Rare disease

Acrocallosal syndrome in a young hypertensive male

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Summary

Acrocallosal syndrome is an extremely rare genetic disorder with autosomal recessive inheritance. It is characterised by moderate to severe mental retardation, hypotonia, agenesis of the corpus callosum and preaxial polydactyly involving both feet and the facial features like broad forehead and hypertelorism. The authors report a case of a young hypertensive male who presented with unprovoked seizures for the first time who had multiple craniofacial, digital dysmorphic features with moderate mental retardation. The diagnosis of acrocallosal syndrome was arrived at after neuroimaging showed agenesis of corpus callosum with interhemispheric cysts.

BACKGROUND

The acrocallosal syndrome, first described in 1979 by Schnitzel,¹ is a genetic disorder with autosomal recessive inheritance and occasional sporadic incidence. The main characteristics mostly apparent at birth are severe

mental retardation, agenesis of the corpus callosum and preaxial polydactyly involving both feet, prominent broad forehead and hypertelorism. Since Schinzel's original description, only 37 cases of acrocallosal syndrome have been described worldwide.² We report here a case

Figure 1 Photograph showing macrocephaly, broad forehead and downslanting palpebral fissure.

Figure 2 Photograph showing high arched palate.

Figure 3 Photograph showing right third and fourth digit syndactyly, left fifth digit clinodactyly.

of a 21-year-old male with features compatible with the diagnosis of acrocallosal syndrome, which after extensive search from literature was found to be the fourth reported case in India. Since the disease itself is very rare mostly with paediatric presentation, arriving at a

diagnosis is difficult as was in our case. We intent to stress on the necessity of thorough evaluation and management of such patients in conjunction with paediatricians, geneticist, orthopaedic and rehabilitative services to improve the outcome.

Figure 4 Photograph showing bilateral great toe polydactyly and exostoses at base of great toe.

CASE PRESENTATION

A 21-year-old male presented to us with two episodes of generalised tonic clonic convulsions with uprolling of eye-balls and frothing at mouth without any preceding aura. He had history of delayed motor, mental and social milestones since childhood. There was no history of audio-visual disability. His mother denied any history of seizure disorder or myoclonic jerks in childhood. There was no history suggestive of meningism or neuropsychiatric manifestations. He was born of a non-consanguineous marriage with unremarkable antenatal and peripartal history. There was no history of similar complains in any family member.

On examination, radial pulse was 120/min, regular with all peripheral pulsations well felt, no radiofemoral delay. Blood pressure was 160/90 mm Hg. On general examination, patient showed the dysmorphic features like macrocephaly, broad forehead, downslanting palpebral fissure (figure 1), high arched palate (figure 2), right third and fourth digit syndactyly, left fifth digit clinodactyly (figure 3), bilateral great toe preaxial polydactyly and exostoses at base of great toe (figure 4).

Secondary sexual characteristics were normal. His IQ was 50–55 suggestive of moderate mental retardation. The Mini-Mental Score Examination was 16/30 and he

faced difficulty in calculation, reading and following written commands, writing down oral commands, drawing of simple figures. Except for hypotonia, rest of the central nervous system examination was normal. Cardiovascular, respiratory and per abdomen examination were within normal limits.

INVESTIGATIONS

On investigations, haemogram, renal function test, serum electrolytes and urinalysis were normal. X-ray of both hands with digits showed left fifth digit clinodactyly. X-ray of the ankles and toes had postaxial polydactyly of both great toes with bilateral exostoses at base. ECG was suggestive of left ventricular hypertrophy, confirmed on 2D ECHO and colour Doppler. Ultrasonography of abdomen revealed bilateral large polycystic kidneys with normal appearing liver and spleen. Audiometric evaluation was normal. MRI of brain showed agenesis of corpus callosum with interhemispheric cysts in midline and in left paramedian location in parietal region (figure 5). Moderate enlargement of ventricular system showed hypoplasia of cerebellar vermis with mild cerebellar atrophy (figure 6). Karyotyping showed normal 46XY chromosome pattern.

Figure 5 MRI of brain showing agenesis of corpus callosum with interhemispheric cysts in midline and in left paramedian location in parietal region.

DIAGNOSIS

Provisionally, the diagnosis was of 'A case of provoked seizure with reno-parenchymal hypertension, moderate mental retardation and cranio-facio-digital dysmorphism'.

Due to the spectrum of dysmorphic features, some disease syndrome was thought of. Thorough search of literature with the help of paediatric services of tertiary child care centre other than our hospital led us to a diagnosis of 'Acrocallosal syndrome'

TREATMENT

Patient was started on β -blockers and valproate sodium. Opinion of orthopaedic and plastic surgery services was sought and the patient was managed conservatively for his acral defects. Genetic and vocational counselling of patient and family members were done. Renal disease outcome was explained.

OUTCOME AND FOLLOW-UP

Patient is being followed up in OPD with well-controlled hypertension, no recurrent seizures. He is now able to earn

his livelihood as a carpenter in his village and planning to marry in near future.

DISCUSSION

Acrocallosal syndrome is an extremely rare genetic disorder described first by Schinzel in 1979 and the term coined by Schinzel and Schmid in 1980. Also known by synonyms like Schinzel acrocallosal syndrome and hallux duplication, postaxial polydactyly and absence of corpus callosum, its prominent features are involvement of the acra (fingers and toes) and the corpus callosum. It has an autosomal recessive inheritance though sporadic incidence too have been reported. To help determine which chromosome or gene location causes the syndrome, it has been compared with similar disorders closest being Greig cephalopolysyndactyly syndrome. Despite the similarity, linkage studies suggest that this disorder is not allelic to Greig syndrome.³ Though the culprit gene is suspected to be located on chromosome 12p13.3-p11.2,^{4,5} to date, no specific genetic cause for acrocallosal syndrome is known, and the disorder can only be identified by clinical symptoms (table 1). It affects

Figure 6 MRI of brain showing moderate enlargement of ventricular system, agenesis of corpus callosum with interhemispheric cysts and mild cerebellar atrophy.

Table 1 The typical clinical features of acrocallosal syndrome¹

Acral	<ul style="list-style-type: none"> ▶ Postaxial polydactyly of upper and lower limbs ▶ Preaxial polydactyly of feet and hallux duplication ▶ Syndactyly of finer and toes ▶ Fifth finger clinodactyly
Craniofacial	<ul style="list-style-type: none"> ▶ Macrocephaly, dolichocephaly, prominent forehead and occiput, large anterior fontanelle ▶ Hypertelorism, medial epicanthal fold and downslanting palpebral fissure ▶ Small nose, depressed nasal bridge, short philtrum and anteverted nostril ▶ Cleft lip and cleft palate ▶ Malformed ear
Neuropsychiatric	<ul style="list-style-type: none"> ▶ Moderate to severe mental retardation ▶ Hypotonia and hyperreflexia ▶ Delayed development milestones ▶ Seizure ▶ Strabismus and nystagmus ▶ Optic atrophy and decreased retinal pigmentation
Central nervous system	<ul style="list-style-type: none"> ▶ Dysgenesis or absence of corpus callosum ▶ Micropolygyria ▶ Anecephaly ▶ Cerebellar hypoplasia and cysts
Miscellaneous	<ul style="list-style-type: none"> ▶ Cardiac septal defects and pulmonary valves defects ▶ Renal and hepatic cysts ▶ Umbilical hernia ▶ Supernumerary nipples and rib hypoplasia

both males and females with no reported sex predilection. Though it may occur within family lines with consanguinity in parents, affected children may also have unrelated, healthy parents and unaffected siblings.

The diagnosis of acrocallosal syndrome is based on the criteria laid by Courten *et al*⁶ in 1997:

- Total or partial absence of the corpus callosum on neuroimaging;
- Minor craniofacial anomalies (prominent forehead, hypertelorism, short nose with anteverted nostrils and large anterior fontanelle);
- Moderate to severe psychomotor retardation (with hypotonia) and
- Polydactyly.

The presence of three of the four criteria are suggestive of the diagnosis of acrocallosal syndrome. All the four features were noted in our patient. Prenatal diagnosis may not be possible due to the variability of the condition. However, prenatal ultrasound can detect polydactyly and cerebral malformations. This may be especially crucial for a woman who already has an affected child and has a 25% risk of having another affected child.

Treatment includes physical therapy in infancy which may assist in the development of motor skills and muscle

tone. Surgery to remove extra fingers and toes and release fused fingers may improve movement and grasp, may assist in walking and the comfort of footwear. Inguinal hernia repair, orofacial surgeries and dental care show good results when indicated. Antiepileptic therapy for seizure disorder and antihypertensives for renoparenchymal hypertension are to be given. Vocational and psychological training may be required, depending on the level of mental impairment. Genetic counselling is of prime importance, and antenatal diagnosis can be attempted by prenatal ultrasound. Prognosis is variable and depends on the degree of hypotonia and early onset of epilepsy rather than the degree of craniofacial and limb malformations with patient surviving till adulthood. Neonatal respiratory distress and intercurrent infections are the leading cause of early death in 15% of cases. At present, there are no preventive measures for acrocallosal syndrome.

With history of previous child in family with such features, next child born will have a 25% risk of being affected, which can be diagnosed antenatally. Any patient with polysyndactyly and absence of corpus callosum with craniofacial abnormalities should be examined meticulously to rule out this syndrome.

Learning points

- ▶ Acrocallosal syndrome is extremely rare autosomal recessive disorder whose diagnosis is possible with meticulous examination of the craniofacial, acral and callosal malformations.
- ▶ Antenatal diagnosis with simple investigations like fetal ultrasound and additionally genetic counselling of parents can lower the occurrence of such disorder.
- ▶ Teamwork of concerned specialised services can help in better outcome.

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Competing interests None.

Patient consent Obtained.

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