Acquired cutis laxa: an unusual skin manifestation of systemic amyloidosis

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Introduction

Cutis laxa (CL) is a rare connective tissue disorder of the elastin fibre network, predominantly affecting the skin. It may also involve other tissues such as the lung and the gastrointestinal tract (1).

CL is either inherited or acquired. Acquired cutis laxa (ACL) is less common than congenital forms. It often begins in the second and third decades of life. ACL has been reported to be associated with post inflammatory skin diseases, multiple myeloma, lymphoma, systemic lupus erythematosus, rheumatoid arthritis, systemic amyloidosis, sarcoidosis, nephrotic syndrome, celiac disease, syphilis, alpha-1 antitrypsin deficiency and drugs such as penicillamine and isoniazid (2). However, sometimes a cause cannot be identified.

Common cutaneous manifestations of primary amyloidosis include petechiae, purpura, ecchymoses, waxy papules, nodules, plaques or tumefactive lesions (3). Cutis laxa is an unusual clinical manifestation of primary systemic amyloidosis (4).

We report a patient with systemic amyloidosis presented with generalized ACL. We were unable to find a similar case reported in Sri Lanka, previously.

Case Presentation

A 44-year native Sri Lankan Tamil female presented with progressive bilateral ankle oedema and shortness of breath on exertion for three months and reduced urine output for one month. She also reported hoarseness of voice, constipation, hair loss, reduced appetite and weight loss in the last six months.

She had noted wrinkling and laxity of the skin which began around her eyes four years ago and progressed

to the rest of the face, neck, axillae, chest, abdomen and thighs. She had undergone vaginal hysterectomy for third degree utero-vaginal prolapse, which developed few years after the appearance of skin laxity. She has been on treatment for hypertension and ischemic heart disease for one year.

Her skin was wrinkled, loose, and hanging in folds, which were most prominent on the face, neck, axillae, chest, abdomen and groins (Figure 1). She appeared much older than her actual age. Elastic recoil of the affected skin was markedly reduced. The skin lesions were not associated with scaling, erythema, induration or pigmentary changes. Mucosae were not affected. She was pale and had bilateral leg oedema. Her blood pressure was 130/90 mmHg.

Investigations showed normochromic normocytic anaemia (Haemoglobin 8.3 g/dL). Erythrocyte sedimentation rate was 75 mm/hour. Serum creatinine was 314 mol/L. Urine microscopy showed microscopic haematuria, pyuria, granular casts without dysmorphic red cells. The 24-hour urine protein excretion was 2.6 g. Urine culture was sterile and acid fast bacilli were not detected. Serum albumin and globulin levels were low. Anti nuclear antibodies and rheumatoid factor were negative. Complement component C4 was low while C3 was normal. Fasting plasma glucose, thyroid function tests and liver function tests were normal.

Ultrasonography showed normal sized kidneys with increased cortical echogenicity and prominent pyramids. Transthoracic echocardiography showed increased myocardial echogenicity suggestive of early infiltrative disease. Serum protein electrophoresis did not reveal monoclonal gammopathy. Urine Bence Jones Proteins were absent. Bone marrow histology showed a reactive marrow.

Figure 1: Skin wrinkling at different sites

Skin histology did not show any abnormalities on routine Haematoxylin - Eosin staining, but Verhoeff-Van Gieson stain showed marked reduction in the number of elastin fibres throughout the dermis while the remaining fibres were fragmented and shortened (Figure 2).

Rectal biopsy showed deposition of eosinophilic homogenous material in submucous blood vessels which stained positively with Crystal Violet and Congo red suggestive of amyloidosis. The patient died 3 months later and histopathological examination of postmortem tissue from the tongue, myocardium, kidneys and lungs confirmed the presence of amyloid within the blood vessel walls (Figure 3).

Figure 2: Verhoeff-van Gieson stain showing a marked reduction in the number of elastin fibres throughout the dermis

Figure 3: Postmortem tissue confirming the presence of amyloid within the blood vessel walls

Discussion

Loose, sagging skin with reduced elastic recoil and resilience, giving rise to an appearance of premature aging, markedly diminished and fragmented elastin fibers in the dermis are typical of acquired generalized CL.

Ehlers-Danlos Syndrome (EDS) and pseudoxanthoma elasticum (PE) have similar cutaneous manifestations. However in EDS, elastic recoil is preserved. In PE, face is spared. The presence of primary papular lesions at the sites of skin laxity together with the histological finding of calcium deposits on the distorted, fragmented elastic fibers clearly distinguishes PE from CL.

The utero-vaginal prolapse at the age of 43 might be related to the laxity of the elastin fibre network of pelvic organs and their supportive ligaments (5).

Nephrotic syndrome, renal impairment with normal sized kidneys and cardiac infiltration raised the possibility of associated systemic amyloidosis in our patient. The rectal biopsy was suggestive of amyloidosis while postmortem histological examination confirmed it.

The pathogenesis of acquired CL is not clear. Several mechanisms have been proposed including abnormal copper metabolism or copper deficiency, reduced serum elastase inhibitors level, low lysyl oxidase activity, increased elastase activity, and an immune mediated mechanism (6). In cases of myeloma associated with amyloidosis, elastolysis was proposed to be due to direct destruction of elastic fibers by amyloid deposits (7). However amyloid deposition was not demonstrated in the skin biopsy of our patient.

Conclusion

Cutis laxa is a rare skin manifestation of systemic amyloidosis. It can manifest several years before the onset of underlying disease and can be missed easily. Early identification and regular follow up is essential to manage these patients effectively.

Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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References

1. Ringpfeil F, Uitto J. Heritable disorders of connective tissue. In: Bologna JL, Jorizzo JL, Rapini RP. 2nd edition, New Haven, Conn, USA. Mosby Elsevier; 2008: 1485-95.
2. Gveric T, Baric M, Bulat V, Situm M, Pusic J, Huljev D, et al. Clinical presentation of a patient with localized acquired cutis laxa of abdomen: a case report. *Dermatology Research and Practice*, 2010; **40**: 2093.
3. Breathnach SM. Amyloid and amyloidosis. *Journal of the American Academy of Dermatology*, 1988; **18**(1 Pt 1): 1-16.
4. Dicker TJ, Morton J, Williamson RM, Chick J. Myeloma-associated systemic amyloidosis presenting with acquired digital cutis laxa-like changes. *The Australasian Journal of Dermatology*, 2002; **43**(2): 144-6.
5. Paladini D, Di Spiezio Sardo A, Mandato VD, Guerra G, Bifulco G, Mauriello S, et al. Association of cutis laxa and genital prolapse: a case report. *International Urogynecology Journal and Pelvic Floor Dysfunction*, 2007; **18**(11): 1367-70.
6. Turner RB, Haynes HA, Granter SR, Miller DM. Acquired cutis laxa following urticarial vasculitis associated with IgA myeloma. *Journal of the American Academy of Dermatology*, 2009; **60**(6): 1052-7.
7. Yoneda K, Kanoh T, Nomura S, Ozaki M, Imamura S. Elastolytic cutaneous lesions in myeloma-associated amyloidosis. *Archives of Dermatology*, 1990; **126**(5): 657-60.