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CONGENITAL CUTIS LAXA: A RARE GENODERMATOSIS

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ABSTRACT Cutis Laxa (CL) / generalized elastolysis / dermatomegaly is a heterogeneous group of disorders which are related to elastic tissue abnormalities. Depending on extent of abnormal elastic tissue, it may be mild or severe. Severe form presents with loose, inelastic, wrinkled skin resembling ill fitted suit. Infant has characteristic facial features like old man appearance, a hooked nose, a short columella, a long upper lip with long philtrum, and everted lower eyelids. CL is categorised as congenital or acquired and the inheritance can be autosomal dominant or recessive, or X linked. Occasionally a few metabolic disorders like Menkes disease, disorders of glycosylation are associated with Congenital CL. Acquired cutis laxa has developed after a febrile illness and various inflammatory skin diseases. Here we present a case of a full-term SGA (small for gestational age) female child born with features of CL.

KEYWORDS : congenital cutis laxa, dermatomegaly, lax skin, elastolysis.

INTRODUCTION-

CL is a rare heterogeneous group of connective tissue disorders with abnormalities of elastic tissue that may be congenital or acquired[1]. Congenital variety is more common and aggressive than acquired[2]. Inherited CL can be autosomal dominant (AD), recessive (AR) or X linked and amongst these the recessive form is more severe and common [3, 4]. In contrast, the acquired forms of CL which are mild, localized or generalized restricted to only skin involvement, congenital forms may be associated with extracutaneous manifestations. AD forms of congenital cutis laxa (CCL) are caused by mutations in the elastin and fibulin-5 genes[5]. However, the AR forms are associated with mutation in genes encoding Fibulin 4 & 5, ATP6VOA2 and PYCR1 [5,6,7].

Cases of acquired cutis laxa have been seen in patients with inflammatory skin diseases such as lupus erythematosus or erythema multiforme, amyloidosis, urticaria, angioedema [1]. Patients with severe CCL have characteristic facial features like old man look, with sagging jaws, a hooked nose with everted nostrils, a short columella, a long upper lip, and everted lower eyelids. Lax inelastic skin over body resembles like an ill-fitting suit. Unlike Ehlers-Danlos syndrome, hyperelasticity and hypermobility of the joints are not present. We are presenting a case of preterm female neonate born with features of CCL.

CASE REPORT-

A full-term female baby weighing 1452 grams, born of 3rd degree consanguineous marriage to a 28-year-old mother was admitted in the neonatal intensive care unit in view of antenatal scans suggestive of fetal growth restriction. The antenatal history was uneventful. Past obstetric history was suggestive of one neonatal death (NND) on day 4 of life due to sepsis and one intrauterine fetal death (IUFD) in third trimester. Both babies were female and did not have any dysmorphism or lax skin. On admission our patient was active, euthermic, vitals were stable. Arthrometric measurements revealed head circumference (26 cm), length (36 cm) and both were below 10th percentile of normal suggestive of baby being small for her gestational age. Neonate was having characteristic features of CCL in form of old man's look with thin translucent wrinkled, lax skin all over the body with visible non-distended veins all over the body (Fig1). Facial dysmorphism was seen in form of microphthalmia, low set ears and wide-open fontanelles. Lower limbs showed bilateral everted feet and hands showed slight overlapping of fingers. Rest of the systemic examination was normal. All joints were normal, there was neither hypermobility nor hyperextensibility of joints.

On examination our initial differentials were cutis laxa or neonatal progeria. Child was started on breast feeds and weight gain was monitored. Computed tomography brain was done in view of large fontanelles showed wormian bones along coronal, sagittal and lambdoid sutures with normal brain anatomy. Genetic workup was done and it was suggestive of mutations in PYCR1 gene, autosomal recessive type of Cutis laxa type IIB and IIIB. There was no history of cutis laxa in family members. Child was managed conservatively and genetic counselling was done. The neonate had uneventful neonatal course and was discharged with advice to follow up regularly.

Fig 1 Neonate Has Generalised Loose Wrinkled Translucent Skin With Visible Veins

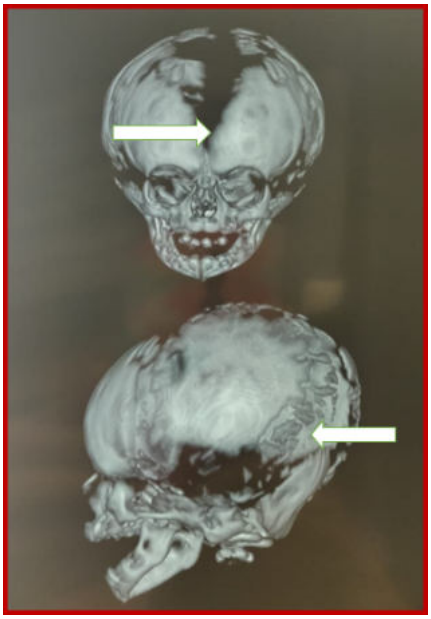

Fig 2a. 3D CT Scan Of Skull Shows Wide Open Anterior Fontanelle With Wormian Bones In Sutures.

DISCUSSION-

CL is a rare heterogenous group of connective tissue disorders with abnormalities of elastic tissue. [1] It may be congenital or acquired. Congenital variety is more common. The abnormal elastin metabolism results in decreased dermal elastin component making skin inelastic and lax. It may be associated with growth and psychomotor retardation, genitourinary abnormalities, gastrointestinal diverticuli, diaphragmatic hernias, cor pulmonale, pneumothoraces, peripheral pulmonary artery stenosis, aortic dilation and orthopaedic problems[1,2,7]. Mode of inheritance is varied; it can be AD, AR or linked. Amongst all AR type is more common and associated with severe multisystem complications manifesting in infancy[8]. Characteristic facial features of AR type CCL include downward slanting palpebral fissures, a broad, flat nose, and large ears, lax skin like ill-fitting suit. Patients with AR variety of CCL have shortened life span as compare to the normal life expectancy seen in AD variety of CCL.[1,2]

AD type of CCL is benign type and onset of skin involvement often is delayed until adult life[6]. The third type CCL with X linked inheritance also called as occipital horn syndrome (also called Ehlers-Danlos type IX syndrome or mild Menkes syndrome) ascribed to ATP7A deficiency.[3,8] Etiopathogenesis of cutis laxa include reduction of elastin fibres due abnormal copper metabolism/copper deficiency, decreased serum elastase inhibitor, low lysyl oxidase activity, increased elastase activity, post-inflammatory elastolysis and immune-mediated mechanisms [9,10]. Our patient was born of 3rd degree consanguineous marriage; however there was no family history of cutis laxa present. Genetic diagnosis of our patient had shown mutations in PYCR1 gene confirming autosomal recessive type of Cutis laxa type IIB and IIIB.

Differential diagnosis of cutis laxa include Ehler - Danlos syndrome, Acrodermatitis chronica atrophicans, Anetoderma, Costello syndrome, Debarsy syndrome, Lipodystrophy, Pseudoxanthoma elasticum, Wrinkly skin syndrome [11,12]. In pseudoxanthoma elasticum, the skin may be lax but it is associated with yellowish discoloration. In the Ehlers-Danlos syndrome, the skin is hyperextensible but not lax and it recoils quickly[5]. Costello syndrome can be differentiated by presence of hyperkeratotic changes of palms and soles, abnormally flexible finger joints and presence of papillomata around mouth and nostrils[13].

Diagnosis of CCL is usually based on clinical features. For confirmation, skin biopsy and genetic evaluation can be done. Histology of skin shows reduced number of dermal elastic fibres, with existent fibres being shortened, clumped, granular or fragmented. In severe cases elastic fibres are completely absent and may present like fine dust like particles scattered throughout the dermis. Electron microscopy is suggestive of degenerative changes in elastic fibres [2]. There is no definitive therapy for this disorder but, early diagnosis and multidisciplinary approach are needed for treatment of multisystem extracutaneous complications in patients with CCL [14,15].

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