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AARSKOG Scott Syndrome Presenting As Syndromic Growth Failure and Speech Delay

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Abstract
Aarskog Scott syndrome is a rare disorder characterized by facial, skeletal and genital abnormalities, intellectual disability and short stature. It has X-linked recessive inheritance primarily affecting males though female carriers can manifest subtle signs. We report a case associated with prematurity, low birth weight, severe developmental delay, congenital heart disease (OS-ASD) and clinodactyly of all limbs.
Keywords: Aarskog-scott syndrome, short stature, mental retardation, craniofacial dysmorphism.

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INTRODUCTION

Aarskog Scott syndrome is a rare genetic disorder also known as facio-digital-genital syndrome predominantly transmitted by X-linked inheritance primarily affecting males.[1] It was first described independently by Dagfin Aarskog and CI Scott in two families in the years 1970-71.[2] It is primarily characterised by facial, skeletal and genital abnormalities and can cause intellectual disability and short stature. The classical FDG1 gene present on short arm of X-chromosome is associated with the syndrome in approximately 20 percent of all patients. The FDG1 protein family acts through the CDC42 (cell division control protein homologue 42) to affect the EGFR1 pathway to cause remodelling of extracellular matrix and remodelling of cranial bone structures.[1,3] Here we present a case of male child presenting to our hospital with poor growth and intellectual disability.

CASE HISTORY

A 5 year old male child, first offspring of non-consanguineous couple born after taking 4 years of infertility treatment. He was brought to this hospital for evaluation of poor weight gain. Younger sibling is unaffected three year old male child. Mother was a known case of polycystic ovarian disease and hypothyroidism. She was diagnosed with oligohydramnios and intrauterine growth restriction during antenatal evaluation, so pregnancy was terminated at 32 weeks of gestation. Baby's birth weight was 1.9 kg, cried spontaneously and required no resuscitation. He remained in hospital for a week due to poor suck and cry.

Milestones were moderately delayed in all spheres with maximum delay in language milestones. Head control was achieved in 1 year, sitting in 20 months, standing by 23 months and walking at 30 months. He started reaching for objects 7 months, object transference by 10 months, pincer grasp >1 year, scribbling 3-years and was able to eat food by self at 4-years. Cooing started at 3 months, monosyllables by 2 year, bisyllables at 3 year and presently able to speak only single words. Social smile appeared at 7 months and still doesn't plays with other children. History of mouthing frequently with hand writhing movements are present. Examination was essentially normal except mild hypotonia in all limbs with joint laxity. Reflexes were essentially normal including plantars.The child had severe growth retardation with weight 12 kg (-3SD), height 94cm (-2.9SD), occipitofrontal circumference 50 cm (50th centile), arm span 99cm and US/LS ratio of 1. He had multiple dysmorphic facial features such as triangular face with widow's peak, frontal bossing, hypertelorism, downslanting eyes with long eyelashes and low set small ears. Skeletal dysmorphism with clinodactyly of bilateral little finger and toes, bilateral flat feet and mild joint laxity were present. A classical finding of shawl scrotum was also present. Genetic evaluation for FDG1 gene was negative. 2D Echo revealed ostium-secundum Atrial septal defect. Blood counts, biochemistry, thyroid stimulating hormone (4.3 µIU/ml), IgA TTG (2.18 U/ml) were within normal limits, hand X-rays revealed bone age 3 years, magnetic resonance and ultrasonography abdomen was unremarkable. The child is presently under nutritional management and speech therapy was started to improve communication skills. He is presently going to a normal school albeit in a lower standard than his age to compensate for intellectual disability. Serum insulin growth factor levels were found to be normal, so growth hormone therapy was not started.

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DISCUSSION

Aarskog Scott syndrome is a rare syndrome also known as facio-genital dysplasia causing characteristic facial, urogenital and limb deformities associated with genetic short stature and rarely intellectual and learning disabilities.[4] It is a X-linked disorder which characteristically manifests in males; however, carrier females are also known to have subtle features such as short stature and widow's peak5. They also may exhibit hand and face anomalies.[5] It is known to be caused due to mutations in FDG 1 gene located on chromosome Xp11. It is also sometimes associated with attention deficit-hyperactivity disorder and a form of syndromic X-linked mental retardation (MRXS16) are also caused by mutation in the FGD1 gene. Therefore, some cases of may present with behavioural problems and intellectual deficits.

Boys with this syndrome have characteristically similar facial expression. The cardinal features are broad forehead, hypertelorism, widow's peak, downward slanting palpebral fissures, short nose, anteverted nares, thick lower lips and sometimes crease below lower lip. There can also be wide philtrum, maxillary hypoplasia and abnormal auricles. Cleft lips and palate, delayed teeth eruption, round face and short neck are sometimes present. Skeletal abnormalities can include short stature, short legs, small and broad hands and palms with single crease, particularly short fifth finger with single crease, brachydactyly, syndactyly, clinodactyly, camptodactyly and striking joint laxity which is particularly prominent in phalanges. Other skeletal abnormalities can include genu recurvatum, talipes, odontoid hypoplasia with cervical ligamentous laxity, scoliosis, metatarsus adductus and splayed toes with bulbous tips. Genital abnormalities include typical shawl scrotum, cryptorchidism and inguinal hernia. Fertility is usually maintained if there is no cryptorchidism or it is corrected early. Life expectancy is also normal.

Growth is slow, anthropometric parameters are usually below 10^{th}centiles and can rarelybe below 3^{rd}centile. Puberty is often delayed but eventually occurs and is associated with prolonged growth spurts. Intelligence is variable with normal IQ to moderate mental subnormality. Cognitive deficits are more common. Attention deficit hyperactivity disorder and behavioural problems are also be associated in few subjects. The reported case had severe growth delay, moderate mental subnormality, global developmental delay associated with severe speech delay which was associated with typical phenotypic findings. In addition, child had clinodactyly of both little fingers and last toes.

CONCLUSION

Aarskog Scott syndrome is a facio-digital-genital syndrome characterized by typical facies, skeletal/ genital abnormalities with short stature and mental subnormality and should be considered in the differential when presented with such findings. FDG1 gene (Xp11) mutations can be present in a minor subset of patients. Early recognition and management can benefit the patient to lead a more productive life.

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