Cutis laxa is an uncommon condition characterized by loose and redundant skin. Biopsy results are positive for a reduction in or an absence of elastic fibers in the dermis. Cutis laxa is acquired or congenital. The acquired form is either a generalized insidious form (type I) or a form associated with prior inflammation (type II). Cardiovascular, pulmonary, gastrointestinal, and urologic complications may occur. In the past, cutis laxa was associated with plasma cell dyscrasia. We report on a characteristic case of cutis laxa to alert clinicians to this uncommon manifestation of multiple myeloma.

Cutis laxa results from injury to cutaneous elastic fibers. The skin is loose, has redundant folds, and is soft to the touch. Fine wrinkling may be evident, and there is decreased recoil of the skin. Under an electron microscope, granular degeneration of elastic fibers is visible. Microfibrils remain normal, but elastin in skeletal fibrils is diminished.

Congenital cutis laxa is usually inherited as an autosomal-recessive condition. The X-linked recessive form of cutis laxa is thought to result from deficiency in lysyl oxidase and is classified as type IX Ehlers-Danlos syndrome. Acquired cutis laxa may occur as a generalized insidious loss of elastic fibers beginning in adulthood (type I). Development of an urticarial or nondescript, erythematous, and papular vesicular eruption sometimes precedes the onset of generalized cutis laxa. Type II cutis laxa (Marshall syndrome) is most often encountered in females of African or South American descent. Development of inflammatory skin lesions is followed by localized loss of elasticity.

Both congenital and acquired cutis laxa may be associated with internal abnormalities including

**GOAL**
To recognize cutis laxa as a possible manifestation of multiple myeloma

**OBJECTIVES**
Upon completion of this activity, dermatologists and general practitioners should be able to:
1. Recognize the clinical features of cutis laxa.
2. Explain the possible etiologies of cutis laxa.
3. Describe an algorithm for evaluating patients with suspected cutis laxa.

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diverticula of the gastrointestinal tract and bladder, rectal prolapse, pulmonary manifestations (eg, emphysema, pulmonary fibrosis), inguinal or hiatal hernias, and vascular abnormalities. Cardiomegaly, congestive heart failure, pulmonary stenosis, and aortic dilatation may occur. Uncommon associations with cutis laxa include multiple myeloma, other plasma cell dyscrasias, amyloidosis, penicillamine therapy, and a reaction to penicillin or isoniazid therapy. Middermal elastolysis results from intense ultraviolet radiation exposure and also may be considered a form of cutis laxa; an unusual localized acral variant has been noted.

Case Report
A 62-year-old woman with a history of multiple myeloma presented for evaluation of age-related changes. Diagnosis of the disease had been made 5 years earlier; present results of bone-marrow aspirate were positive for immunoglobulin G (IgG) multiple myeloma. A bone-marrow smear included 40% plasma cells, but lytic lesions were not evident on a bone scan.

Treatment began with vincristine, melphalan, doxorubicin, cyclophosphamide, and prednisone therapy, and the patient improved markedly. She received interferon, granulocyte-macrophage colony-
stimulating factor, thalidomide, and occasional dexamethasone pulse therapy. At presentation, she was taking prednisone 50 mg every other day and thalidomide 100 mg daily, with the thalidomide gradually being increased to a total of 400 mg daily.

Family history included malignant melanoma in the patient’s brother and father. Evident on physical examination of the patient was marked skin laxity with redundant folds on the face, neck, chest, and back. She denied any prior inflammatory skin disorder or exanthema. Non-sun-exposed sites were involved (Figures 1 and 2). Biopsy results were positive for loss of elastic fibers but negative for inflammatory infiltrate (Figures 3 and 4). Results of serum protein electrophoresis showed raised levels of human gamma globulin (1.98 g/dL; reference range, 0.5–1.4 g/dL) and \( \beta_2 \)-microglobulin (2.3 mg/L; reference range, 0.3–1.9 mg/L).
Homogenous bands to IgG and the κ region were evident on immunofixation electrophoresis. Results of urine monoprotein analysis showed monoclonal κ light chains, and results of monoclonal protein serum analysis showed raised levels of κ (3340 mg/dL; reference range, 534–1267 mg/dL) and IgG (8040 mg/dL; reference range, 717–1411 mg/dL). Erythrocyte sedimentation rate, serum copper level, and ceruloplasmin level were all unremarkable. On review of systems, no rectal or vaginal prolapse problems, emphysema, or cardiac problems were detected.

**Comment**
Acquired cutis laxa may present without an obvious underlying cause or may be associated with prior inflammation. Several studies have linked cutis laxa with plasma cell dyscrasia or multiple myeloma. Our patient’s skin condition coincided with her diagnosis of multiple melanoma. A clear association between cutis laxa and the treatment our patient received for multiple myeloma has not been established.

The etiology of cutis laxa is unknown, but a decrease in serum elastase inhibitors (eg, α1-antitrypsin)
Cutis Laxa Associated With Multiple Myeloma

is thought to be a factor. Elastase activity is increased in fibroblasts of patients with acquired cutis laxa. Elastolysis also may result from increased fibroblast matrix metalloproteinase (MMP) activity. In some studies, MMP1, MMP3, and MMP9 were found to have increased levels of messenger RNA activity. MMP1 and MMP3 degrade elastin.

Another possible factor in elastolysis is copper metabolism. Lysyl oxidase is a copper-dependent enzyme necessary for elastic fiber synthesis. Linear polypeptides connected by desmosines contribute to the formation of elastin. A decrease in serum copper level affects lysyl oxidase activity and therefore may affect elastic fiber synthesis (our patient's serum copper level was normal).

Immunologic factors also may play a role in elastolysis. Immunoglobulins may induce elastolysis by complement fixation. IgG may bind to dermal elastic fibers and lead to complement fixation and subsequent elastic fiber degradation. We suspect that our patient may have had a unique protein that, when combined with elastic fibers, caused complement fixation and elastolysis. Immunoglobulin A deposits are found in some patients with blepharochalasis.

A possible algorithm for evaluating cutis laxa is outlined in the Table. Although the exact nature of the association between cutis laxa and multiple myeloma is unclear, clinicians should be alert to this uncommon association because identification of cutis laxa may point to underlying plasma cell dyscrasia.

REFERENCES