Acquired cutis laxa of face with multiple myeloma

Sir,

Cutis laxa is a rare dermatosis characterized by diffuse laxity of skin resulting in a prematurely aged appearance. It is most commonly an inherited condition. The acquired form is rare and has been associated with various conditions, including multiple myeloma, monoclonal gammopathy of undetermined significance, and heavy chain deposition disease. Cutis laxa usually follows a progressive course and there is no definitive treatment available.[1] We describe a 44-year-old female with multiple myeloma and cutis laxa localized to the face. She developed anasarca, which subsided following treatment for multiple myeloma leaving lax and wrinkled skin all over the body. Lax skin improved spontaneously elsewhere but persisted on the face.

A 44-year-old female presented to us with a two-year history of loosening of skin over the face. Two years back, she had developed severe anaemia with associated anasarca and exertional dyspnea. She also had heavy proteinuria, hypoproteinaemia and progressive renal failure. A kidney biopsy was performed which revealed mesangial cell proliferation and lobular accentuation of glomerular tufts with marked mesangial matrix deposition and eosinophilic periodic acid Schiff (PAS) positive nodules. Immunofixation electrophoresis on a 24-hour urine sample was positive for kappa light chains. Serum immunofixation electrophoresis (IFE) revealed a stable monoclonal IgG-λ M-spike (0.5 g/dL).

Serum β₂-microglobulin was increased. Bone marrow examination revealed 14% plasma cells. Based on these findings, a diagnosis of early multiple myeloma with nephrotic syndrome was made. She was started on a chemotherapy regimen consisting of thalidomide (100 mg/day), oral cyclophosphamide (150 mg/day) both for the first five days in every month with weekly intravenous dexamethasone (40 mg/week) along with loop diuretics. In addition, the patient was prescribed bortezomib which was discontinued by the patient after two months. Following one year of treatment, the anasarca subsided leaving behind loose wrinkled skin all over the body. Over the next one year, the skin over the extremities and the abdomen reverted back to normal; however, loosening of skin persisted over the face.

Examination revealed a healthy-appearing woman, who appeared older than her stated age [Figure 1]. She had loose, sagging skin on the face and neck giving her a hound-dog facies [Figure 2]. Skin over the ear lobules was lax. On stretching of the skin over face, no elastic recoil was seen. Her systemic examination was also normal. Hematoxylin and eosin (H and E) stained sections from a skin biopsy from the face showed a mixed cell infiltrate of lymphocytes and occasional neutrophils [Figure 3]. A special stain to demonstrate elastic tissue (Verhoff van Gieson) showed fragmented and clumped elastic fibers [Figure 4].

Based on her clinical features, a diagnosis of acquired cutis laxa localized to the face following multiple myeloma was made and she was referred to a plastic surgeon for surgical correction of redundant folds.

Cutis laxa is a rare condition characterized clinically by lax, pendulous skin and histologically by loss of elastic tissue in the dermis. It is a heterogeneous condition, which may be inherited as a dominant, recessive or X-linked recessive disease, or it may be acquired. The face and neck are often affected, which produces a ‘bloodhound’ appearance of premature aging. Mild trauma can lead to purpura due to skin fragility and this may lead to formation of fibrotic nodules over the bony prominences. There may be widespread, massive folds of lax skin, or the changes may be mild and confined to a limited area. Such cases may be confused as having anetoderma. The acquired cephalic form of localized cutis laxa presents characteristically as large, hanging loose ear lobes, blepharochalasis and lax nasolabial folds. Organs other than the skin may also be involved. Internal organ abnormalities like emphysema,
gastric fibromas and tracheobronchomegaly have been reported.\(^2\)

Histologically, the skin is of normal thickness, but the elastic fibers are sparse, short, fragmented and clumped, particularly in the upper dermis, and they show granular degeneration.\(^3\) The elastic fibers are found to be deficient in elastin, though their microfibrils appear normal. Similar changes in elastic fibers may occur in the lungs and aorta.\(^4,5\) There are occasional case reports of multiple myeloma and other plasma cell dyscrasias associated with cutis laxa.\(^6\)

It is likely that paraproteinemia resulting in the deposition of immune complexes possibly leads to the release of inflammatory cytokines and subsequent destruction of elastic fibers. Surgical repair seems to be the only therapeutic choice, but the results are variable and temporary.

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Obesity-associated lymphedematous mucinosis

Sir,

Obesity-associated lymphedematous mucinosis is a newly recognised entity with only a few patients reported to date. Though this condition can clinically mimic pretibial myxedema, it is differentiated from the latter by microscopic findings and a lack of thyroid disease.[1,2]

A 71-year-old female presented to us with swelling, erythema, and discoloration on both her legs; these symptoms had been present for 1 year. She had been overweight for 30 years (height 160 cm, weight 95 kg, and body mass index 37.1). Dermatologic examination revealed pink-red plaques on both legs, especially the left leg. Several circular, semi-translucent, papulo-nodular lesions of 1-2 cm diameter were noted surmounting these plaques [Figure 1a and b].

Blood tests including total protein, immunoglobulin levels, and thyroid function tests were all normal. No cardiac or renal failure was detected. A skin biopsy taken from a lesion showed a basket-weave stratum corneum with focal hyperkeratosis and mild acanthosis. Dermal edema was noted, with mucin deposition around vessels in the superficial papillary dermis, the deposits staining with PAS, Alcian blue, and mucicarmine stains. Dermal capillaries were increased in number and thickness; perivascular lymphocytes and increased dermal stellate fibroblasts were also seen [Figure 2a and b].

The patient was treated initially with pentoxyphylline 400 mg thrice daily and clobetasol 17-propionate 0.05% cream, applied daily for the first month and then on alternate days. After 5 months, since the patient no longer wished to continue with the cream, administration of monthly triamcinolone acetonide (40 mg/mL) injections into the nodular lesions was started. Three months later, the plaques had slightly regressed and the papulonodular lesions were smaller [Figure 3]. The patient continued to take pentoxyphylline tablets for another 10 months. Meanwhile, she was referred to a dietician and a low-calorie diet was recommended; however, she only lost 3-4 kg. After 10 months of therapy, there was no significant regression of the lesions so further treatment was stopped; the patient is still following up with us.

Mucin accumulation on the legs is usually considered an indicator of pretibial myxedema.[3] In 1993, Somach et al. reported that pretibial myxedema in euthyroid patients may be histologically different from the pretibial myxedema of hyperthyroidism.[2] Then in 2006, Tokuda et al. reported three cases of “chronic obesity lymphedematous mucinosis,”[4] where mucin accumulation on the legs accompanying lymphedema had histological findings similar to those reported by Somach et al. Most recently, in 2009, Rongioletti et al. reported five cases of obesity-associated lymphedema with mucin accumulation on the legs. They renamed this entity “obesity-associated lymphedematous mucinosis.”[5] The pathogenesis of this condition is unclear but a lymphatic drainage defect may be a cause,[5] leading to excessive high-protein fluid collecting in the interstitium. This in turn could cause thickening of the legs and a peau d’orange appearance.[2]

Clinically, obesity-associated mucinosis is characterized by skin-colored or brown-red papules and/or nodules on an erythematous base on the pretibial region accompanied by edema; rarely, these may occur on the foot or ankle. Patients have long-standing obesity with lymphedema and do not have thyroid disease. Pretibial myxedema, despite being similar, can be differentiated on the basis of histopathological findings and the presence of thyroid disease. Obesity-associated lymphedematous mucinosis shows epidermal atrophy and disappearance of rete ridges with hyper-orthokeratosis, while pretibial myxedema is not associated with epidermal atrophy.[3,4] Both conditions show varying levels of fibrosis associated with stellate or linear fibroblasts and separation of collagen.
