

LETTERS TO THE EDITOR

Chronic urticaria may not be as innocent as we think: A rare case of acquired cutis laxa following chronic urticaria

To the Editor,

Cutis laxa (CL) is a rare connective tissue disorder characterized by sagging, pendulous skin, which may have both acquired and inherited forms.¹ In autosomal-dominant form of inherited CL, pathogenic mutations in the elastin gene give rise to disorganization of the elastic fiber network, which culminates in the loose, sagging skin.² On the contrary, localized and generalized forms of acquired cutis laxa (ACL) may occur in association with monoclonal gammopathies, penicillamine, and inflammatory diseases.^{1,3} Herein, we would like to demonstrate an interesting case of ACL developed secondary to chronic urticaria and emphasize the efficacy of dapsone treatment in ACL.

A 26-year-old woman was admitted to our department due to wrinkling, sagging, and loosening of the facial and abdominal skin leading to an aged facial appearance. Her complaints started from the face and neck 8 years ago and spreaded gradually to the upper arms. In addition, she had a 10-year history of chronic urticaria for

which she used oral antihistamines, systemic corticosteroids, cyclosporine, and azathiopurine treatments with a partial response. The patient was unable to recall the duration, dosage, and onset of any of these treatments, and she was not currently on any other treatment. There were not any affected family members from CL. Before admission to our hospital, she had performed genetic mutation analysis for pseudoxanthoma elasticum, which turned out to be negative. Dermatologic examination revealed sagging, loose skin of the lateral neck, chin, and abdomen with loss of elasticity (Figure 1). Slightly erythematous, annular plaques were discernible upon the arms and back (Figure 1). Our initial diagnoses were cutis laxa, mid-dermal elastolysis, and granulomatous slack skin. One punch biopsy was taken from the chin and showed decrease in the number of elastic fibers with Verhoeff-Van Gieson staining compatible with CL (Figure 2). Two other punch biopsies were taken from the erythematous annular plaques on the leg for Hematoxylin and Eosin staining and direct immunofluorescence (DIF) assay, respectively. Parakeratosis,

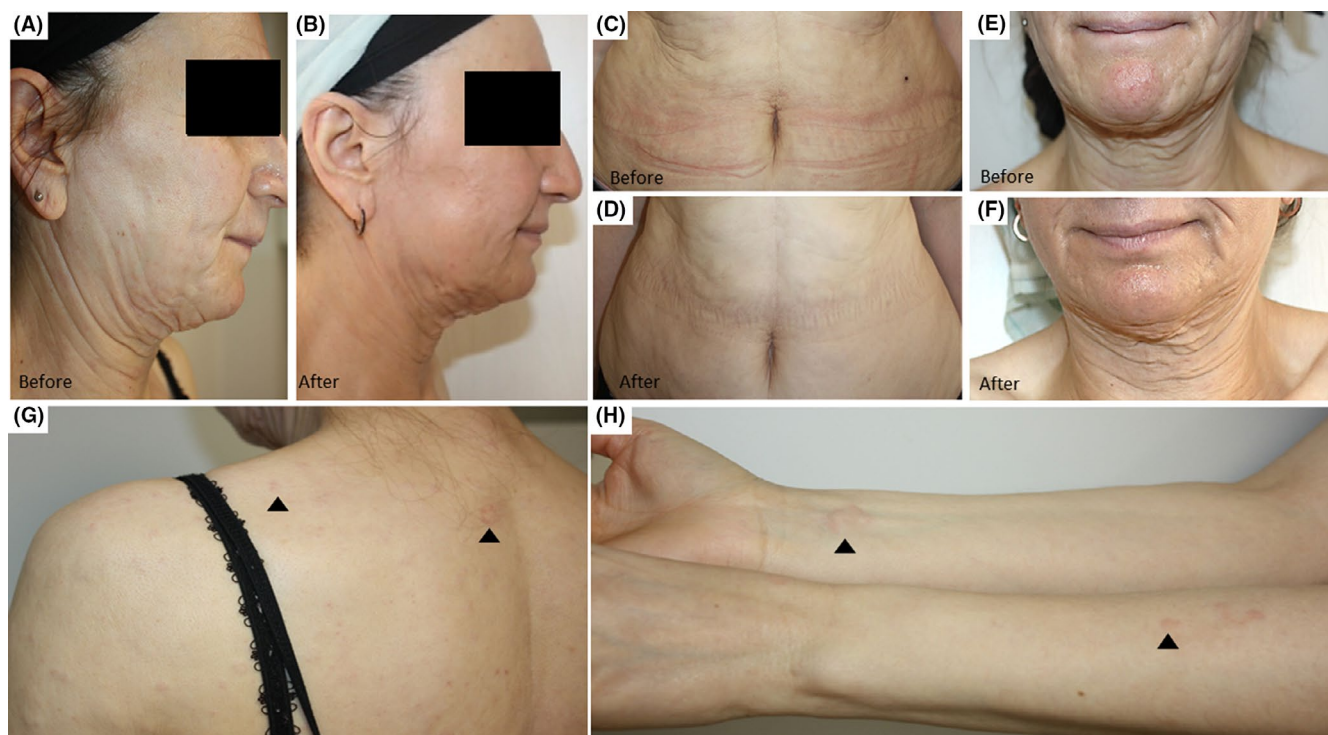


FIGURE 1 First presentation: Saggy, wrinkled skin involving the lateral neck (A), abdomen (C), and chin (E). Subtle, erythematous papules and plaques on the back (G) and on the arms (H) (arrowheads). After 3 months of treatment with dapsone, cessation of progression was observed in cutis laxa lesions involving the lateral neck (B), abdomen (D), and chin (F)

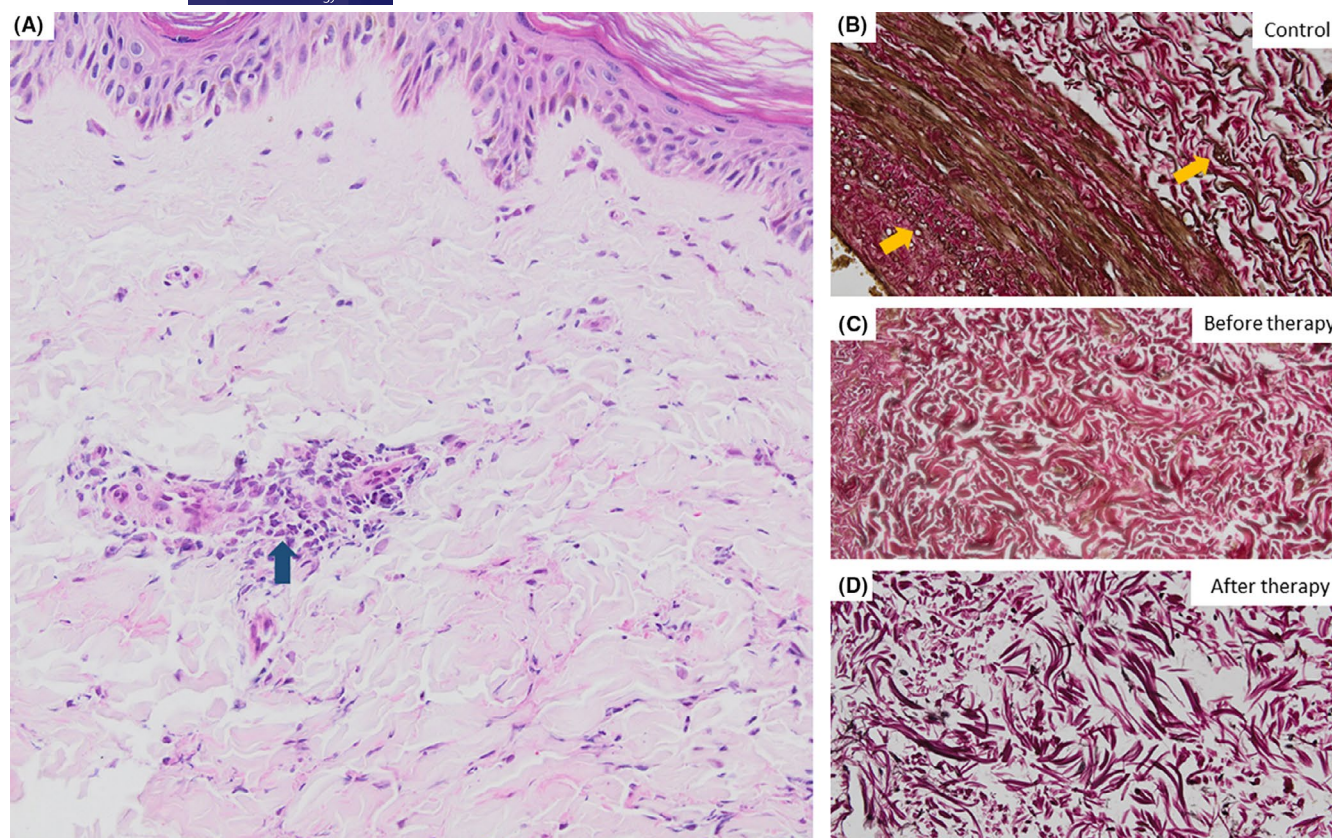


FIGURE 2 Superficial perivascular and interstitial lymphocytic reaction. Endothelial swelling and minimal nuclear dust (A, arrow) (Hematoxylin&Eosin, $\times 200$). Elastic fibers in the wall of an artery as the control (B, arrowheads) (Verhoeff-Van Gieson, $\times 200$). Loss of elastic fibers with Verhoeff-Van Gieson staining compatible with cutis laxa prior to therapy (C) (Verhoeff-Van Gieson, $\times 200$). No change in amount of elastic fibers in the biopsy after therapy (D) (Verhoeff-Van Gieson, $\times 200$)

focal-minimal spongiosis, perivascular lymphocytes in the superficial dermis along with leukocytoclasia were noted (Figure 2). No fibrin deposition was present, and DIF did not reveal any immune deposit. The patient was diagnosed with CL associated with chronic urticaria and was consulted to Medical Genetics Department. She was offered to have whole-exome sequencing analysis but she deferred. There were no abnormal laboratory results, and malignancy screening was negative. Echocardiography did not reveal any valvular (aortic) abnormalities, and abdominal ultrasonography did not show any bladder diverticula. She used 2×50 mg/day dapsone for 1 month and 1×50 mg/day for 2 months. At the end of dapsone treatment for 3 months, another biopsy was taken from the chin, right next to the prior biopsy site; no discernible change was detected by histopathological examination. However, no further progression along with stabilization was noted in CL lesions upon the lateral neck, cheeks, and abdomen (Figure 1). However, starting from the first week of the treatment, urticarial eruption ceased completely.

Cutis laxa manifests as localized or disseminated progressive loosening and wrinkling of the skin, which leads to the formation of deep furrows in the sagging skin.¹ ACL has two types: grouped as type I and type II.⁴ In type I ACL, the disease can be localized or generalized, and extracutaneous involvement such as emphysema, joint laxity, and arterial aneurysms may be accompanied.³ On the

contrary, type II ACL can be defined as localized elastolysis observed in the previous inflammatory skin areas (such as urticaria as in our case) without the involvement of visceral organs.⁴ ACL typically presents in adulthood and various drugs, and systemic inflammatory disorders and plasma cell dyscrasias are implicated in the etiopathogenesis of ACL.³ Chronic urticaria, dermatitis herpetiformis, Sweet syndrome, sarcoidosis, mastocytosis, and connective tissue disease are among the causative factors of ACL.³ Recently, Zheng et al⁵ and Takenaka et al⁶ reported two very similar cases of generalized ACL developing in the setting of urticarial eruption, which were successfully treated with diphenyl sulfone. In the case of urticaria, infiltration of the neutrophils into the elastic fibers, increased elastase activity and dysfunction of elastase inhibitors, may cause fragmentation, thinning, and disorganization in ACL.⁵⁻⁷ Since dapsone inhibits calcium-dependent activities of neutrophils, therapeutic management may be achieved by the use of dapsone.⁸ By looking at the examples of successful treatment with dapsone in ACL patients, we chose to start with dapsone. Even though we were unable to show any significant histopathological change, we believe that 3-month treatment period might not be enough to show any histopathological improvement in CL. Even the cessation of disease progression and complete clearance of urticaria by dapsone might be considered as contributions in CL patients. Surgery and

fractional carbon dioxide laser resurfacing may also provide cosmetic improvement in CL or ACL.^{1,9}

All in all, we would like to present a rare case of ACL developed in the background of urticarial eruption, and we were able to control the progression of skin loosening by dapsone. Our case shows that chronic urticaria is not just an innocent dermatologic disease that only affects patients' quality of life; instead, this chronic inflammatory disease may have significant impact on various skin structures such as elastic fibers causing ACL. We believe that it is possible to prolong the treatment response that can be achieved by different surgical modalities in CL patients; if we can manage to stabilize the disease activity with systemic treatments such as dapsone.

KEYWORDS

acquired cutis laxa, dapsone, urticaria

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CONFLICT OF INTEREST

None.

ETHICAL STATEMENT

Authors declare human ethics approval was not needed for this study.

AUTHOR CONTRIBUTIONS

Ecem Bostan involved in conceptualization, visualization, and writing-original draft. Basak Yalici-Armagan involved in conceptualization, supervision, writing-review and editing. Ozay Gokoz involved in conceptualization, data curation, supervision, and editing.

INFORMED CONSENT

Written informed consent for publication of medical images was taken from the patient.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REFERENCES

- Reddy GP, Mishra B, Upadhyaya DN. Acquired localized cutis laxa: a case report and the role of plastic surgery. *Indian J Dermatol.* 2019;64:55-58.
- Mehta B, Amladi S. Acquired localized cutis laxa of the face: a rare presentation. *Pediatr Dermatol.* 2011;28:421-423.
- Berk DR, Bentley DD, Bayliss SJ, Lind A, Urban Z. Cutis laxa: a review. *J Am Acad Dermatol.* 2012;66:842.e1-842.e17.
- Nabatanzi A, Da S, Male M, Chen S, Huang C. Type II acquired cutis laxa associated with recurrent urticarial vasculitis: brief report. *Allergy Asthma Clin Immunol.* 2020;16:1.
- Zheng BQ, Yan YL, Ou M, Wang XH. Successful treatment of acquired cutis laxa with urticarial eruption by diphenyl sulfone. *Clin Exp Dermatol.* 2021;46:599-603.
- Takenaka Y, Ishiguro N, Kawashima M. Case of acquired cutis laxa with preceding urticarial eruption treated by diphenyl sulfone. *J Dermatol.* 2018;45:e292-e293.
- Paulsen IF, Bredgaard R, Hesse B, Steiniche T, Henriksen TF. Acquired cutis laxa: diagnostic and therapeutic considerations. *J Plast Reconstr Aesthet Surg.* 2014;67:e242-e243.
- Suda T, Suzuki Y, Matsui T, et al. Dapsone suppresses human neutrophil superoxide production and elastase release in a calcium-dependent manner. *Br J Dermatol.* 2005;152:887-895.
- Nathan NR, O'Connor DM, Lee JJ, et al. Fractional carbon dioxide laser treatment for textural improvement and symptomatic relief of acquired cutis laxa of the neck. *Lasers Surg Med.* 2021;53:427-428.

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