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Case report

Acquired cutis laxa associated with cutaneous mastocytosis

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Abstract

Cutis laxa is characterized by dramatic wrinkling of skin that is lacking in elasticity due to inherent defects in dermal elastic fibers. Cutis laxa can be caused by genetic and metabolic disorders. It can also be acquired, possibly resulting from inflammatory processes with destruction of elastic fibers. This report describes a 26-year old woman who developed acquired cutis laxa and cutaneous mastocytosis leading to premature aging. She represents a unique co-occurrence of these two separate disease entities. To our knowledge, there has been only one published case report of acquired cutis laxa occurring in association with urticaria pigmentosa in a 4-year old girl. Our case would be a second case that exhibits the coexistence of these two disorders in an adult female.

Keywords: Mastocytosis, mast cells, cutis laxa, elastolysis

Introduction

Cutis laxa is characterized by dramatic wrinkling of the skin that hangs in pendulous folds lacking in elasticity owing to inherent defects in dermal elastic fibers [1]. Patients with cutis laxa exhibit loose, pendulous skin that produces a wrinkled, prematurely-aged appearance. Cutis laxa can be caused by genetic and metabolic disorders, involving genes that are important in the formation of elastic tissue fibers [2, 3]. It can also be acquired, possibly resulting from inflammatory processes in which the destruction of elastic fibers is primarily confined to areas of inflammation [3]. Some patients with cutis laxa have a preceding or accompanying eruption that had been characterized as eczema, urticarial, or erythema multiforme.

Case synopsis

The patient is a 26 year-old woman who first developed a diffuse pruritic eruption in the skin, consisting of heterogeneous red-brown patches and plaques, four years prior to presentation. Within 24 hours, the lesions had largely resolved. However, in the ensuing months, she had several similar eruptions that failed to resolve. For this condition she took herbal medication for several months, but the eruption did not improve and she discontinued this medication. She soon noticed wrinkle lines on both cheeks and her skin was less tense and firm than before. In the same period, she also noticed extensive pruritus and excessive dryness and wrinkling of the skin on her hands, abdomen, and inner thighs. In the subsequent three years, she had frequent lower abdominal pain and runny stools, often simultaneously with the red-brown eruptions. Her facial and abdominal skin continued to develop a progressive increase in wrinkling and laxity. At the time of her presentation to us, the polymorphous eruption was occurring intermittently, lasting 3-4 days. Notably, compared to her physical facial appearance at age 22, she appeared much older than her chronological age of 26 (Figure 1).

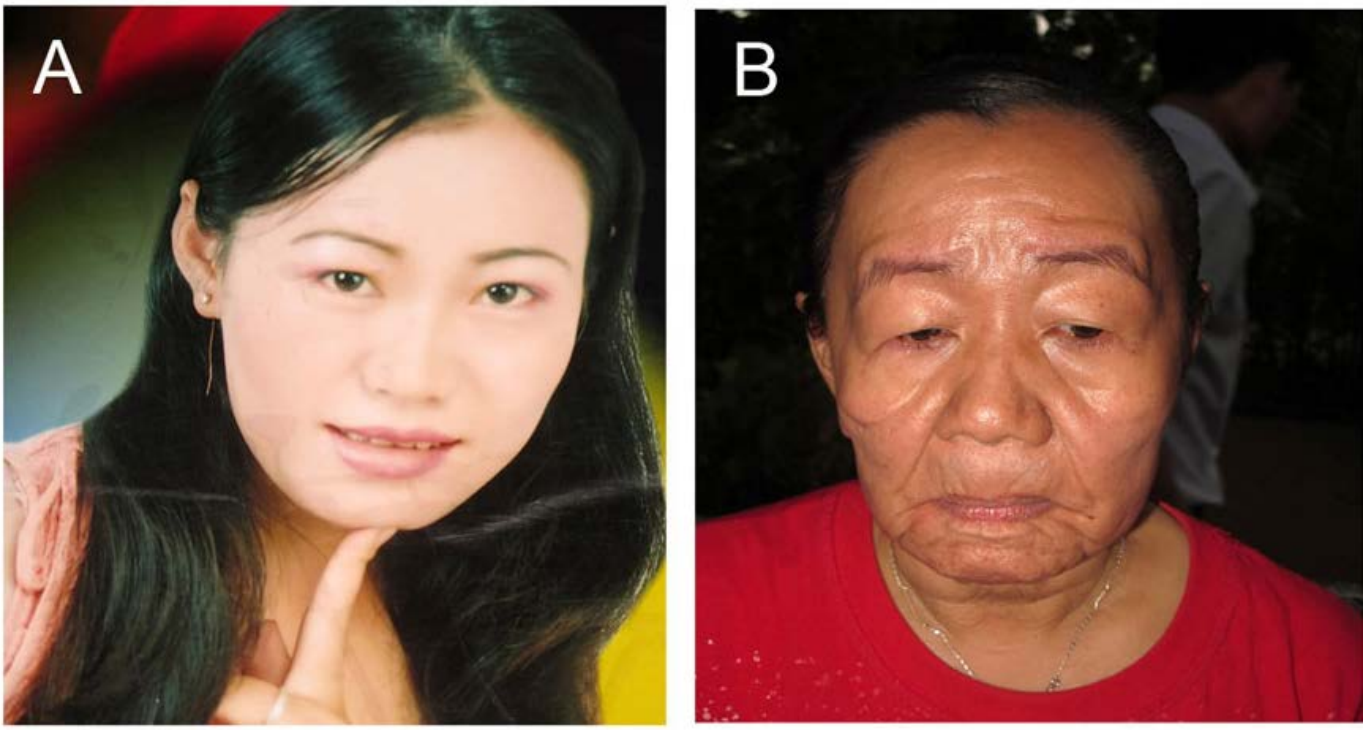

Figure 1. (A) The patient as she appeared at age 22 in a photograph, prior to the onset of cutaneous eruptions. (B) The patient as seen four years later at age 26, when she first presented to the Dermatology Clinic.

A complete medical work-up did not reveal any evidence for systemic mast cell disease. Her urinalysis for histamine was negative and her complete blood cell count and complete metabolic panel were within normal limits. The patient was suspected to have cutis laxa in light of the clinical presentation. A work-up for cutis laxa was also performed, including physical examination and biopsies of skin areas with erythema and laxity. On physical exam, she was found to have loose and wrinkled skin in the neck, axilla, chin, abdomen, and thighs. Abundant erythematous macules and patches were present diffusely on the face, trunk, and extremities with extensive wrinkling and laxity of the skin in these areas (Figures 2A-B). Of note, the areas of loose skin were observed to overlap with areas of erythema. Other parts of her skin that did not have erythematous eruptions appeared normal and without laxity (Figure 2C).

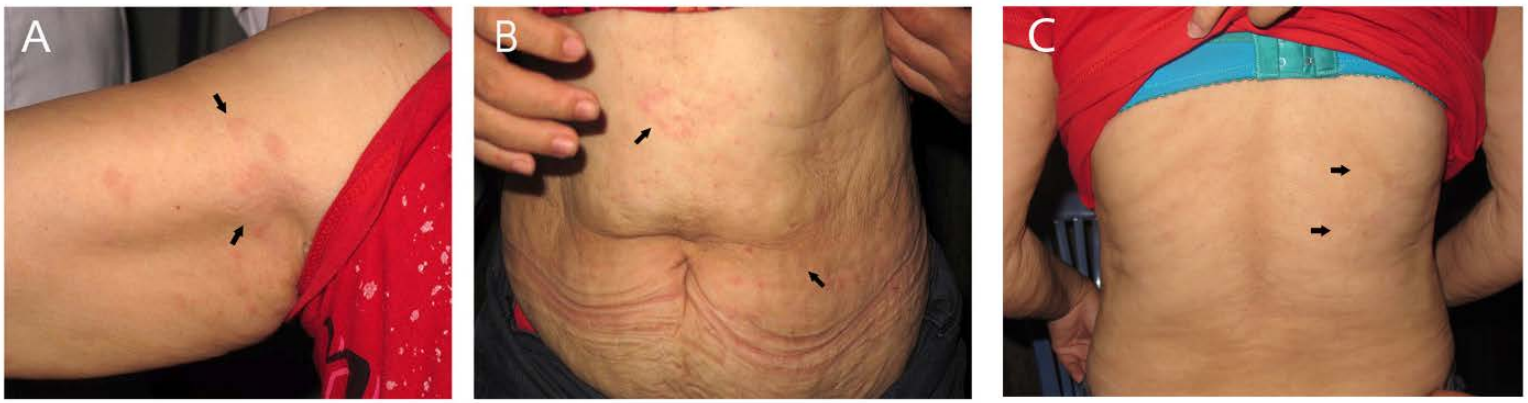

Figure 2. (A) Erythematous macules and papules on the patient's inner arm and axilla (arrows). (B) The patient had a diffuse erythematous eruption on the trunk and abdomen (arrows). Extensive wrinkling was also present. (C) Areas of skin that appeared normal and without laxity did not have erythematous eruptions (arrows).

Punch biopsies of the skin lesions on the patient's face, axilla and elbow showed normal epidermis. Within the dermis, there was a superficial and deep lymphohistiocytic infiltrate with a slight increase in the number of mast cells around the vascular plexus and in the interstitium (Figures 3A-B). Eosinophils were not prominent in any of the biopsies. These findings were supported by immunostains for c-Kit (CD117), which is expressed in mast cells and showed a significant increase in the number of mast cells in the dermis (>10 cells per high power field) (Figures 3C-D). We did not have normal skin from this patient for comparison. However, normal skin obtained from another patient showed abundant elastin fibers as seen on Verhoeff-van Gieson (VVG) elastin stains (Figures 3E-F). VVG stains of lesional skin from the case patient showed a significant loss of elastin fibers as compared with normal skin (Figures 3G-H). The remnant elastin fibers appeared thin and partially fragmented.

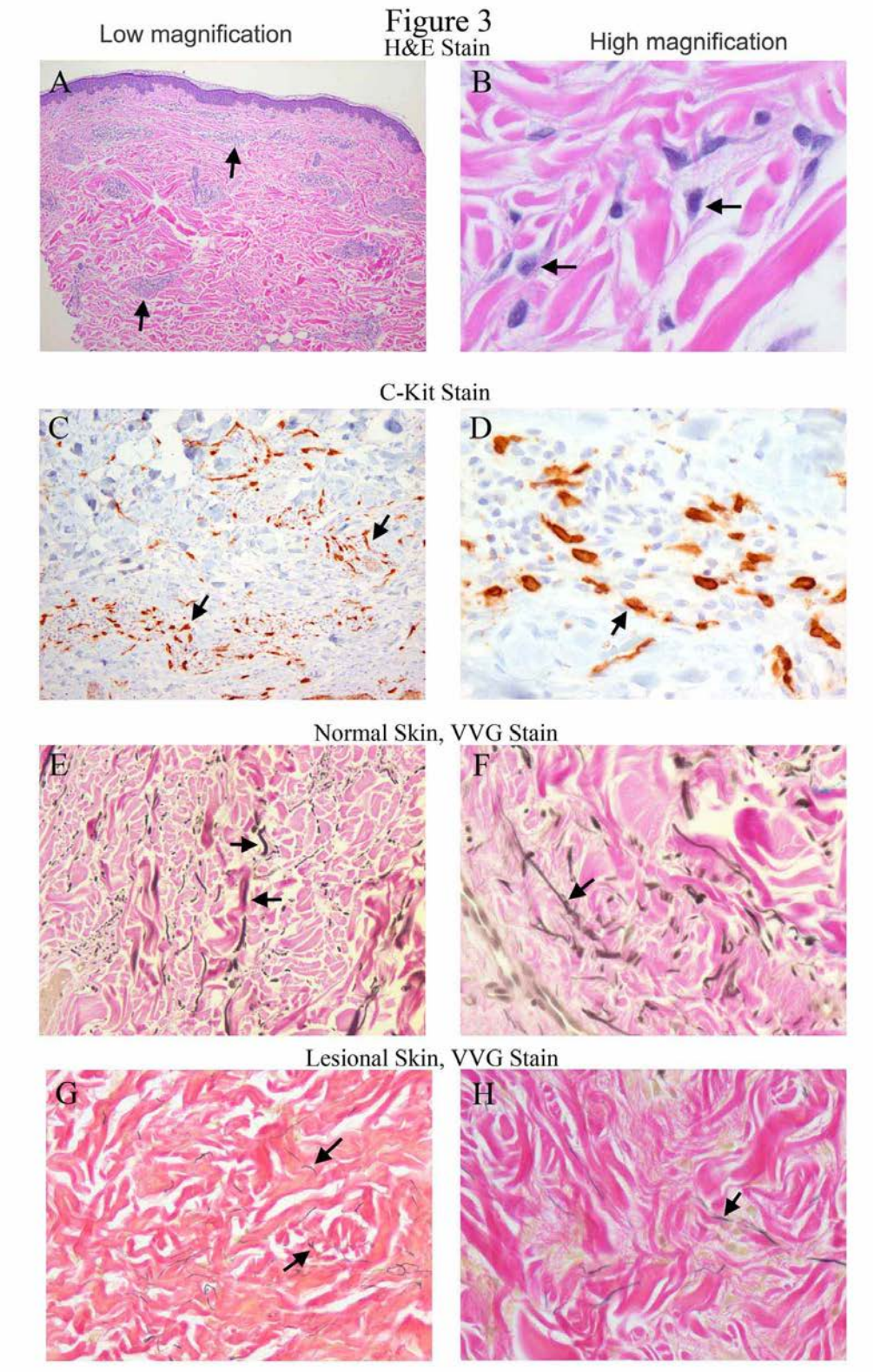

Figure 3. (A) Punch biopsy of an active erythematous area shows a superficial and deep perivascular inflammatory infiltrate of predominantly lymphocytes and histocytes on hematoxylin & eosin (H&E) stain (arrows, magnification X40). (B) Mast cells with granular cytoplasm are present in increased numbers within the reticular dermis (arrows, magnification X400). (C) c-Kit (CD117) immunohistochemical stain of a biopsy taken from an "active lesion" shows increased number of perivascular and interstitial mast cells (brown-stained cells, arrows, magnification X200). (D) A higher magnification of c-Kit-positive mast cells (magnification X400). (E) Verhoeff-van Gieson (VVG) stain of a biopsy of normal skin shows normal elastic tissue fibers (dark-stained fibers, arrows, magnification X200). (F) A higher magnification of VVG stain of normal skin (arrow, magnification X400). (G) VVG stain of lesional skin with extensive laxity shows almost complete loss of elastic fibers (arrows, magnification X200). (H) A higher magnification of VVG stain of lesional skin (arrow, magnification X400).

For her mastocytosis, the patient was treated with anti-histamine, including fexofenadine (180 mg), cyproheptadine (4 mg), and cimetidine (400 mg) for several months. For her cutis laxa, she was treated twice, each time one year apart, with CO_2 fraxel laser (100 milliseconds, 5 joules) plus topical tacrolimus (0.1%) and pimecrolimus (0.1%). In long-term follow up for over a year, she had significant reduction in the number of polymorphous eruptions with treatment. She experienced improvement in some areas of loose skin, mainly around the eyes, forehead, and proximal arm. However, areas with significant loose skin folds, such as the cheeks, chin, and neck, did not show much improvement with treatment and may need plastic reconstructive surgery in the future.

Discussion

Cutis laxa is characterized by dramatic laxity of the skin due to inherent defects in dermal elastic fibers [1]. Cutis laxa can be caused by genetic and metabolic disorders, involving genes that are important in the formation of elastic tissue fibers [2, 3]. It can also be acquired, possibly resulting from inflammatory processes in which the destruction of elastic fibers is primarily confined to areas of inflammation [3].

To our knowledge, there has been only one published case report of acquired cutis laxa occurring in association with mast cell disease. In this published report, a 4-year old girl who had urticaria pigmentosa with recurrent episodes of erythematous confluent plaques developed finely wrinkled and lax skin [4]. Our case is that of an adult female and represents a unique co-occurrence of these two separate diseases in the same patient. The patient underwent a work-up for systemic mast cell disease, which included urinalysis for histamine, complete blood cell count, and complete metabolic panel, which were all within normal limits. The blood level of tryptase to evaluate mast cell activation was not performed owing to lack of such diagnostic test at the medical facility in Vietnam. A work-up for cutis laxa was also performed, including physical examination and biopsies of skin areas with erythema and laxity. Skin biopsies revealed an increased number of mast cells and fragmentation of elastin fibers, consistent with histologic features of cutaneous mastocytosis and cutis laxa. Although it is not possible to prove a cause-and-effect relationship between cutis laxa and mastocytosis in this patient, one can postulate that the inflammatory milieu created by mast cells in the skin may subsequently affect the integrity of dermal elastic tissue in individuals who have a predisposition to elastic tissue disorder. Mast cells release many inflammatory cytokines, which can result in the proteolysis of connective tissues [5]. In addition, neutrophils and eosinophils can also be recruited to areas of degranulated mast cells. The release of elastase by neutrophils may contribute to the destruction of elastic tissue fibers [6, 7]. The inflammatory environment created by mast cells can potentially lead to accelerated alteration and destruction of elastic fibers that already have inherent structural defects. This may explain why mast cell disorders alone in otherwise healthy individuals do not typically lead to cutis laxa.

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