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A CASE REPORT OF RARE DISEASE ACROCALLOSAL SYNDROME

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ABSTRACT

Acrocallosal syndrome (ACS) 1,2 is characterised by post-axial polydactyly, duplication of the hallux, and abnormality of corpus callosum including agenesis or dysgenesis, occasional anencephaly, and/or Dandy–Walker malformation, characteristic craniofacial abnormalities, and moderate-to-severe mental retardation. One year old male child admitted in view of convulsions who has dysmorphicfacies, polydactyly, Hallux duplication, undescended testis. MRI brain showed carpus callosal agenesis and Whole exon sequencing – KIF 7 gene mutation. Acrocallosal syndrome is rare with only a limited number of cases being described in the literature. Early recognition of the condition is necessary to intervene surgically and to counsel the parents regarding the genetics of the disease and dedicated follow-up of the affected child in special OPDs. Molecular testing should be done in all suspected cases.

INTRODUCTION

Acrocallosal syndrome (ACS)[1,2] was first described by Schinzel in 1979, as a conundrum of findings, including post-axial polydactyly, duplication of the hallux, and abnormality of corpus callosum including agenesis or dysgenesis, occasional anencephaly, and/or Dandy–Walker malformation, characteristic craniofacial abnormalities, and moderate-to-severe mental retardation. In clinical practice, however, the clinical, physical, and imaging findings vary over a spectrum and hence vary with the age of presentation. The inheritance pattern of ACS is autosomal recessive with the gene situated on chromosome 12p caused due to mutations in the KIF7 gene[3,4,5]; however, sporadic cases have also been reported.

CASE PRESENTATION

1 year old mch born of 3 degree consanguineous marriage h/o multiple admissions for seizures, operated for inguinal hernia O/E dysmorphic facies (frontal bossing, hypertelorism, depressed nasal bridge, low set ear, short neck), polydactyly, Hallux duplication, undescended testis.

MRI BRAIN – corpus callosal agenesis

2D Echo – 6 mm ASD, Dextrocardia

Whole exon sequencing – KIF 7 gene mutation

DISCUSSION

Acrocallosal syndrome is rare with only a limited number of cases being described in the literature. Most of the cases have reported an autosomal recessive inheritance and a history of consanguineous marriage. Recent studies have shown mutations in the genes of kinesis KIF and transcription factor Gli3 which are involved in the ciliary signaling pathway involving the sonic hedgehog which is responsible for the formation of midline structures. The disruptions in the development of the corpus callosum occur during the 5th–16th week of pregnancy. Courtens et al. have given the diagnostic criteria for ACS as the presence of any three out of the four features, which include: (1) absence/ hypoplasia/ dysgenesis of the corpus callosum, (2) craniofacial dysmorphism, (3) polysyndactyly, and (4) psychomotor retardation.

With the increase in the number of cases being reported, there is a definite phenotypic variation as shown below
A) Clinical manifestations 1.Macrocephaly 2. Seizures/ abnormal EEG 3. Hypotonia 4. Hypertelorism and frontal bossing

B) Neurological manifestations 5. Agenesis/ hypoplasia of corpus callosum 6. Cerebellar hypoplasia (including dandy walker malformation) 7. Brainstem dysplasia, joubert syndrome, hippocampal malrotation 8. Optic atrophy 9. Olfactory bulb agenesis and olfactory tract abnormalities

C)Musculoskeletal manifestations 10. Hallux duplication 11. Pre- and post-axial polydactyly of toes and fingers 12. Cranial synostosis 13. Orofacial malformations 14. Rib anomalies 15. CTEV

D)Cardiac manifestations 16. Congenital heart disease 17. Dextro position of the heart 18. Cyanotic spells.

The prognosis of ACS depends on the degree of hypotonia and age of onset of seizures in addition to the associated malformations Life span of patients range from stillbirth to relatively normal lives with variable degrees of developmental delay. A periodic follow-up of the patient with a paediatric neurologist, cardiologist, otolaryngologist, speech therapist, and child psychologist is recommended to the parents. Since there is a 25% chance of recurrence of this syndrome in the next child, genetic counselling of the parents is given utmost importance in detected cases. Central nervous system malformations and polysyndactyly can be readily detected on antenatal scan and hence a judicious imaging follow-up in all future pregnancies is advised for mothers detected with ACS in one offspring.

CONCLUSION

Acrocallosal syndrome is a rare anomaly and only a few cases have been reported in the Indian population. Imaging plays an important role in antenatal diagnosis of this condition. Postnatally, imaging is essential for the diagnosis of corpus callosum agenesis along with other associated cranial, facial, and digital anomalies that distinguish it from other syndromes. Early recognition of the condition is necessary to intervene surgically and to counsel the parents regarding the genetics of the disease and dedicated follow-up of the affected child in special OPDs. Molecular testing should be done in all suspected cases.

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