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Acquired cutis laxa secondary to neutrophilic urticarial dermatosis with panniculitis: A case report

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Abstract

Cutis laxa is a heterogeneous group of dermatoses characterized by sagging and inelastic skin. They are often present as neutrophilic dermatosis before acquired cutis laxa. Herein, we describe a rare case of acquired cutis laxa secondary to neutrophilic urticarial dermatosis with panniculitis and review the literature for previously reported cases. A 22-year-old female had reported a 6-month history of wrinkled and loosening skin on the face. Base on clinical, laboratory and histopathological findings, we made a diagnosis of acquired cutis laxa secondary to neutrophilic urticarial dermatosis with panniculitis. She was treated with colchicine and thalidomide. And in time, the lesions disappeared, without any obviously change in skin sagging. According to the patient's treatment response, we put forward a viewpoint that the histopathological appearance of our case may be attributed to the end-stage of histopathologic alterations of subcutaneous Sweet syndrome.

Keywords

Cutis laxa; Neutrophilic urticarial dermatosis; Panniculitis; Case report.

Abbreviations

CL: Cutis laxa; NUD: Neutrophilic urticarial dermatosis; SPTCL: Subcutaneous panniculitis-like T cell lymphoma.

Introduction

Cutis laxa (CL) is a heterogeneous group of diseases, which can be characterized by sagging and inelastic skin due to the damage of dermal elastic fibers. It can be either inherited or acquired. According to the clinical characteristics, acquired CL is divided into two groups: Type 1 (generalized acquired elastolysis) and type 2 (Marshall's syndrome). To date, a lot of etiological factors have been reported to be related

to acquired CL type 1, which include malignancies, infections, connective tissue diseases, and medications. Marshall's syndrome usually presents itself as a post-inflammatory phenomenon without any evidence of extra cutaneous involvement. Herein, we describe a rare case of acquired CL secondary to Neutrophilic Urticarial Dermatosis (NUD) with panniculitis and review the literature for previously reported cases.

Case Report

A 22-year-old female was referred to our hospital with wrinkled and loosening skin on the face which had developed over the last 6 months. The patient had a two-year history of recurrent urticaria-like plaques and papules on various parts of her body. In particular, on the proximal limb and chest, they were asymptomatic and could spontaneously subside. The biopsy from another hospital showed a perivascular and interstitial neutrophilic infiltrate with intense leukocytoclasia but without vasculitis. The patient was otherwise in good health. She denied trauma and proceeding or concurrent illnesses.

Cutaneous examination revealed sporadic erythematous papules on her trunk and limbs (Figure 1A). The patient appeared much older than her actual age as a result of the sagging and wrinkling of her facial skin (Figure 1B). Two skin biopsies were taken, one from the loosening skin without erythema of the face, one from the asymptomatic erythematous nodules on the left upper extremity. The face biopsy revealed a normal epidermis with scarcely dermal interstitial neutrophilic infiltrates (Figure 2A). Special stains for elastin revealed rarefaction and fragmentation of elastic fibers (Figure 2B). Surprisingly, the biopsy from the left upper extremity showed lymphocyte-rich lobular panniculitis (Figure 2C), with some eosinophils, and plasma cells (Figure 2D). Laboratory examinations were unremarkable in her full blood count, serum immunoglobulin E, serum and urine immunofixation electrophoresis, anti-nuclear antibody, or anti-phospholipid antibody.

In view of the clinical, laboratory and histopathological findings, we made a diagnosis of acquired Cutis laxa (CL) secondary to Neutrophilic Urticarial Dermatosis (NUD) with panniculitis. The patient received treatment of oral colchicine and thalidomide. Following-up on this, all lesions disappeared in 3 months, without any obviously change in skin sagging. The patient has given her consent to her case to be reported.

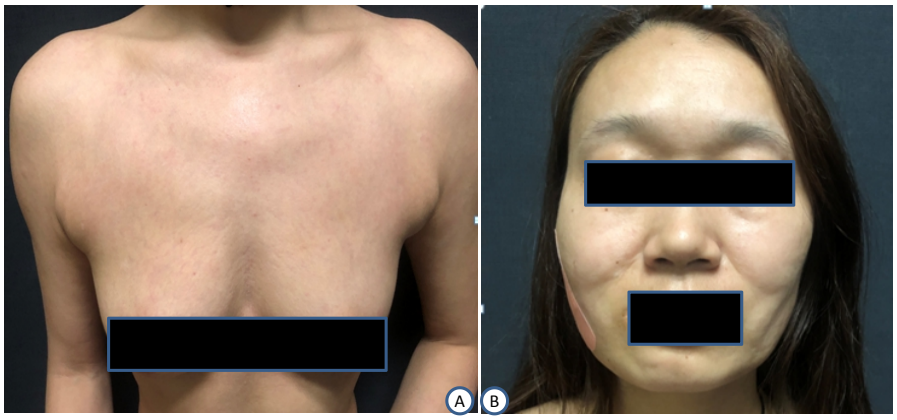

Figure 1: Clinical appearance.(A) sporadic and poorly-defined erythematous papules on her trunk;(B) wrinkled and loosening skin on her face,presenting a prematur-aging appearance.

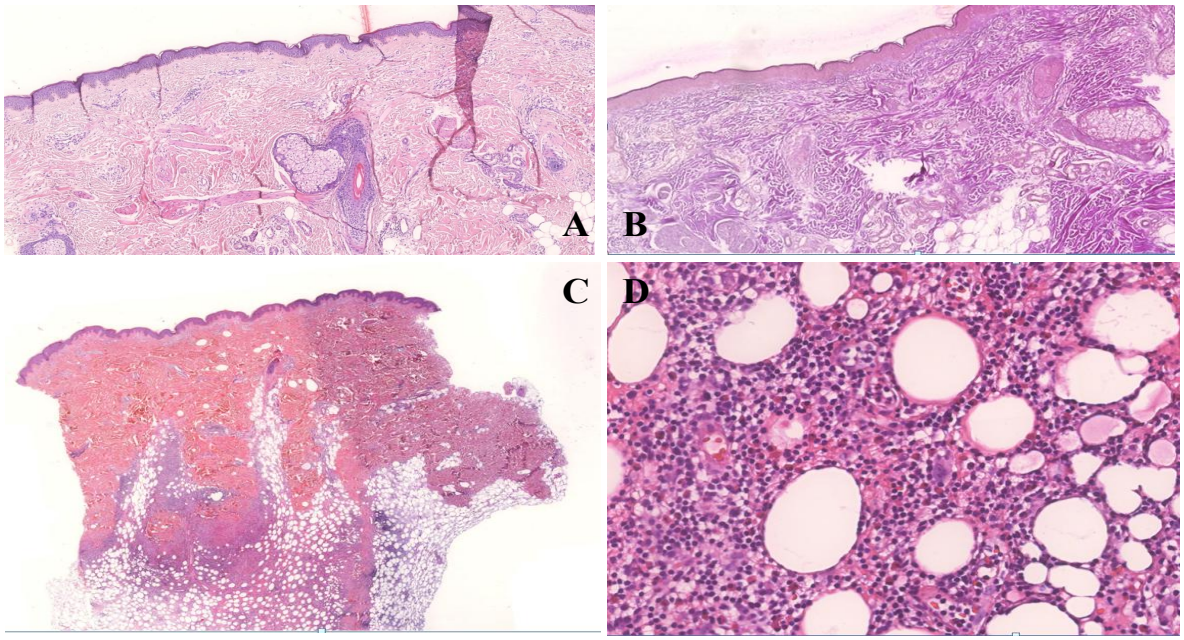

Figure 2: Results of histopathologic.(A)The face biopsy revealed a normal epidermis with scarcely dermal interstitial eutrophilic infiltrates(H&E staining, ×100);(B)Special stains for elastin revealed rarefaction and fragmentation of elastic fibers(Verhoeff elastic staining, ×100 X;(C)The biopsy from the left upper extremity showed a normal epidermis and interstitial infiltration in the dermis,with lobular panniculitis(H&E staining, ×23);(D)The infiltrating lymphocytes are uniform in shape and size.

Discussion

Cutis laxa (CL) is a heterogeneous group of diseases, which is characterized by stagging and inelastic skin. It can be inherited or acquired. Inherited forms of CL include autosomal dominant cutis laxa, autosomal recessive cutis laxa, Urban–Rifkin–Davis syndrome, macrocephaly-alopecia-cutis laxa-scoliosis syndrome, arterial tortuosity syndrome and X-linked cutis laxa [1]. As mentioned before, acquired CL is divided into two groups: Type 1 (generalized acquired elastolysis) and type 2 (Marshall's syndrome). Heretofore, a lot of etiologic factors such as medications, malignancies, infections, connective tissue diseases have been reported to be associated with acquired CL type 1 [2-4]. we performed laboratory tests of this patient to identify the underlying disease.

Acquired CL type 2 (Marshall's syndrome) usually presents itself as a post-inflammatory phenomenon without any systemic involvement evidence [5]. Typically, the course of the disease includes two stages, separated into an eruptive phase and an elastolysis phase. The onset of disease can be insidious and prolonged for months to years. In the eruptive phase, red papules and plaques appear in the head, trunk and limbs, which often manifest as an NUD. Unlike the common urticaria, the urticarial eruptions in this condition usually last more than 72 hours. Angioedema and facial swelling are rarely seen. Compared with urticaria vasculitis, neutrophilic urticarial dermatosis is characterized by an urticarial lesion with the histopathologic features of a perivascular and interstitial neutrophilic infiltrate with leukocytoclasia but without vasculitis or dermal edema. In the elastolysis phase, the skin lesion becomes wrinkled and stagging, giving the patient a premature-aging appearance. Base on the clinical, laboratory and histopathological findings, Marshall' syndrome is currently considered for the patient's diagnosis. NUD may be idiopathic or associated with systemic diseases including adult-onset still's disease, systemic lupus erythematosus, and

Schnitzler syndrome [6]. Hence, these patients need long-term follow-up.

After histopathological examination, acquired CL is suggested to be divide into 4 histopathologic stages [7]. Beginning at stage 1, lesions will show mild elastic fibers damage until stage 4, where the elastic tissue is finally burnout. This behavior suggests that elastic fibers degradation in acquired CL is an initial process, instead of the byproduct of inflammation. Each stage can simultaneously appear varying severity of dermatitis. The patient we reported had three skin biopsies. Very Under high magnification, the infiltrating lymphocytes are uniform in shape and size without obvious atypia. In order to exclude lupus, we also performed direct immunofluorescence, which is negative. We observed that these panniculitis-like nodules disappeared in few days without any trace after prescribed oral colchicine and thalidomide. This phenomenon is highly suggestive of subcutaneous Sweet syndrome which vanish spontaneously or usually has a rapid response to corticosteroids [8]. The typical histopathologic manifestations of subcutaneous Sweet syndrome is neutrophilic lobular panniculitis with obvious leukocytoclasis and mild fat necrosis. However, we did not see evidence of neutrophils infiltrating in our case. As the fact that most panniculitis start with neutrophilic infiltrates and then transform into different conditions, we attributed this biopsy finding to the end-stage of histopathologic alterations of subcutaneous Sweet disease.

The pathogenesis of acquired CL is not clear, but according to the histopathology, the destruction and reduction of elastin fibers play a decisive role in the pathogenesis. As we know, elastase is the crucial enzyme to degrade elastin fibers, which is mainly produced by macrophages, neutrophils, and fibroblasts. Hence, it is possible that recurrent inflammation may stimulating elastase activity resulting in progressive elastolysis. Our case also supports a role for inflammation in the pathogenesis of acquired CL.

The main differential diagnosis of Marshall's syndrome includes anetoderma dermal elastolysis and granulomatous skin laxity. Anetoderma is characterized by small round papules usually with normal skin color and hernia sac tactile sensation. Mid dermal elastolysis shows significant features in histopathology that the elastic fibers in the dermal reticular middle layer was reduced or completely absent, while the elastic tissue of the dermal papilla and the lower reticular layer were less involved. Granulomatous skin laxity is considered to be a rare subtype of mycosis fungoides, which usually occurs in the axilla and groin. Pathologically, it is characterized by lymphoid cell infiltration, multinucleated giant cell granuloma formation, and loss of elastic fibers. In this case, we also need to differentiate from a group of primarily-lobular panniculitis such as lupus panniculitis, Subcutaneous panniculitis-like T cell lymphoma (SPTCL), and so on. Lupus panniculitis often presents itself with erythematous nodules in areas (including the upper arm, shoulder, face, scalp and buttocks) less commonly affected by other types of panniculitis. The typical histopathological manifestation is lobular lymphocytic panniculitis. The lymphatic follicular panniculitis. The usually has a good response to hormone and hydroxychloroquine. Patients with SPTCL typically present with one or more usually painless subcutaneous nodules or poorly circumscribed indurated plaques. The diagnosis of SPTCL is mainly based on pathology which is characterized by subcutaneous infiltration of atypical T cells that distinctly surround the individual fat cells, as well as by a unique immunophenotype (expression of CD3, CD8, and TCR, but negative for CD4 and CD56).

At present, there is no satisfactory treatment for acquired CL. Some people suggest dapsone and topical corticosteroid may be benefit in the inflammatory phase [9,11,12]. However, it cannot reverse or

prevent disease progression. Biologics may have better prospects. For patients who have a strong need to improve their appearance, it seems that plastic operation may be the only way, but the duration of appearance after surgery is uncertain.

Note that neutrophilic dermatosis precedes the occurrence of acquired CL. We searched PubMed for articles on CL and neutrophilic dermatosis from 1980 to 2022 and found 24 reports of this condition (table 1) [9-11,13-32]. 13 cases were associated with Sweet syndrome that preceded the onset of CL, and 10 cases were associated with NUD.

Conclusion

In conclusion, the diagnosis of acquired cutis laxa is based on clinic and pathology. Systematic examination is very important for disease classification and therapeutic schemes. Acquired CL associated with panniculitis is a rare skin disease. As far as we know, it has not been reported before. In addition, more study is needed to fully explore the pathological mechanism for this rare disease and to find more effective treatment.

Table 1: Reports of acquired cutis laxa after neutrophilic dermatosis.

Author (Year)	**Preceding dermatosis**	**Age at onset**	**Sex**	**Remarks**
Weir et al. (1977)	Sweet's syndrome	N/A	N/A	Cardiovascular involvement
Christensen et al. (1983)	Sweet's syndrome	17 months	F	Aorta were affected
Muster et al. (1983)	Sweet's syndrome	16 months	N/A	Aorta were affected
Chun et al. (1995)	Urticarial papules	28 years	M	No laboratory abnormalities
Hwang et al. (1995)	Sweet's syndrome	16 months	N/A	Alpha-1 antitrypsin deficiency
Bouloc et al. (1999)	Urticarial papules	15 years	F	No laboratory abnormalities
Guia et al. (1999)	Sweet's syndrome	7 months	M	Aorta were effected
Prasad et al. (2002)	Sweet's syndrome	1 months	F	Fever and neutrophilia
Timmer-de Mik et al. (2009)	Sweet's syndrome	8 months	M	Fever and neutrophilia
Haider et al. (2010)	Erythematous plaques	14 months	F	Fever, neutrophilia, high IgE
Guhamajumdar et al. (2011)	Sweet's syndrome	2 years	F	Cardiovascular involvement
Sun et al. (2011)	Urticarial papules	15 years	M	No laboratory abnormalities
Ma et al. (2012)	Sweet's syndrome	11 years	M	Fever and leukocytosis
Fontenelle er al. (2013)	Urticarial papules	6 years	M	No laboratory abnormalities
Kluger et al. (2014)	Urticarial papules	40 years	M	Joints were affected
Paulsen et al. (2014)	Urticarial papules	30 years	F	No laboratory abnormalities
Ercan et al. (2015)	Urticarial papules	19 years	M	Pituitary microadenoma, high IgE
Aslan et al. (2017)	Sweet's syndrome	28 years	M	No laboratory abnormalities
Takenaka et al. (2018)	Urticarial papules	35 years	F	No laboratory abnormalities
Knöpfel et al. (2020)	Sweet's syndrome	10 years	F	Fever and neutrophilia
Jagati et al. (2020)	Sweet's syndrome	3 years	F	Fever,neutrophilia,anemia
Fauconneau et al. (2021)	Urticarial papules	34 years	M	No laboratory abnormalities
Rosier et al. (2022)	Sweet's syndrome	51 years	M	No laboratory abnormalities
This report (2022)	Urticarial papules	22 years	F	No laboratory abnormalities

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