Cutis Laxa: A Rare Entity

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Abstract
Cutis laxa is a heterogeneous group of connective tissue disorders related to abnormalities in elastic tissue. It may be autosomal recessive (Type I and Type II), autosomal dominant, X-linked recessive or acquired. Inborn errors of elastin synthesis and structural defects of extracellular matrix proteins lead to decreased elasticity and redundant, sagging skin in affected patients. It involves skin, lungs, endocrine system, gastrointestinal tracts, cardiovascular system and genitourinary tracts. Clinical manifestations of cutis laxa depend on the type of disease, whether X-linked, autosomal dominant, recessive or acquired. Clinical features of these different types may overlap in a patient. We report a case of cutis laxa in an infant, solely diagnosed on the basis of history and physical examination of the case reported. The clinical features and complications of the case and review of the literature are discussed.
Keywords: Cutis laxa, connective tissue disorder, genetic, acquired, genetic skin disorder, inborn error.
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Introduction

Cutis laxa (Generalized Elastolysis, Chalazoderma, Dermatochalasia, Dermatolysis, Deratomegaly, Generalized Elastorrhexis and Pachydermatocele) is a rare, inherited or acquired connective tissue disorder in which the skin becomes inelastic and hangs loosely in folds. All forms of cutis laxa are very rare and no precise data about the prevalence is available to this date[1-3]. It frequently involves internal organs of the body. The characteristic skin finding of loose skin is mainly found around the eyes, face, neck, shoulders and thighs resulting in a prematurely senile appearance[4,5]. Cutis laxa may be preceded by an inflammatory rash or it may develop spontaneously[4]. It presents at an early age and affects persons of all races, both men and women equally. We present herein a case of cutis laxa that came in pediatric emergency ward of Abbasi shaheed hospital. The presence of characteristic clinical features led the diagnosis of cutis laxa. To our knowledge, a pediatric case of cutis laxa has not been reported to this date locally.

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Case Report

A 9-month old baby girl presented through the emergency ward with complaint of cough for three weeks. Her past history showed that she has been experiencing difficulty of breathing after feeding frequently since three months of age. She had an episode of febrile fit, characterized as generalized tonic clonic with uprolling of eyes. The baby had been admitted previously twice in the hospital for similar complaints of cough and difficulty in breathing. There is no history of blood transfusion or drug reaction. She has been getting treatment for recurrent episodes of difficulty of breathing and cough from general practitioners and from a local hospital. She has three siblings, none of which had a congenital or similar illness however; her first cousin suffers from a similar congenital disease. Her parents are married in consanguinity. She was delivered at full term via spontaneous vaginal delivery. There is no history of maternal illness or drug exposure or premature rupture of membranes. She had neonatal jaundice for one week. Her vaccination history was incomplete as she had still not received the measles vaccine. Baby was still on mother's feed exclusively. There is no developmental delay of milestones to this date.

On examination, an active and responsive baby girl with occipito-frontal circumference between 25th

and 50th centile, weight and length below 5th centile, temperature 100°F, respiratory rate 56/min, heart rate 120 beats/minute and pallor. She had long fingers, periorbital wrinkles, generalized loose skin, barrel shaped chest, bilateral marked skin folds on ankles and wrists and normal external genitalia. On auscultation of chest, fine crepitations were found bilaterally in upper zone of lungs. In precordium, a systolic murmur of grade II intensity was audible at P2 area. Her liver span was found to be 6 cm with round edges, smooth surface. Her spleen was 7cm palpable. Central nervous system (CNS) examination findings were unremarkable anterior fontanel was open. Complete blood picture, showed a normochromic normocytic anaemia.

The follow up of this child was not possible. The parents were reluctant to bring the child to the hospital again, despite repeated counseling.

Discussion

Cutis laxa is an uncommon disease and may present with salient features of skin involvement and multiple systemic complications. The most reported causes of cutis laxa include abnormal copper metabolism/copper deficiency, decreased serum elastase inhibitor level, low lysyl oxidase activity increased elastase activity, post inflammatory elastolysis, immune-mediated mechanism, decreased elastin gene expression[4].

The skin findings include loose, inelastic and hanging folds of skin[5], loose hanging skin around the face and neck giving the bloodhound appearance[1,2,5]. The patient appears much older than his/her actual age with reduced elastic recoil when skin is stretched[4,5]. In addition, presence of sagging jowls, downward slanting palpebral fissures, a broad flat nose or a hooked nose with everted nostrils, large ears, short columella, long upper lip, everted lower eyelids and normal tensile strength is also found[2]. Many infants have hoarse cry probably because of laxity of the vocal cords [2]. All of these findings were prominent in our case except the short columella, long upper lip, everted lower eyelids and hoarse cry.

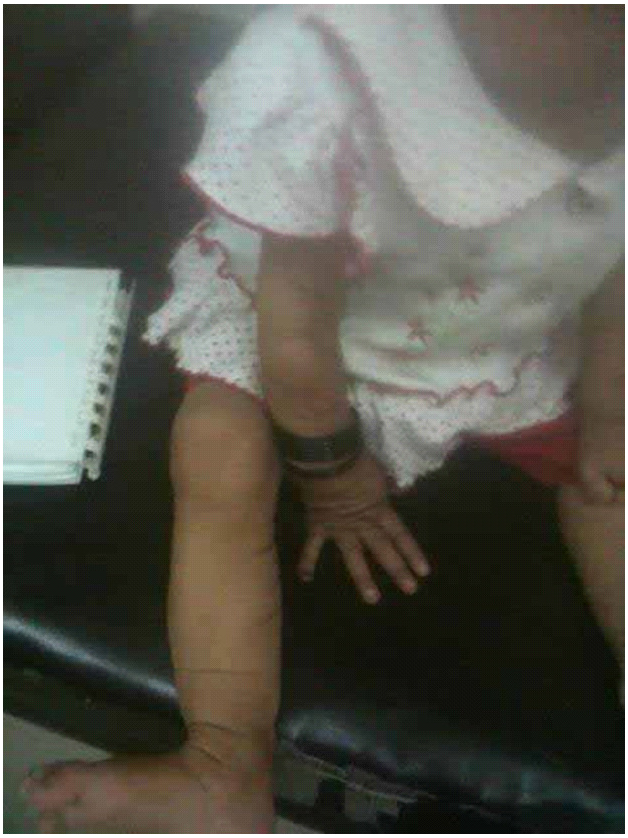
Autosomal dominant form have benign course, with only skin and connective tissue changes mainly and may begin at birth or early childhood[1]. Loose hanging skin may be the only feature and facial involvement is universal. Systemic manifestations are uncommon [5]. Life expectancy of patient may be normal. It may associate with intrauterine growth restriction, lax ligaments and delayed closure of fontanels[2]. Pulmonary emphysema and cardiovascular manifestations may also occur. Associated features include cardiac valve anomalies and hernias. Early emphysema may occur, but gastrointestinal symptoms are uncommon [1].

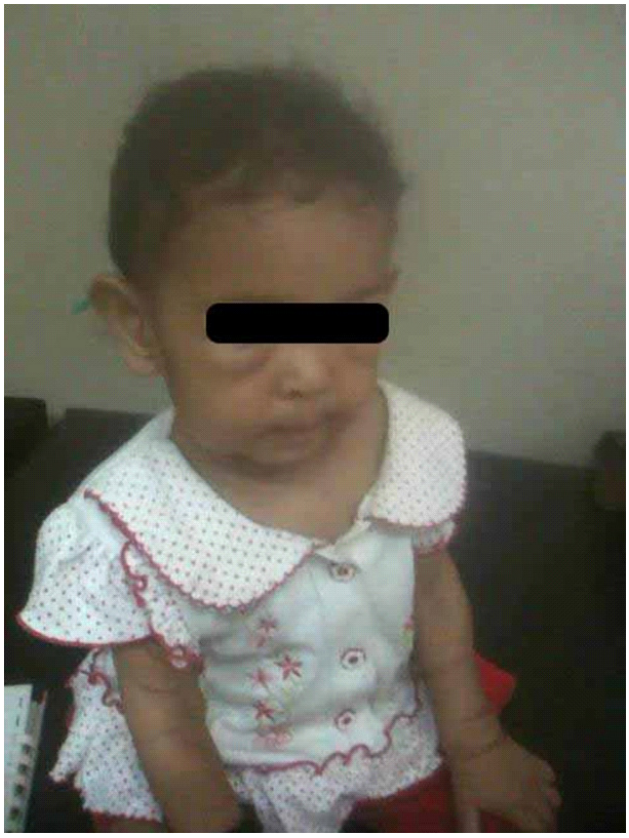
Autosomal recessive form of disease has an onset in infancy with loose skin, bone abnormalities (e.g. delayed joining of skull bones, hip dislocation, spinal curvature)[5], multiple hernias, rectal prolapse, diaphragmatic atony, diverticula of the gastrointestinal and genitourinary tracts, cor pulmonale, emphysema, pneumothoraces, peripheral pulmonary artery stenosis and aortic dilatation[2]. A combined disorder of N- and O-linked glycosylation has been described in association with severe CNS involvement, brain migration defects, seizures, and hearing loss[4]. There is only single case of autosomal recessive form of cutis laxa reported with congenital hypothyroidism owing to isolated thyrotropin deficiency suggesting that it may also present with endocrine abnormalities[6].

One study suggests that autosomal recessive cutis laxa (Debré type) initially considered a dermatologic syndrome, is a multisystem disorder with cobblestone-like brain dysgenesis manifesting as developmental delay and an epileptic neurodegenerative syndrome[7]. It might represent a metabolic cause of Dandy-Walker malformation. It shares many similarities with muscle-eye-brain syndromes[7].

The X-linked cutis (occipital horn syndrome) is currently classified in the group of copper transport diseases[4]. The main features include loose joints (joint hyperextensibility), bone abnormalities such as hooked nose, pigeon breast and funnel breast, frequent loose stools, urinary tract blockages and

Figure 1 & 2. Nine month old baby girl with loose, inelastic and hanging folds of skin around the face, neck giving bloodhound appearance. The patient appears older than her actual age and has everted nostrils. Loose skin is also seen on the limbs especially at the joints.





mild mental retardation[5]. These features such as loose joints, pigeon shaped chest, frequent loose stools, urinary tract blockage and mental retardation was not present in this case.

The acquired form of disease develops after febrile illness, inflammatory skin diseases such as systemic lupus erythematous (erythema multiforme), amyloidosis, urticaria, angioedema, hypersensitivity reactions to penicillin and in infants whose mothers were taking penicillamine[2,4]. The features of acquired cutis laxa are mainly loose skin, especially in areas of previous inflammation. It has also occurred in association with complement deficiency (C2 and C3), systemic lupus erythematous, sarcoidosis, multiple myeloma and systemic amyloidosis[4,5].

Ehlers Danlos Syndrome resembles cutis laxa mostly but in the former hypermobility of the joints is present[2]. Other diseases with cutis laxa like skin changes may include De Barsy syndrome, Lenz-majewski syndrome, SCARF (skeletal abnormalities, cutis laxa, ambiguous genitalia, retardation, and facial abnormalities) syndrome, wrinkling skin syndrome and Costello syndrome [2,4].

Although no routine laboratory findings are present in cutis laxa. Complete blood count may reveal normochromic normocytic anaemia, while total protein and beta-2 microglobulin levels may be elevated[4]. Serum protein electrophoresis and quantitative immunoglobulins can be performed to assess for myeloma. Direct immunofluorescence studies for IgG, immunoglobulin A (IgA), immunoglobulin M (IgM), C2, C1q, and fibrin may be performed to assess for related conditions, such as lupus erythematous[4]. Serum copper, zinc, ceruloplasmin, alpha-1 antitrypsin, C3, rapid plasma reagent, and antinuclear antibody levels can be measured. Serum and urine elastin peptide levels may be el-

evated [4].Thyroid function tests may be considered in newborns with cutis laxa[4]. Imaging studies include echocardiogram and chest radiograph to check for any pulmonary and cardiac involvement. One study suggests that evaluation and follow up of bone mineral density is necessary in order to prevent osteoporosis in a patient with cutis laxa[8]. Skin or bone marrow biopsy may be performed. Throughout the dermis, reduction of elastic fibers with fragmentation, distension and clumping of elastic fibers is evident histologically[2,4].

Treatment of cutis laxa includes supportive care and rehabilitation of the child with counseling of the parents as the cornerstone. No specific treatment exists to this date in order to prevent disease progression. Bisphosphonate therapy can be given in a child with cutis laxa to treat osteoporosis[8]. Dapsone can be given in acquired cutis laxa to control swelling[4].

Conclusion

Cutis laxa is a rare entity with limited number of cases reported locally. The sole principle of managing such patients is to counsel their parents and treat them symptomatically.

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