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Case Report

Neonatology Section

A Term Female Neonate with Achondroplasia: A Case Report

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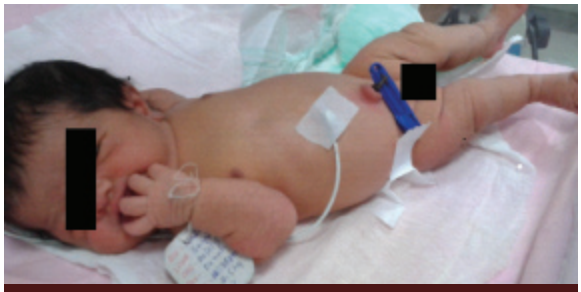
ABSTRACT

Achondroplasia is one of the commonest causes of dwarfism, inherited as autosomal dominant trait. Majority of the cases are due to mutation in the Fibroblast Growth Factor Receptor 3 (FGFR3). The mutation results in gain of FGFR3 function, which affects cartilaginous growth plate in the growing bone causing the skeletal changes. At birth it manifest as short limbs, large head with midfacial hypoplasia and narrow trunk. Diagnosis is mainly based on clinical features and skeletal radiography. Complications are hypotonia, delayed development, hydrocephalus, recurrent ear infections and dental malocclusion.

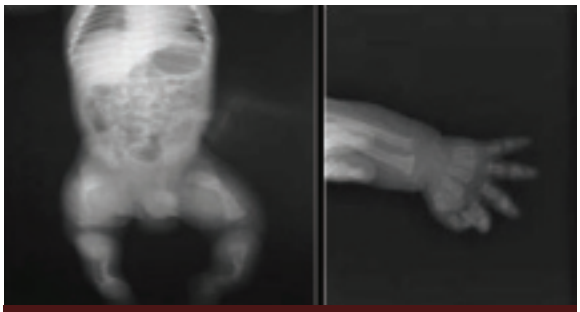
Keywords: Dwarfism, FGFR3 gene, Mutation, Trident hand

CASE REPORT

A 2800g, 38 weeks female neonate was born by elective caesarean to a gravida II. Maternal age was 38 years and paternal age of 45 years. Respiratory distress was reported soon after birth for which the infant required NICU admission. Antenatal ultrasound showed polyhydramnios, shortening of proximal limbs and a large head. Previous one male sibling was normal. There was no history of similar illness in the family. The neonate at birth had typical features of achondroplasia like short proximal limbs, large head, depressed nasal bridge, excess skin creases, short stubby fingers along with trident hand [Table/Fig-1]. Respiratory distress was due to transient tachypnoea of the newborn and settled with oxygen therapy within 6 hours. Skeletal X-ray showed short iliac bones with flat acetabular roof and short tubular bones [Table/Fig-2,3]. Consent for genetic analysis was taken from parents, which showed G1138A mutation in the FGFR3 gene located on chromosome 4p16.3. Based on perinatal history, clinical features and investigations a diagnosis of achondroplasia was made. She was discharged on the 5th day. They were also counselled regarding prognosis and chances of recurrent respiratory infections. Follow-up at 6 months showed a well baby with normal development and short stature without any other complications.



[Table/Fig-1]: Clinical photograph revealing short extremities, flat facial profile, small chest, short stubby fingers, excess skin folds.



[Table/Fig-2]: X-ray showing short iliac bones with flat acetabular roof. **[Table/Fig-3]:** Short tubular bones and trident hand.

DISCUSSION

Achondroplasia is the most common form of chondrodysplasia that causes dwarfism in humans. It is rare, affecting about 1 in 10-30,000 people. More than 95% of patients have the same point mutation in the FGFR3 gene and majority of these are new mutations [1]. Affected babies appear short at birth and grow slowly throughout childhood. The limbs are relatively shorter than the trunk with predominant involvement of the proximal limbs. The head appears large with prominent forehead and a flat nasal bridge. The hands and feet appear small and wide with short fingers and toes [2,3].

Achondroplasia can be confirmed by skeletal radiography. The cranial bones are large compared to cranial base and a facial bone, which appears small .The vertebral pedicles are short with reduced interpeduncular distance. Iliac bones are short and round with flat acetabular roofs. The tubular bones are short with flaring of metaphysis [4].

Genetic studies involve mutations in FGFR3 gene. During early foetal development, much of our skeleton is made up of cartilage. Normally, most cartilage converts into bone later. But in achondroplasia, a lot of the cartilage doesn't convert to bone. This is caused by mutations in the FGFR3 gene. The FGFR3 gene is needed for the synthesis of a protein which is necessary for the bone growth and maintenance. Mutations in this gene can cause abnormal skeletal development. All patients with the classical features of achondroplasia will have the same glycine to arginine substitution at position 380 (G380R), which maps to the transmembrane domain of the receptor [3]. The signalling pathways for FGFR3 activation are signal transducer and activator of transcription (STAT), Mitogen-Activated Protein Kinase (MAPK), and phospholipase C-pathway. STAT signals inhibit chondrocyte proliferation, whereas MAPK signals disrupt terminal differentiation and post-mitotic matrix synthesis. Genetic studies shows that FGFR3 signals through multiple pathways down regulate growth-promoting molecules, leading to reduced proliferation and differentiation of chondrocytes in growing bones resulting in bony deformities [5,6].

Although, the majority of affected children will be healthy, approximately 10% can develop significant complications.

Musculoskeletal complications include early hypotonia of the limbs with delayed motor development which later subsides as age advances. Later they can develop thoracic kyphosis and lumbar lordosis subsequently. Approximately 10% of children may develop significant bowing of the tibia, which may require corrective surgery if there is recurrent knee or ankle pain or frequent falls.

Neurological complications include hydrocephalus requiring a neurosurgical intervention by the age of 5 years. The main risk of this problem is in the first two years of age. Another rare complication is cervicomedullary compression which can present with recurrent episodes of apnoea. In the adolescent and adult, compression of nerve roots in the spinal canal may occur presenting as sensation of numbness or weakness in the legs.

A recurrent middle ear infection is a common problem and there is a risk of developing conductive hearing loss. Therefore, regular hearing assessment is recommended in patients with achondroplasia. Older children may present with dental malocclusion. Morning headache, poor concentration and school performance may be seen in those with sleep-associated breathing problems [7,8].

There is no specific treatment but constant monitoring can detect early the occurrence of complications. Most of the children will adjust with the problems arising from their short stature. Occupational adaptations at home or at school will allow such children to participate in all activities. Growth hormone treatment has no role in the treatment of achondroplasia. C-type natriuretic peptide antagonism of Fibroblast Growth Factor Receptor 3 signals are under trial and require further studies to prove the efficacy [9].

CONCLUSION

We report a term female neonate with achondroplasia, characteristic clinical and radiological features confirmed by chromosomal analysis coupled with advanced parental age suggestive of denovo mutation, makes this case unique.

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