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Case Report

Neuroimaging findings in a case of autosomal recessive cutis Laxa syndrome: a case report

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ABSTRACT

Cutis laxa is a heterogeneous group of inherited and acquired connective tissue disorders characterized by a loose skin and variable systemic involvement. One Autosomal dominant and three autosomal recessive forms of cutis laxa have been described. The diagnosis of CL syndrome is based on clinical assessment of typical skin features and the associated extracutaneous finding. Magnetic resonance imaging of brain in evaluation of cutis laxa syndrome has not been described in literature till date. We describe MR neuroimaging in a case of type 2 AR cutis laxa syndrome.

Keywords: Cutis laxa, Magnetic resonance imaging, Perivascular spaces

INTRODUCTION

Cutis laxa (CL) is a heterogeneous group of inherited and acquired connective tissue disorders characterized by a loose skin and variable systemic involvement. Inherited forms may follow autosomal dominant, autosomal recessive or x-linked recessive patterns. Acquired forms are typically associated with previous inflammatory skin disorder like urticaria. The hallmark of CL is deficiency of elastic fibers in skin.[1] Autosomal dominant cutis laxa, often caused by mutations in the elastin gene, is usually considered benign but carries an increased risk for pulmonary emphysema and aortic root dilatation. Three autosomal recessive forms of cutis laxa have been identified. Type 1 recessive cutis laxa (caused by LTBP4, FBLN4 or FBLN5 mutations) primarily affecting the pulmonary and cardiovascular system. Type 2 (associated with mutations in ATP6V0A2, ATP6V1E1 or ATP6V1A) often present with skeletal and central nervous defects.[2] Type 3 recessive cutis laxa presents with skeletal involvement as well as ocular features such as corneal clouding and cataract.[3] The diagnosis of CL relies on clinical evaluation of characteristics skin findings and associated extracutaneous features. Notably, Type 2 AR cutis laxa syndrome demonstrates distinct neuroimaging features although magnetic resonance imaging findings of the brain in such cases remain poorly described in the literature till date. In this case report we present MRI neuroimaging findings in a case of Type 2 AR cutis laxa syndrome.

CASE REPORT

A 5 years old boy, the child of related parents (3º consanguineous marriage) present to OPD with complaint of loose wrinkled skin, frequent falls and dropping of things from hands on his own and exaggerated startle. There was no significant birth history. He had history of global developmental delay. He is able to stand without support, however not able to walk without support. Pincer grasp not yet attained however palmer grasp attained at the age of 2 years. He is unable to dress/ undress himself. He is able to speak phrases at the age of 3 years. He is not able to follow three step command, however plays with the kids of his own age. His dentition was delayed and have a history of dental caries. On examination the child was lean, thin and undernourished. The weight and height

were 15 kgs (<3rd percentile) and 103 cm (<3 percentile) respectively. The face had a senile appearance with lax wrinkled skin and delayed recoil. He had low set ears, retrognathia, medial epicanthal fold, downward slanting of palpebral fissures, hypertelorism, broad flat nasal bridge, long philtrum. There was patent anterior fontanelle. He had protuberant abdomen with umbilical hernia. His bone age<chronological age. His oral and genital mucosa appeared normal. He had developmental dysplasia of right hip with unequal lengths of lower limbs (left>right), limited abduction in bilateral lower limbs and positive Galeazzi sign in right hip. He had genu valgum bilaterally.

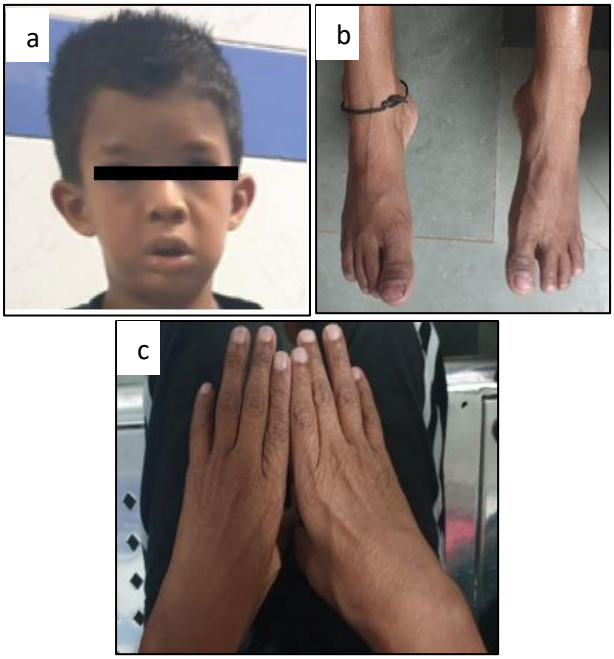

Figure 1 (a-c): 5-year male child with senile appearance with lax wrinkled skin and delayed recoil. There are low set ears, retrognathia, medial epicantal fold, downward slanting of palpebral fissures, hypertelorism, broad flat nasal bridge, long filtrum.

Figure 2: Developmental dysplasia of right hip with unequal lengths of lower limbs (left>right), limited abduction in bilateral lower limbs and positive Galeazzi sign in right hip.

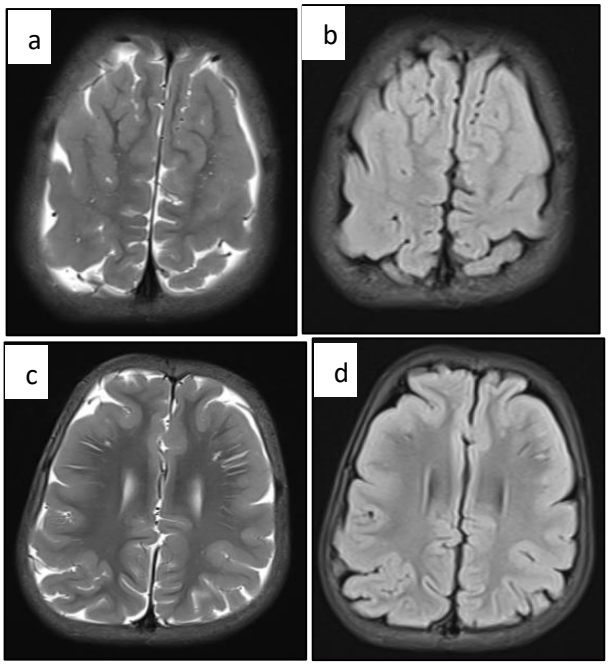

Figure 3 (a-d): T2/FLAIR axial images showed reduction in the number of frontal gyri and marked thickening of frontal cortex with smooth cortical surface suggestive of pachygyria. Few of gyri are abnormally shallow in bilateral frontal location and cortex reaching up to subcortical grey matter in left frontal region likely FCD variant.

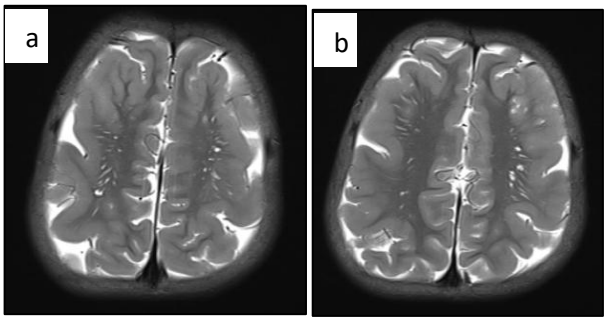

Figure 4 (a and b): T2 axial images showing abnormally enlarged round as well as linear perivascular spaces are noted with radial disposition in bilateral centrum semiovale and frontal deep white matter.

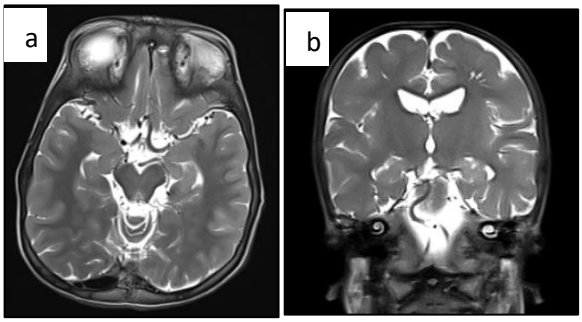

Figure 5: (a, b) T2 axial and coronal images showing tortuous intracranial vessels.

Chest, abdomen and cardiovascular examination was normal. On CNS examination, Power was 3/5, reduced in all the four limbs with normal (2+) deep tendon reflexes. Routine tests showed normocytic, normochromic anemia. Routine biochemical investigations results were normal. Ophthalmological examination was normal. Chest X-ray was normal Echocardiography showed outpouching at dorsal aortic valve, measuring 1.1×1.4 cm, not communicating with right ventricle- congenital aneurysm. ECG was normal. EEG showed abnormal awake records. Osteopenia was seen in DEXA scan.

On skin biopsy, there was absence of elastin fibres in dermis on VVG stain (Verhoeff-Van Gieson stain). Histopathological examination of dermis and epidermis was unremarkable.

Imaging findings

In view of global developmental delay, magnetic resonance imaging (MRI) brain was carried out on Siemens Somatom 3T MR Scanner. It revealed Microcephaly with pachygyria and abnormally enlarged perivascular spaces (PVS) in bilateral frontal distribution with tortuous intracranial vessels, prominent cisterns and ventricular system with few T2/FLAIR hyperintensities. Abnormally shallow gyri in bilateral frontal location and cortex reaching up to subcortical grey matter in left frontal region likely FCD variant.

DISCUSSION

Cutis laxa is an uncommon connective tissue disorder typically identified by loose sagging skin folds. Histologically, alterations in dermal elastic fibers are evident. This condition usually follows a genetic inheritance pattern. The autosomal recessive variant is linked with both skeletal and neurological manifestations.

We present a patient with a cutis laxa, autosomal recessive, type II. This form of the syndrome has only been documented in a limited number of cases. Moreover, limited data are available regarding neuroimaging.

In our patient, tortuous intracranial vessels were identified and were predominant on Willis's polygon circle. This is concordant with the description in the Sinnige et al, review, where tortuous vessels were present mostly on arteries, only two patients were described with venous tortuosity and only on the cerebral and basilar arteries.[4] Martinelli et al, suggested that this tortuosity could be secondary to abnormal proline metabolism, affecting the production of proline-rich connective tissue proteins such as elastin and collagen and then leading to defective interactions between the extracellular matrix and vascular smooth muscle.[5] The patient exhibited significantly enlarged perivascular space (PVS) predominantly in the cerebral frontoparietal white matter. Small perivascular spaces can often be seen on magnetic resonance imaging (MRI) in any age group and are a common finding in children.[6,7] However large dilated PVS distributed throughout the cerebrum are unusual in children and their clinical significance is unknown. Morava and colleagues documented three patients, born to consanguineous parents, all presenting with cutis laxa, having small head size, wide anterior fontanel and brain malformation.[8]

Okanishi et al, reported a female infant with cutis laxa, short stature, microcephaly, wide anterior fontanel and bifrontal cortical malformation. Biochemical testing revealed abnormal plasma transferrin and apolipoprotein C-III patterns suggestive of defective N- and O-glycosylation.[9]

CONCLUSION

The neuroimaging findings in the patient with cutis laxa syndrome are presented. Pachygyria, focal cortical dysplasia, microcephaly, intracranial vascular tortuosity and wide perivascular spaces were the most notable imaging findings. The data on our patient enlarge the spectrum of neuroimaging findings. Our data indicate that neuroimaging should be included as part of baseline surveillance in patients of cutis laxa syndrome.

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