A RARE CASE OF ACHONDROPLASIA- SHORT LIMB

B. Ravichander[1], Sreemayee Kundu[2]

[1]Professor and HOD, Department of Paediatrics, MVJ Medical College and Research Hospital, Bangalore.
[2]Junior Resident, Department of Paediatrics, MVJ Medical College and Research Hospital, Bangalore.

ABSTRACT

BACKGROUND

A 6-year-old boy was presented to the paediatric department with shortening of all the limbs and delay in growth. Clinical examinations revealed height less than third percentile along with other abnormalities like frontal bossing, midfacial hypoplasia, flattened nasal bridge, short neck and rhizomelic type of shortening of all the limbs. These clinical features raised the diagnosis towards achondroplasia, which was further supported by radiologic evidence. Achondroplasia is a disorder involving growth of bone. The conversion of cartilage to bone is hampered. The affection is particularly seen in the long bones of arms and legs. The characterising features of this disorder are dwarfism, limitation in range of motion at the elbows, enlarged size of head, small fingers, but with normal intelligence. Other complications like apnoea, obesity, recurrent ear infections and lordosis of the spine are often associated with achondroplasia. The basic defect in achondroplasia lies in mutations of the FGFR3 gene. It is an autosomal dominant disorder.

KEYWORDS

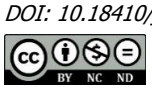
Achondroplasia, Rhizomelic, Hypoplasia, Cartilage, Dwarfism, Autosomal.

HOW TO CITE THIS ARTICLE: Ravichander B, Kundu S. A rare case of achondroplasia- Short limb. J. Evid. Based Med. Healthc. 2017; 4(18), 1058-1061. DOI: 10.18410/jebmh/2017/207

BACKGROUND

Achondroplasia is one of the commonest bone dysplasia, which generally affect the growth of tubular bones along with skull and spine. It is characterised by rhizomelic shortening of limbs. It is one of the most common short limb dwarfism syndrome. Its prevalence is 1 in 15,000 to 40,000.[1] It is an autosomal dominant disorder. An 80% of these cases are due to de novo mutation. The leading pathology is mutation in the FGFR3 gene (fibroblast growth factor receptor gene 3), which limits the ossification of cartilage, especially in long bones resulting in short limb pattern of dwarfism.[2,3] The mutation causes a gain of function of the FGFR3 gene resulting in reduced endochondral ossification, inhibition of proliferation of chondrocytes in growth plate cartilage, reduced cellular hypertrophy and reduced production of cartilage matrix, which leads to a variety of manifestations and complications. Achondroplasia is generally diagnosed by clinical and radiographic findings, which are characteristic of this disorder.[4,5] The common clinical features are short stature, shortened length of arms and legs, enlarged size of head along with hypoplastic face. Additional features can be present, which are bow legs, long thin trunk, reduced muscle tone, spinal stenosis and limited extension at elbow.[4] Radiographic features diagnostic of achondroplasia include narrowing of the caudal spine, notching over sacroiliac groove, short and thick long bones and metaphyseal flaring. Diagnosis of achondroplasia is done on the evidence of clinical and radiological findings.[5]

Financial or Other, Competing Interest: None.
Submission 13-02-2016, Peer Review 20-02-2017,
Acceptance 01-03-2017, Published 02-03-2017.
Corresponding Author:
Dr. Sreemayee Kundu,
No. D504, 80/3, Grand Edifice Apartment,
Amani Doddakere, Hoskote,
Bengaluru, Karnataka-562114.
E-mail: draritramaji@gmail.com
DOI: 10.18410/jebmh/2017/207



CASE SUMMARY

A 6-year-old boy was brought to the paediatric department with chief complaints of shortening of limbs and delay in growth as compared to his age. There was no developmental delay. He attained the milestones as per normal age. However, the child was not in school despite being in the school going age group. Clinical examinations revealed height less than third percentile (73 cms). There was frontal bossing with midfacial hypoplasia, flattened nasal bridge and short neck. Both upper and lower limbs presented with rhizomelic type of shortening. His motor system was intact with normal muscle power in all the four limbs and normal mobility in all the joints. Speech was not affected. Head circumference was 48 cms, upper segment to lower segment ratio was 1.25 and arm span was 60 cms (13 cms more than height). Abdomen was distended, but there was no evidence of organomegaly or presence of free fluid. Systemic examinations revealed no abnormalities. Skeletal survey showed large cranial vault with small skull base, platyspondyly in thoracolumbar and sacral vertebrae, posterior vertebral scalloping, progressive decrease in interpedicular distance in lumbar vertebrae and champagne glass type pelvic inlet. In the limbs, there was trumpet bone type appearance, rhizomelic shortening, short and sturdy metacarpals and phalanges, delayed appearance of carpal epiphysis. All these features, both clinical and radiological are suggestive of achondroplasia. Informed and written consent has been taken from the child's parents (both father and mother) for publication as a case report.

Figure 1

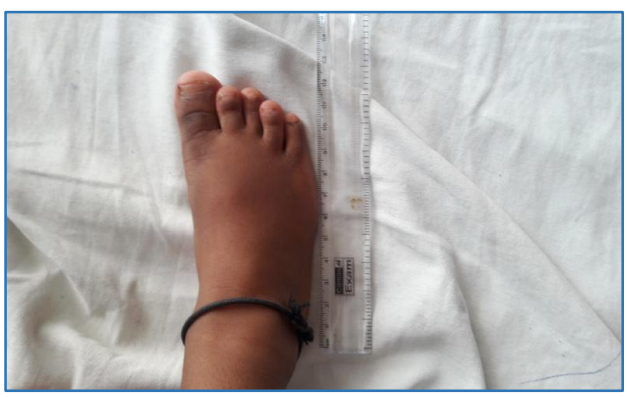


Figure 2

Figure 3

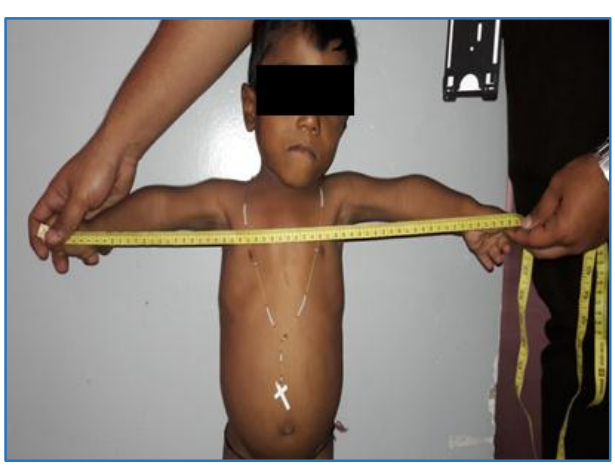


Figure 4

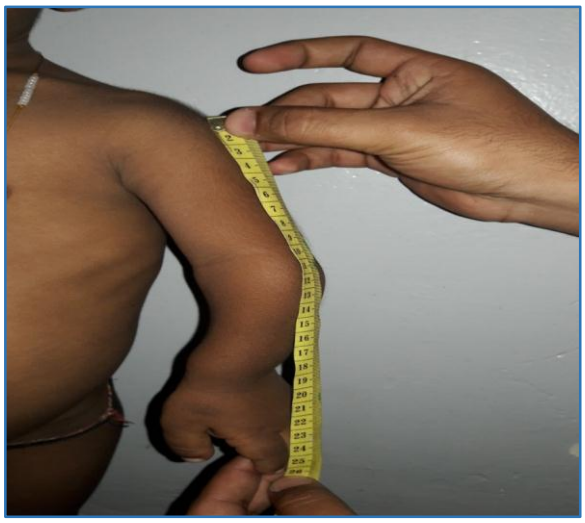


Figure 5

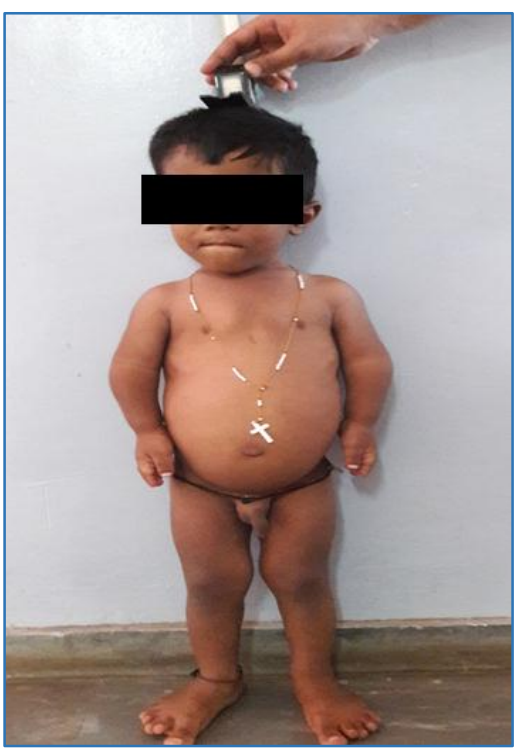


Figure 6

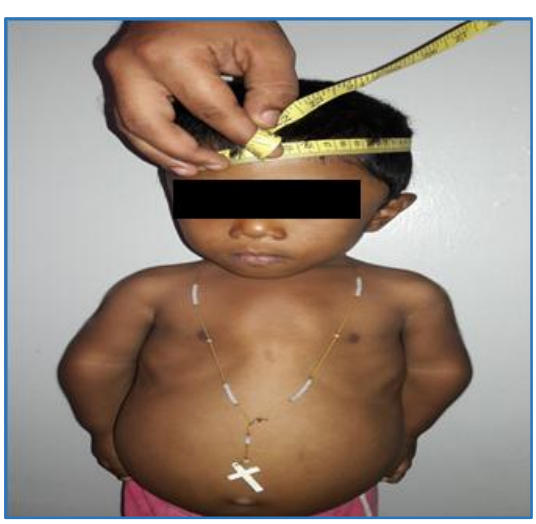


Figure 7

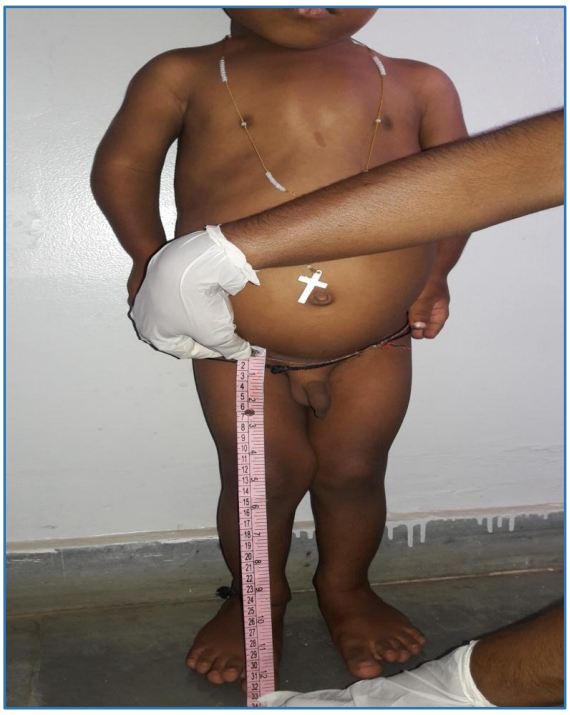


Figure 8

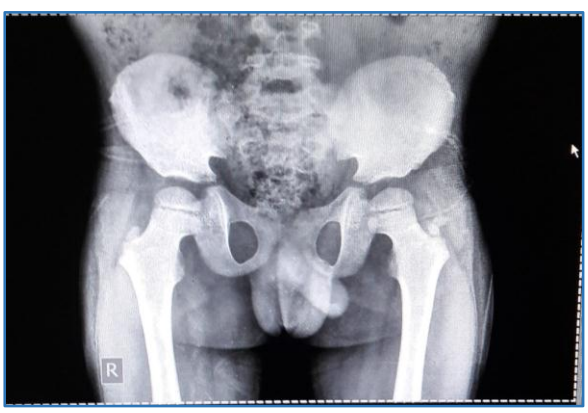


Figure 9

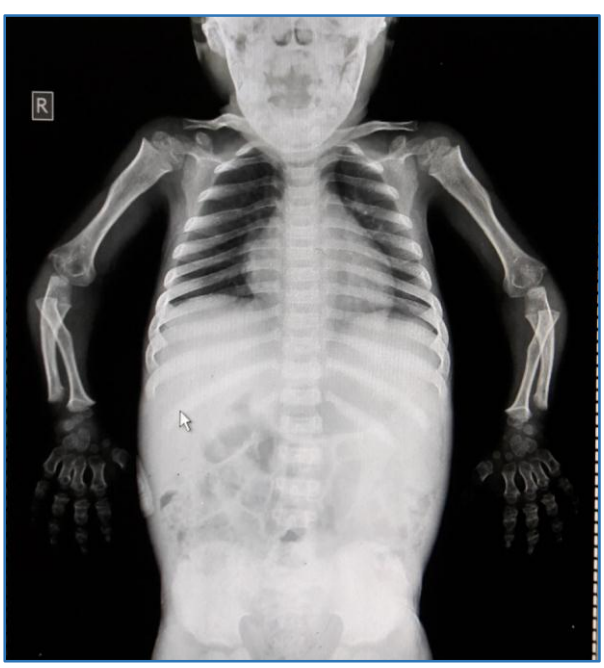


Figure 10

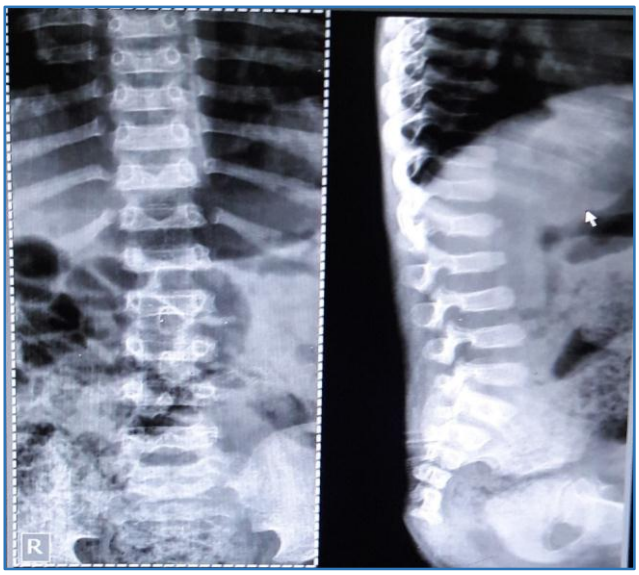


Figure 11

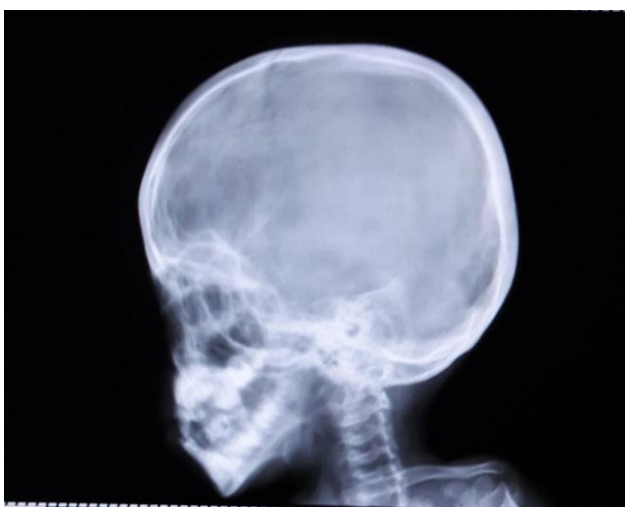


Figure 12

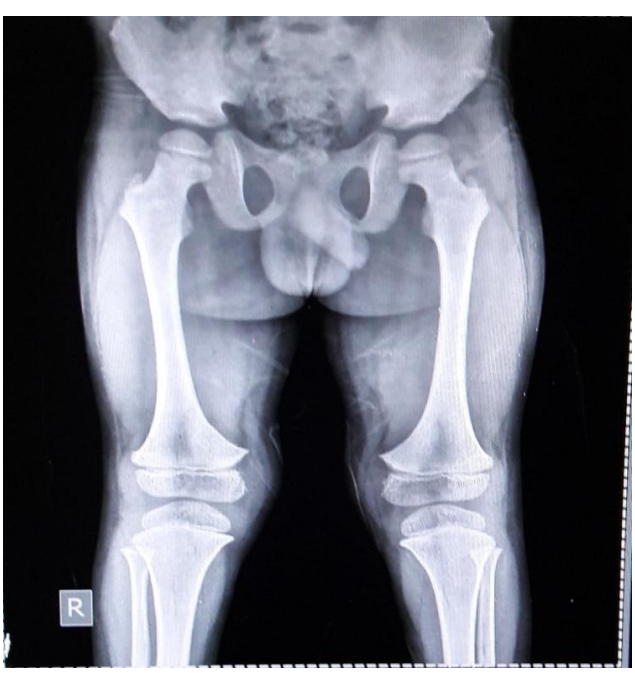


Figure 13

DISCUSSION

Achondroplasia is the prototype chondrodysplasia. It typically affects at birth with rhizomelic shortening of limbs, long trunk and large head with prominent forehead and midfacial hypoplasia. It is seen in 1 in 15,000 to 40,000 livebirths.[1] It is an autosomal dominant disorder with 80% cases occurring as de novo mutation. The defect lies in the FGFR3 (fibroblast growth factor receptor 3 gene) codon 380. The mutation maps to the transmembrane domain of the receptor and is thought to stabilise receptor dimmers that enhance receptor signals.[2,3] The FGFR3 gene encodes for a protein involved in the development of bone and brain tissue. This protein limits the ossification of cartilage in the long bones.[4,5] The consequences of this inhibit linear bone growth resulting in short-limbed dwarfism. Almost, all cases of achondroplasia result from two specific mutation in the FGR gene. Most cases are caused by a G to A point mutation at nucleotide 1138 whereas a few of them are caused by a G to C point mutation at nucleotide 1138.[2,3,4,5] These mutations result in overactive protein, which interferes in development of skeletal system leading to improper bone growth. In achondroplasia, there is usually one normal copy of the fibroblast growth factor receptor 3 gene and one mutant copy.[6,7] Two copies of the mutant gene will have fatal effect before or shortly after birth. However, most cases of achondroplasia have carrier parents who do not have the condition. This results from de novo mutation.[4,5,6,7] Diagnosis of achondroplasia is based on clinical features and skeletal radiographs. Surgical limb lengthening and growth hormone treatment have been used to increased height, however, both these modalities of treatment are controversial. Growth hormone therapy has been used to facilitate growth in such cases.[8] Study results from growth hormone use in achondroplasia are inconsistent. An increase in growth velocity, especially after first 2 years of use have been evident in some studies. However, orthopaedic complications arising from abnormal bone deposition is a major concern in growth hormone use.[9] Surgeries like limb lengthening procedures, lumbar laminectomy and spinal fusion have proven to be beneficial. Neurologic improvement has been invariably seen after surgeries done to relieve craniomedullary compression.[8,9] Prognosis for achondroplasia depends on the severity of the disorder. Approximately, 5% of newborns with extremely severe form of achondroplasia die within first year of life, although majority with the disease live a normal life span.[8,9] In spite of the fact that patients with achondroplasia rarely reach the height of 5 feet, they usually have a normal level of intelligence. Genetic factor that is homozygosity or heterozygosity for the abnormal FGFR3 gene determines the severity of the disease.[6,7] Thus, genetic testing and counselling is of high importance in achondroplasia. It also serves as means for patient education about this familial disorder. Families affected by these diseases can also seek the help of various support groups.

CONCLUSION

Despite achondroplasia being a well-documented cause of disproportionate short stature, it is difficult to diagnose in early infancy owing to the inherent disproportion of child in infancy as compared to older children or adults. It is important to recognise this disease early for appropriate counselling of the ignorant parents. As diagnosis of achondroplasia is difficult in infancy, hence careful history, clinical examination and skeletal survey are the essential tools for detecting achondroplasia in infants. Detecting the condition early in life would help counsel the parents about the disease and to attempt for betterment of the patient's life.

REFERENCES

[1] Bellus GA, Heffron TW, Horton WA. Achondroplasia is defined by recurrent G380R mutations of FGFR3. Am J Hum Genet 1995;56(2):368-373.
[2] Sobetzko D, Braga S, Rüdeberg A, et al. Achondroplasia with the FGFR3 1138g-->a (G380R) mutation in two sibs sharing a 4p haplotype derived from their unaffected father. J Med Genet 2000;37(12):958-959.
[3] Gooding HC, Boehm K, Thompson RE. Issues surrounding prenatal genetic testing for achondroplasia. Prenatal diagnosis 2002;22(10):933-940.
[4] Horton WA, Hall JG, Hecht JT. Achondroplasia. Lancet 2007;370(9582):162-172.
[5] Mettler G, Fraser CF. Recurrence risk for sibs of children with sporadic achondroplasia. Am J Med Genet 2000;90:250-251.
[6] Shiang R, Thompson LM, Zhu YH, Church DM. Mutation in the transmembrane domain of FGFR3 cause the most common genetic form of dwarfism achondroplasia. Cell 1994;78:335-342.
[7] Cohen MM. Some chondrodysplasias with short limbs: molecular perspectives. Am J Med Genet 2002;112(3):304-313.
[8] Langer LO Jr, Baumann PA, Gorlin RJ. Achondroplasia. Am J Roentgen 1967;100:12-26.
[9] Wallace DC, Exton LA, Pritchard DA, et al. Severe achondroplasia: demonstration of probable heterogeneity within this clinical syndrome. J Med Genet 1970;7(1):22-26.