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Case Report

Cutis laxa with systemic involvement

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Abstract Cutis laxa is a disorder of skin due to defective elastin synthesis. In both the inherited type and the acquired type, the internal organs are frequently involved. A case of a 27-year-old female patient suffering from cutis laxa is reported who developed severe pulmonary and cardiac involvement in adulthood.

Key words
Cutis laxa, elastin.

Introduction

Cutis laxa (CL) is a rare, inherited or acquired connective tissue disorder in which the skin becomes inelastic and hangs loosely in folds.[1] The clinical presentation and the mode of inheritance show considerable heterogeneity. The clinical features of cutis laxa are thought to be due to defective elastin synthesis that results in sparse and abnormal elastic fibres in the affected tissues.[2] We report here a case of 27-year-old female patient of CL who developed severe pulmonary and cardiac involvement in adulthood.

Case report

A 27-year-old female presented in the emergency department of Services Hospital, Lahore, with 2-year history of progressively increasing loosening of skin on the face especially on the eyelids. She developed drooping of upper eyelids and exertional dyspnea with cough which was productive of large quantities of sputum for the last 18 months. She also had vomiting for last 5 days. Her problem started when she developed urticarial lesions on her upper eyelids bilaterally followed by periorbital puffiness, which later on progressed to drooping of her upper eyelids in 6 months. She also developed umbilical hernia during this period. She noticed her skin becoming loose especially in the skin folds, arms, neck and on her abdomen. There were no other significant symptoms. Her family history was negative for any similar illness. On general physical examination, she looked much older than her actual age. She was oriented in time, place and person. She was in obvious respiratory distress. There was ptosis and periorbital edema (**Figure 1**). The skin was lax and inelastic (**Figure 2**). She had a raised JVP, clubbing of fingers, macroglossia (**Figure 3**), umbilical hernia (**Figure 4**) and oral thrush.

She was febrile with a temperature of 101ºF, heart rate of 110 beats per minute, blood pressure of 90/60 mmHg and a respiratory rate of 24/min. Cyanosis was present and there was

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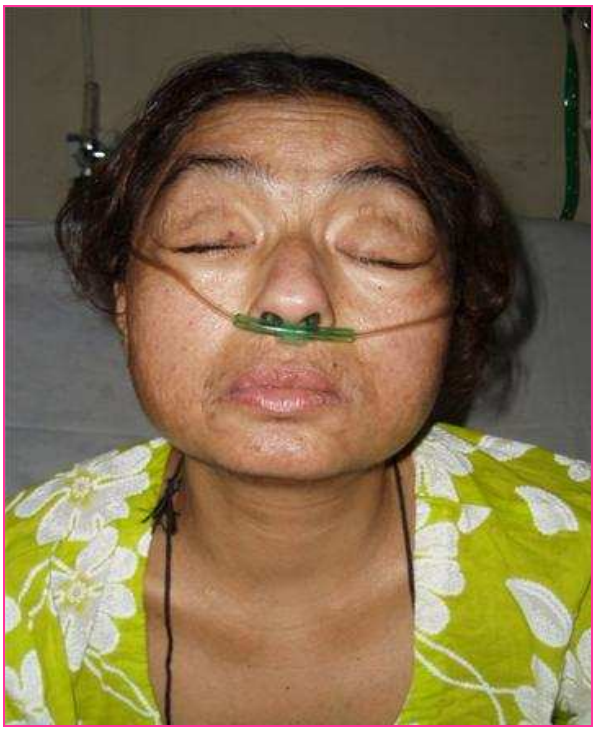

Figure 1 Periorbital edema and ptosis.

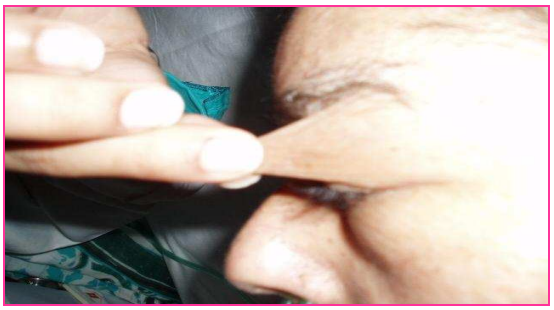

Figure 2 Laxity of upper eyelid skin.

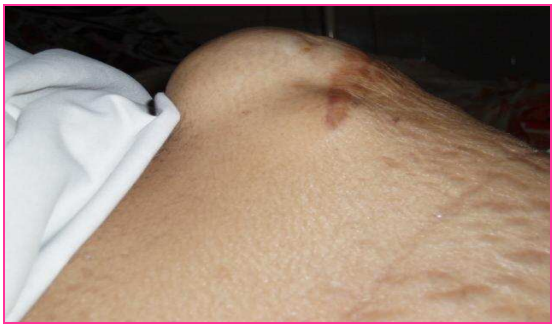

Figure 4 Abdominal hernia and striae formation.

Figure 3 Macroglossia.

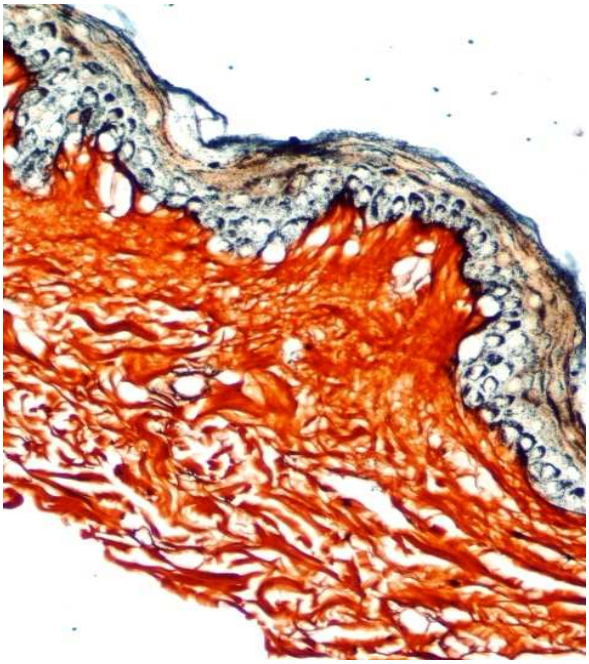

Figure 5: Reticulin stained sparse and fragmented elastic tissue.

pedal edema with pitting. There were no lymph nodes palpable. Her liver was palpable two fingers below the costal margin with an increased span. She had diffuse crepitations with wheeze heard all over her chest. Cardiac examination showed left parasternal heave, loud P_2 and a grade 2 pansystolic murmur on tricuspid area. The rest of the systemic

examination was normal. The investigations revealed: hemoglobin = 9.2 g/dL, TLC = 13,000/µL, hematocrit = 32%, ESR = 25mm/hr, total bilirubin = 1.5 mg/dL, ALT = 64 U/L, AST = 56 IU/L, serum creatinine = 2.1 mg/dL, Urea = 57 mg/dL, total proteins = 6.2 g/dL, albumin = 2.9 g/dL. Serum electrolytes, thyroid function tests, coagulation profile and blood sugar levels were normal. Her complete urine analysis showed pH = 6.0, specific gravity = 1,020, proteins = +++, RBCs = 24/HPF, pus cells = 3-4/HPF, glucose = nil, ketones = nil, bilirubin = nil, urobilinogen = normal, casts = nil. 24 hour urinary proteins were 0.4 g/24 hrs. Her arterial blood gases showed compensated respiratory acidosis with an oxygen saturation of 80.6% on room air. X-ray chest PA view showed moderate right sided pleural effusion and scattered irregular opacities. High resolution CT scan of chest showed thickening of airways, cysts, mucous plugs and decreased vascularity. Pulmonary function tests revealed obstructive pattern with decreased FEV_1 and decreased FEV_1/FVC. Echocardiography revealed pulmonary hypertension with tricuspid regurgitation. Ultrasonography of abdomen revealed hepatomegaly with markedly thick walled gallbladder and biliary ducts. Mild ascites was also noted.

A skin biopsy was done that revealed short, sparse, clumped and fragmented elastic fibres particularly in the upper dermis (**Figure 5**).

She presented at a late stage of her disease and was given symptomatic treatment which included cardiac support, diuretics, antibiotics and supplementary oxygen; however, she succumbed to death. The most striking feature of the disease in our patient was her severe pulmonary involvement which is rare to find in a patient with systemic cutis laxa syndrome.

Discussion

CL, also known as 'dermatolysis', 'generalized elastolysis', and 'pachydermatocele'[3], is a group of rare connective tissue disorders mainly involving the skin but can also affect heart, lungs, arteries, joints and other organs as well when severe. It is inherited in an autosomal dominant, autosomal recessive or X-linked recessive forms but it can also be acquired. It may occur spontaneously or in 50% of cases develop following episodes of urticaria or angioedema or extensive inflammatory skin disease (e.g. eczema, erythema multiforme, blistering eruption)[4] as in our patient. CL may be caused by mutations in the genes: ELN, ATP6V0A2, ATP7A, FBLN4,[5] and FBLN5.[2,6]

The underlying etiology of this disorder is unknown but is related to the reduction of elastic fibres. Some of the mechanisms responsible for this reduction are increased elastase activity,[6] decreased serum elastase inhibitor level, decreased elastin gene expression, abnormal copper metabolism/copper deficiency and low lysyl oxidase activity.[7]

According to some reports isolated cases of cutis laxa have been reported in patients undergoing D-penicillamine therapy (copper chelator) such as those with Wilson's disease due to the elastolytic effect of D-penicillamine.[8]

CL is characterized by degenerative changes in the elastic fibers resulting in loose, pendulous skin. The skin is sagging, redundant, and stretchable with reduced elastic recoil. The cutaneous findings of CL may be striking, but the elastic fiber network is even more important for pulmonary and cardiovascular function.[9] There may be furrowing of the skin of the whole body that is particularly obvious in neck, axillae, and groin. The face has a typical droopy

appearance with eyelid ptosis and droopy cheeks. Overall the face shows a picture of premature aging.[1] Hernias especially inguinal and incisional can also appear very commonly in such patients. A distinguishing feature of the skin is that it does not spring back into position and is inelastic as compared to Ehlers-Danlos syndrome in which the skin becomes hyperelastic.[10,11]

Elastic fibre degeneration in pulmonary system leads to pulmonary emphysema which if worsened can lead to bronchiectasis and cor pulmonale. Hollow viscus diverticulae such as intestinal diverticulae, esophageal dilatation and rectal and uterine prolapse can also be found due to the same reason.[12,13]

Costello syndrome, which should be included in the differential diagnosis of cutis laxa, has distinctive features such as nasal papillomata, coarse facies and mental retardation.[14,15] Pseudoxanthoma elasticum (PXE) is another disorder similar to cutis laxa. In PXE, there is mineralization (accumulation of calcium and other minerals) and fragmentation of the elastin-containing fibers in connective tissue, but primarily in the midlaminar layer of the dermis and the midsized arteries.[16] Usually, pseudoxanthoma elasticum affects the skin first, often in childhood but frequently, later. Small, yellowish papular lesions form and cutaneous laxity mainly affects the neck, axillae, groin, and flexural creases.

Our patient when presented to us in the medical emergency had developed severe dyspnea due to superadded pulmonary infection on already bronchiectatic lungs (as evident on the CT-scan lungs). The long standing bronchiectasis resulted in proteinuria (due to amyloidosis of the kidneys).[17] Echocardiography supported the diagnosis of right heart failure due to cor pulmonale. However, there was no evidence of pulmonary or aortic stenosis on the echocardiography which could be seen in some cases of systemic CL.[18] The extensive pulmonary involvement led to the demise of the patient despite supplementary oxygen and cardiac support. Isolated cutis laxa on the other hand has a very good prognosis as microsurgeries are very effective in treating the aesthetic aspect of the disease. The success of plastic surgery in CL is also due to the fact that wound healing is not affected by the disease process.[19] Botulinum toxin injection in isolated facial CL has also a good prognosis.[20] Apart from the various supportive therapies there is no absolute cure of the disease and the prognosis is worse in systemic involvement. Dapsone is sometimes used to slow the progression of the disease but the data are very limited.[21]

It is difficult to state with certainty whether our case had acquired or congenital form of CL. There was no family history and the disease was of late onset. These features are suggestive of an acquired condition. The causes of the acquired forms are not known.

References

1. Fazio MJ, Olsen DR, Uitto JJ. Skin aging: Lessons from cutis laxa and elastoderma. *Cutis* 1989; **43**: 437-44.
2. Hu Q, Loeys BL, Coucke PJ *et al.* Fibulin-5 mutations: mechanism of impaired elastic fibre formation in recessive cutis laxa. *Hum Mol Genet* 2008; **15**: 3379-86.
3. James WD, Berger TG, Elston, DM, eds. *Andrews' Diseases of the Skin: Clinical Dermatology, 10th edn*. Philadelphia: Saunders; 2005.
4. Musaliar S, Nair SP, Yogirajan K, Kumari L. Acquired cutis laxa. *Indian J Dermatol Venereol Leprol* 2003; **69** (Suppl): S48-S9
5. Hucthagowder V, Sausgruber N, Kim KH *et al*. Fibulin-4: a novel gene for an autosomal recessive cutis laxa syndrome. *Am J Hum Genet* 2006; **78**: 1075-80.

6. Bouloc A, Godeau G, Zeller J *et al.* Increased fibroblast elastase activity in acquired cutis laxa. *Dermatology* 1999; **198**: 346-50.
7. Khakoo A, Thomas R, Trompeter R *et al.* Congenital cutis laxa and lysyl oxidase deficiency. *Clin Genet* 1997; **51**: 109-14.
8. Hill VA, Seymour CA, Mortimer PS. Penicillamine-induced elastosis perforans serpiginosa and cutis laxa in Wilson's disease. *Br J Dermatol* 2000; **142**: 560-1.
9. Chhabra SK, Gupta RK, Singh T. Cutis laxa and pulmonary emphysema. *Indian J Chest Disease Allied Sci* 2001; **43**: 237.
10. Itin PH, Burgdorf WHC, Happle R *et al*. Genodermatoses. In: Schachner LA, Hansen RC, eds. *Pediatric Dermatology*. Philadelphia: Mosby; 2003. P. 263-384.
11. Sarkar R, Kaur C, Kanwar AJ, Basu S. Cutis laxa in seven members of a North-Indian family. *Pediatr Dermatol* 2002; **19:** 229-31.
12. 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.
13. Torrent JMG, García FC, Gómez MC, Gómez MG. Alteraciones cardiovasculares en el síndrome de cutis laxa congénita. *Rev Esp Cardiol* 1999; **52**: 204-6. (Spanish).
14. Platton MA, Baraitser M. Cutis laxa and the Costello syndrome (Letter). *J Med Genet* 1993; **30**: 622..
15. Davies SJ, Hughes HE. Costello syndrome: natural history and differential diagnosis of cutis laxa. *J Med Genet* 1994; **31**: 486-9.
16. Gheduzzi D, Sammarco R, Quaglino D *et al.* Extracutaneous ultrastructural alterations in pseudoxanthoma elasticum. *Ultrastructural Pathol* 2003; **27**: 375-84.
17. Newton JA, Mckee PH, Black MM. Cutis laxa associated with amyloidosis. *Clin & Exp Dermatol* 1986; **11**: 87-91
18. Dasouki M, Markova D, Garola R *et al.* Compound heterozygous mutations in fibulin-4 causing neonatal lethal pulmonary artery occlusion, aortic aneurysm, arachnodactyly and mild cutis laxa. *Am J Med Genet A* 2007; **143A**: 2635-41.
19. William TO, Michael MH, Randall CD. Congenital cutis laxa: a case report and review of loose skin syndromes. *Ann Plas Surg* 1993; **30**: 252-56.
20. Tamura BM, Lourenço LM, Platt A *et al*. Cutis laxa: Improvement of facial aesthetics by using botulinum toxin. *Dermatol Surg* 2004; **30**: 1518-20.
21. Fisher BK, Page E, Hanna W. Acral localized acquired cutis laxa.. *J Am Acad Dermatol* 1989; **21**: 33-40.