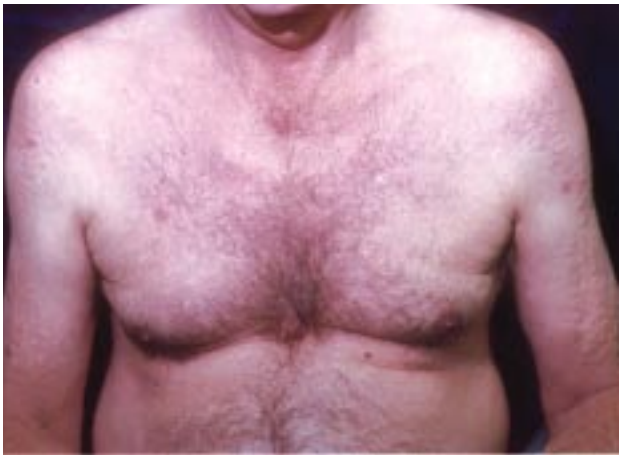

Figure 1. Urticarial papules and plaques on the lateral arms. Fine wrinkling and perifollicular papules are not present.

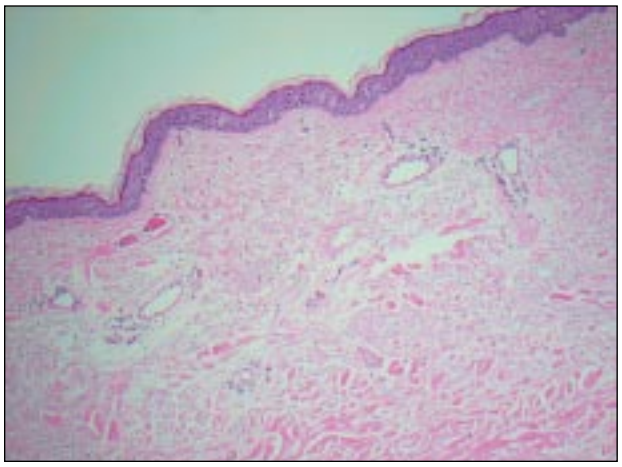

Figure 2. Scant perivascular inflammation (H&E, original magnification ×100).

Laboratory evaluation yielded the following values: phosphorus, 8.9 mg/dL (reference range, 2.5–4.5 mg/dL); ferritin, 1550 ng/mL (reference range, 27–377 ng/mL); alkaline phosphatase, 145 U/L (reference range, 26–118 U/L); intact parathyroid hormone, 536 pg/mL (reference range, 10–65 pg/mL); creatinine, 12.8 mg/dL (reference range, 0.8–1.6 mg/dL); blood urea nitrogen, 53 mg/dL (reference range, 9–28 mg/dL); hemoglobin, 12.8 g/dL (reference range, 14–18 g/dL); hematocrit, 37.2% (reference range, 42%–52%); total iron-binding capacity, 204 µg/dL (reference range, 228–428 ug/dL); unsaturated iron-binding capacity, 131 µg/dL (reference range, 159–359 µg/dL); bicarbonate, 17 mEq/L (reference range, 22–33 mEq/L); and aspartate aminotransferase, 4 U/L (reference range, 11–34 U/L). All laboratory analyses were considered consistent with CRF and hemodialysis.

Biopsy of a lesion from the right upper arm demonstrated a healthy epidermis and several slightly thick-walled dilated venules with a patchy mononuclear cell infiltrate. Substantial solar elastosis was seen in addition to a slight increase in the number of mast cells (Figure 2). No stains for elastin were done. Approximately 11 weeks later, 2 repeat biopsies were performed on lesions of the right and left upper arms. Both biopsies demonstrated mildly increased cellularity within the upper and mid-reticular dermis. Additionally, there was a sparse perivascular mononuclear cell infiltrate surrounding ectatic blood vessels within the upper dermis. Giemsa stain revealed a mildly increased number of perivascular and interstitial mast cells, and elastic tissue stain demonstrated a well-demarcated area with loss of elastic fibers within the superficial and mid-reticular dermis (Figure 3).

UVB light therapy was initiated and was successful at decreasing the patient's pruritus; however, there had been no change in his clinical appearance with follow-up for more than a year.

Comment

Originally described by Shelley and Wood[1] in 1977, MDE is characterized as well-circumscribed patches of fine wrinkling with a bandlike loss of elastic tissue localized to the mid dermis. A less common second type of MDE also has been reported as multiple perifollicular papules with central umbilication and similar mid-dermal absence of elastic tissue.[4] Lesions of MDE generally occur on the trunk and arms, and rarely on the thighs or face. The majority of cases reported involve white women aged 30 to 50 years.[5]

Many reports of MDE have failed to recognize an inciting event, though Shelley and Wood[1] cited a history of urticaria prior to their initial case and other researchers have observed a history of intense UV light exposure or inflammation prior to the onset of symptoms.[5-7] Mid-dermal elastolysis has been associated with other conditions, including eczema, granuloma annulare, rheumatoid arthritis, silicone mammoplasty, false-positive serology for *Borrelia burgdorferi*, Hashimoto thyroiditis, and acute febrile neutrophilic dermatosis, and was reported as a feature of Keutel syndrome with a mutation of the matrix G1a protein gene, *MGP*.[3,8-11]

Currently, the pathogenesis of MDE is unknown; however, some researchers have postulated that matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) are key components in the pathogenesis of MDE. In fact, Patroi et al[9] examined biopsy specimens from 7 patients with MDE and found intense staining for MMP-9 in the cellular infiltrate located in the mid dermis. In addition, Gambichler et al[10] demonstrated increased staining for MMP-1 and MMP-12, and decreased staining for TIMP-1 was reported in one patient with MDE.[9] Matrix metalloproteinases are secreted by a variety of structural and inflammatory cells, and stromelysin, gelatinase, MMP-2, MMP-9, and MMP-12 are thought to affect elastic tissues. Tissue inhibitors of metalloproteinases act in opposition of MMPs, and the balance between these 2 components regulates the breakdown of connective tissues.[9,12]

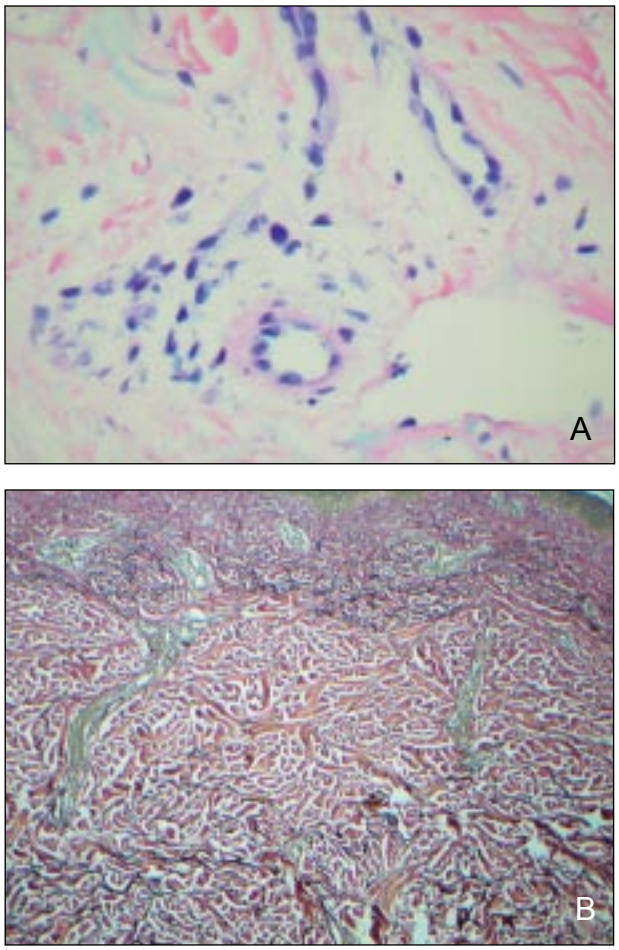

Figure 3. Perivascular mast cells (A)(Giemsa, original magnification ×400). Mid-dermal loss of elastic tissue (B) (Verhoeff–van Gieson, original magnification ×200).

Patients on hemodialysis have shown increased expression of MMP-9 messenger RNA (mRNA) in peripheral monocytes. Ebihara et al[13] evaluated 40 patients with CRF on hemodialysis, 20 patients on chronic peritoneal dialysis, 20 patients with CRF not on dialysis, and 20 healthy volunteers. The group on hemodialysis showed greater MMP-9 mRNA expression in peripheral monocytes than the other groups.[13] This finding led us to consider the possibility that chronic hemodialysis may have resulted in an increase of

MMP-9 expression in our patient, which resulted in MDE.

The presence of mast cells was an interesting finding in our patient's biopsy specimens, which is not often described in MDE. Mast cells have demonstrated substantial MMP-9 activity, especially after inflammatory events.[12,14] Additionally, the presence of mast cells and mast cell degranulation may have led to tissue edema and contributed to the atypical presentation of urticarial plaques in our patient instead of the fine wrinkling or perifollicular papules that are typically experienced.

Reported treatments for MDE have proven largely ineffectual and include colchicine, topical retinoic acid, topical corticosteroids, moisturizers, and sunscreens.[2,15] Surgical removal of affected tissue has been ineffective because of MDE recurrence at the surgical site.[2] We elected to use UVB light therapy, which decreased the patient's pruritis but unfortunately had no effect on the clinical appearance.

Conclusion

Our case demonstrates several features not typically described in MDE, and to our knowledge, there have been no reported cases of MDE in patients with CRF undergoing hemodialysis. Our patient did not display fine wrinkling or perifollicular papules but rather large coalescing urticarial papules and plaques. Although the presentation was atypical, the characteristic location of the lesions and selective loss of elastic fibers in the mid dermis were consistent with the diagnosis of MDE.

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