



Autosomal Recessive Cutis Laxa Type 1: A Rare Case Report

Authors

**Samriti Sood¹, Saru Thakur^{2*}, Mudita Gupta³, Reena K Sharma⁴, GR Tegta⁵,
Mohit Bajaj⁶**

^{1,2}Post graduate student, ³Assistant Professor, ⁴Senior Resident, ⁵Professor and Head, Deptt. of Dermatology, Venereology and Leprosy, Indira Gandhi Medical College, Shimla, Himachal Pradesh

⁶Post graduate student, Deptt. of Paediatrics, Indira Gandhi Medical College, Shimla, Himachal Pradesh

*Corresponding Author

Saru Thakur

Deptt. of Dermatology, Leprosy and Venereology, Indira Gandhi Medical College, Shimla,
Himachal Pradesh, India

Abstract

Cutis laxa is an acquired or inherited disorder of connective tissue characterized by wrinkled and inelastic skin. This is attributed to inborn errors of elastin synthesis and structural defects of extracellular matrix proteins. The inherited form of cutis laxa is uncommon as compared to the acquired form. We present a ten months boy of autosomal recessive cutis laxa type 1 with pulmonary involvement.

Keywords: *cutis laxa, recessive, sagging skin, type 1.*

Introduction

Cutis laxa is an acquired or inherited skin disorder characterized by lax pendulous skin that recoil slowly when pulled. Various modes of inheritance have been described as autosomal dominant, autosomal recessive and x-linked recessive. Autosomal recessive types (ARCL1 and ARCL2) are the most common.⁽¹⁾ Autosomal recessive cutis laxa (ARCL) is a genetically heterogeneous condition exhibiting variable phenotype in different patients. Three common types are known with generalized loose skin and increased elasticity, being a common feature in all the three types.⁽²⁾ The loose skin is most easily noticeable on the face giving a prematurely aged appearance. Systemic complications are seen in ARCL. We present a ten months old boy with ARCL type 1

due to rarity of its occurrence with pulmonary involvement.

Case Report

A ten months male infant, second born of non-consanguineous marriage, presented to the emergency department in respiratory distress with fever and cough for 1 week. His birth history was uneventful and developmental history was normal for age. He presented to dermatology department with the complaints of loosely hanging skin since birth and a non contributory family history. The skin over the face had a wrinkled appearance with sagging of cheeks and earlobes. Ears were large with broad flat nose. The laxity was more appreciable at the axillary and thigh folds (Figure 1) and neck (Figure 2). Lax and pendulous skin

was observed, which was recoiling slowly on being pulled (Figure 3).



Figure 1: Lax skin can be observed at the axillary, elbow and thigh folds



Figure 2: Redundant skin folds at the neck and the chest

There was no joint hyper extensibility and increased skin fragility. On systemic examination, the patient was febrile and had intercostal and subcostal muscle retraction with crepitations in bilateral lower lobes. The patient had an oxygen saturation of 66%, respiratory rate 54 per minute and heart rate of 132 beats per minute. The other systems were also examined for any abnormalities and the examination was found to be within normal limits. Slit-lamp examination of the eyes revealed no angioid streaks. He was started with

continuous positive airway pressure and injectable antibiotics. Routine investigations were within normal limits except for a raised total leucocyte count of 20 thou/microL. Emphysema with collapsed right lower lobe was seen on chest radiography. The histopathological examination of skin revealed normal epidermis with diminished elastic fibres and no infiltrate in upper dermis with normal number and thickness of collagen bundles on hematoxylin and eosin staining (Figure 4). The elastic fibres present were fragmented, stained uneven and showed granular appearance, as evidenced in Verhoeff-van Gieson stain. Von-Kossa stain did not show any calcification. The findings were consistent with cutis laxa.



Figure 3: Lax skin over abdomen which recoiled slowly on being pulled

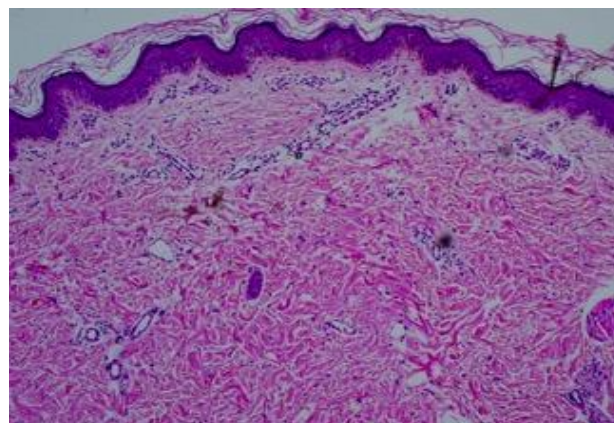


Figure 4: Skin biopsy shows normal number and thickness of collagen bundles with markedly reduced elastic fibres.

Discussion

Cutis laxa is a rare disorder of elastic tissue characterized clinically by loosely hanging skin folds. It can be acquired or hereditary. Acquired Cutis laxa has been seen after a febrile illness, inflammatory skin diseases such as Lupus erythematosus or Erythema Multiforme, Amyloidosis, Urticaria, Angioedema and Hypersensitivity reactions to penicillin.⁽³⁾ In hereditary forms, the clinical presentation and the mode of inheritance show considerable heterogeneity and presents as autosomal dominant (ADCL), autosomal recessive (ARCL) and X-linked inheritance (XRCL).⁽⁴⁾ However, the underlying genetic etiology in the majority of cases of severe ARCL is still unknown in a few children.

The genetic mutations can lead to errors of elastin synthesis or structural defects of extracellular matrix proteins leading to the decreased elasticity and redundant, sagging skin in patients with cutis laxa.⁽⁵⁾ Cutis laxa variably affect connective tissue in the skin as well as other parts of the body, including the heart, blood vessels, joints, intestines and lungs.⁽¹⁾

ARCL is classified into three types, out of which, ARCL type I is the most severe form and is fatal at an early age due to cardiac or pulmonary complications. In this, mutations are seen in the fibulin-5 (FBLN5)⁽⁶⁾ and the fibulin-4 (FBLN4, EFEMP2) genes⁽⁷⁾ encoding the extracellular matrix proteins fibulin-5 and fibulin-4 which is EGF-containing fibulin-like extracellular matrix protein 2. The skin manifestations affect the whole body and are usually recognised from birth. The excessive sagging skin is more prominent around the axillae, groins, neck and on the face, giving patient an aged appearance with ptosis and drooping cheeks. Pulmonary emphysema develops early in the life often leading to respiratory failure. Our patient also presented to emergency department with respiratory complaints and was suffering from similar episodes since past 5 months. Other features which may be seen include vascular anomalies such as arterial aneurysms,

fibromuscular artery dysplasia and stenosis, gastrointestinal or genitourinary system diverticulae, cranial anomalies, late closure of the fontanel, joint laxity, hip dislocation, arachnodactyly and bone fragility. These systemic anomalies were absent in our patient. Intelligence is normal in ARCL type I.⁽⁸⁾

ARCL type II along with cutis laxa presents with developmental delay, and associated skeletal abnormalities. ARCL Type III (De Barsy syndrome) is characterised by the presence of progeroid appearance with athetoid movements and corneal clouding. In contrast autosomal dominant cutis laxa caused by mutation in elastin gene, is associated with mild condition without systemic abnormalities⁽⁹⁾. The third type of cutis laxa is transmitted by X-linked inheritance (OMIM 304150), it is also termed occipital horn syndrome which is allelic to menkes disease.⁽¹⁰⁾

Histopathological examination reveals normal thickness of epidermis. The elastic fibres are sparse, short, fragmented and clumped, particularly in the upper dermis and show granular degeneration.⁽¹⁾ Electron microscopy demonstrates moth-eaten appearance, abnormal elastin fiber branching and lose microfibrils and therefore is diagnostic in most types of autosomal recessive cutis laxa. Besides the characteristic frayed elastic fibers, reduced in number and density, the skin collagen fibril network could be fully normal.

The differential diagnosis includes other inherited disorders of connective tissue like Pseudoxanthoma elasticum (PXE) and Ehler Danlos Syndrome (EDS). The child could be differentiated from PXE by the absence of the characteristic yellow color of PXE and lack of calcification with Von Kossa stain. Absence of skin fragility, easy bruisability and joint involvement ruled out EDS.

Treatment is limited and is based on alleviating the comorbidities. Surgical correction of redundant skin folds, prolapses or hernias may be undertaken. However, surgery often produce temporary benefit. Botulinum toxin injections are

being considered for improving the agent appearance and facial defects.

Conclusion

Autosomal recessive cutis laxa type1 is a rare inherited disorder of connective tissue. Severe systemic manifestations like cardiopulmonary involvement leading to respiratory failure may be seen in these patients.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms, in which, the patient's attendant has given his consent for his child's images and other clinical information to be reported in the journal. The attendant understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Conflict of Interest: Nil

Sources of Support and Sponsorship: Nil

References

- Burrows N. Genetic Disorders of Collagen, Elastin and Dermal Matrix In: GriffithsC, Barker J, Bleiker T, Chalmers R, Creamer D eds, Rook's, Textbook of Dermatology. 9th ed. John Wiley & Sons, Ltd 2016. p. 72.11.
- Kornak U, Reynders E, Dimopoulou A, van Reeuwijk J, Fischer B, Rajab A, *et al*. Impaired glycosylation and cutis laxa caused by mutations in the vesicular H⁺- ATPase subunit ATP6V0A2. *Nat Genet* 2008;40:32- 4.
- Dhale SN, Rathod AD, Sonawane S. A Case Report of Cutis Laxa. *Bombay Hospital Journal* 2012; 54:186-7.
- Morava E, Guillard M, Lefeber DJ, Wevers RA. Autosomal recessive cutis laxa syndrome revisited. *Eur J Hum Genet* 2009;17:1099- 110.
- Urban Z, Gao J, Pope FM, Davis EC: Autosomal dominant cutis laxa with severe lung disease: synthesis and matrix deposition of mutant tropoelastin. *J Invest Dermatol* 2005; 124: 1193-9.
- Elahi E, Kalhor R, Banihosseini SS *et al*: Homozygous missense mutation in fibulin-5 in an Iranian autosomal recessive cutis laxa pedigree and associated haplotype. *J Invest Dermatol* 2006; 126: 1506-9.
- Huchtagowder V, Sausgruber N, Kim KH, Angle B, Marmorstein LY, Urban Z: Fibulin-4: a novel gene for an autosomal recessive cutis laxa syndrome. *Am J Hum Genet* 2006; 78: 1075- 80.
- Kielty CM: Elastic fibres in health and disease. *Expert Rev Mol Med* 2006; 8: 1–23.
<https://doi.org/10.1017/S146239940600007X>
- Tassabehji M, Metcalfe K, Hurst J *et al*: An elastin gene mutation producing abnormal tropoelastin and abnormal elastic fibres in a patient with autosomal dominant cutis laxa. *Hum Mol Genet* 1998; 7: 1021– 1028. *Eur J Hum Genet* 2008; 16:28– 35.
- Hbibi M, Abourazzak S, Idrissi M, Chaouki M, Atmani S, Hida M. Cutis Laxa Syndrome: a case report. *Pan Afr Med J.* 2015; 20:3.
<https://dx.doi.org/10.11604%2Fpamj.2015.20.3.5878>.