Review Article

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Rare Case of Achodroplasia Couple Delivering Normal Baby

Ashok Kr Maji[1], Aritra Maji[2]

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[1]Senior Consultant, [2]Junior Consultant, Department of Obstetric and Gynecology, Aakash Hospital, Siliguri, West Bengal 734001, India.

Corresponding Author: Aritra Maji, Junior Consultant, Department of Obstetric and Gynecology, Siliguri, West Bengal 734001, India.

E-mail: draritramaji@gmail.com

Abstract

Achodnroplasia is one of the most prevalent form of dwarfism. There is very less literature or protocol for antenatal management of achondroplasia mother. We had a case of an achondroplasia mother who came in labour at 34 weeks of gestation. Her partner was also achondroplasic. Emergency LSCS was done and a healthy baby was extracted. Baby had no features of achondroplasia with normal radiologic and karyotypic evaluation. As achondroplasia is an autosomal dominant disease, the chances of healthy baby for aachondroplasia couple is very rare. There is a 25% chance of healthy baby if both the parents are heterozygouslyachondroplasic.

Keywords: Achondroplasia; Autosomal; Karyotype; Heterozygous; Mutation; Rhizomelic; Hypoplastic.

Introduction

Background

Achondroplasia is a common form of bone dysplasia, where generally the growth of tubular bones along with skull and spine are affected. The characteristic feature is rhizomelic shortening of limbs. It is the most common cause of short limb dwarfism syndrome with prevalence of 1 in 15,000 to 40,000[1]. 80% of this autosomal dominant disorder are due to de novo mutation. The major pathology is mutation in the FGFR3 gene (fibroblast growth factor receptor gene 3), which prevents the ossification of cartilage, especially in long bones resulting in short limb dwarfism.[2,3] The mutation causes increased activity of the FGFR3 gene which result in inhibition ofendochondral ossification, limitation of proliferation of chondrocytes in growth plate cartilage, decreased cellular hypertrophy and reduced formation of cartilage matrix. Achondroplasia is generally diagnosed by clinical and radiographic findings, which are characteristic of this disorder.[4,5] The diagnostic features are short stature, shortened length of arms and legs, enlarged size of head along with hypoplastic face. Additional features like bow legs, long thin trunk, reduced muscle tone, spinal stenosis and limited extension at elbow may also be evident.[4] Diagnostic radiographic features of achondroplasia include narrow caudal spine, notching over sacroiliac groove, shortened and thickened long bones and metaphyseal flaring.[5] Achondroplasia is diagnosed based on the evidence of clinical and radiological findings.Prenatal diagnosis of achondroplasia can be accomplished by ultrasound evaluation with characteristic features of shortening of long bones and confirmed by molecular analysis of DNA either by amniocentesis, chorionic villi sampling or non-invasive methods like of DNA.[10,11]

Case Summary

27 year old primigravidae woman with achon-

droplasia visited opd at 30 weeks of gestation. Her partner was achondroplastic too. Her height was 121 cm and weight was 54 kg. Fig. 1 showing arm expansion of the lady. Fig. 2 showing height of the lady. Thorough physical examination was done. Her extremities were short while her head size was normal with hypoplastic face. There was no other obvious deformities. Physician and cardiologist opinion was taken which proved insignificant. Her partner also shared the common features characteristic of achondroplasia. Her NT scan and Anomaly scan showed no obvious congenital fetal anomaly. At 34 weeks of gestation she came in labour. In view of cephalopelvic disproportion emergency LSCS was planned. A live, male baby weighing 1.7 kg was delivered with length of 42cm and APGAR score of 8/10 & 9/10. Baby was doing well, with no apparent features of achondroplasia as evaluated by neonatologist. Fig. 3 showing the length of the baby. Fig. 4 showing the head circumference of the baby. Mother and baby was discharged on day 7 of LSCS. Radiographic evaluation was normal and karyotyping studies showed no fibroblast growth factor receptor 3 mutation. At the time of penning down the case study, baby was growing normally and achieving milestones normally.

Fig. 2: Height of Achondroplasia Mother.

Fig. 1: Arm circumference of Achondroplasia Mother.

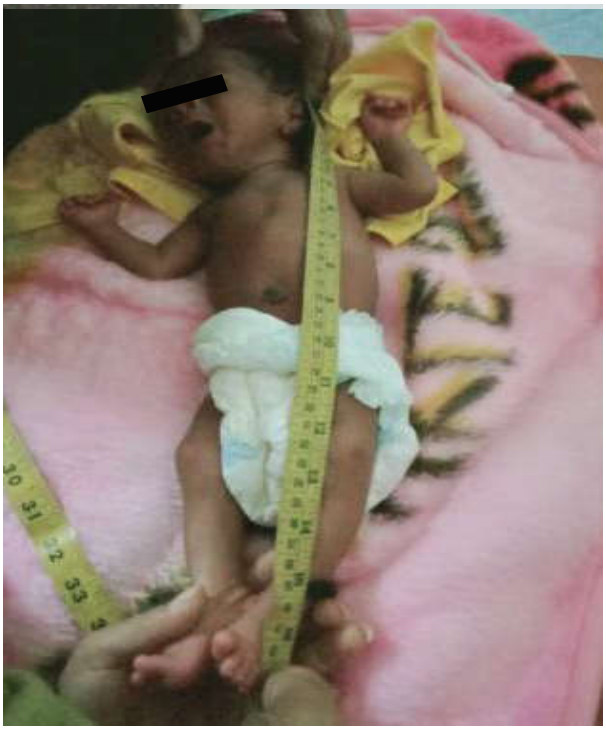

Fig. 3. Length of Baby.

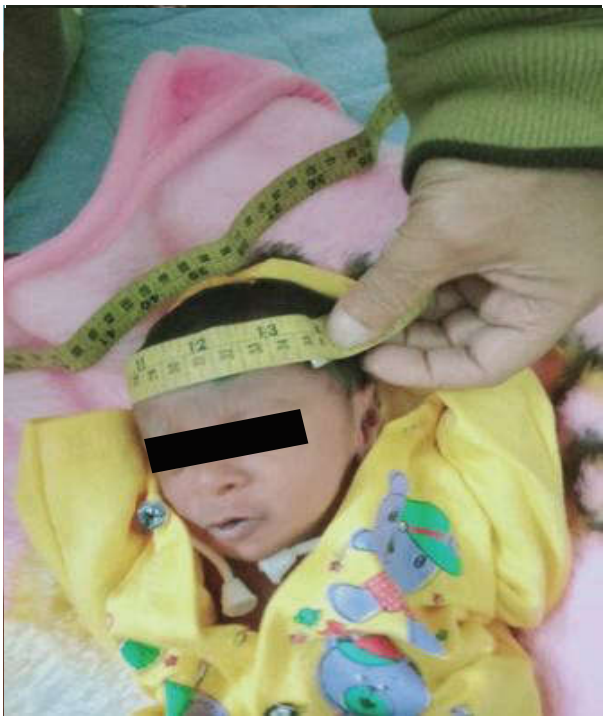

Fig. 4: Head Circumference of Baby

Conclusion

Achondroplasia is an autosomal dominant disease. Hence it is very rare that a normal healthy baby is born to an acnondroplasia couple. There is a 25% probability that an acondroplasic couple could give birth to a normal baby in case both the parents have heterozygous gene mutation. Such was the case in this case which we have reported.

Discussion

Achondroplasia is the prototype chondrodysplasia usually affecting at birth with typical features of rhizomelic shortening of limbs, long trunk and large head with prominent forehead and midfacial hypoplasia. It is found in 1 in 15,000 to 40,000 livebirths.180% cases of this autosomal dominant disease occurs as de novo mutation due to defect in the FGFR3 (fibroblast growth factor receptor 3 gene) codon 380. The mutation is in the transmembrane domain of the receptor which stabilise receptor dimmers that enhance receptor signals.[2,3] The FGFR3 gene encodes for a protein which inhibits the ossification of cartilage in the long bones.[4,5] This limits linear bone growth resulting in short-limbed dwarfism. Most cases of achondroplasia are due to a G to A point mutation at nucleotide 1138 while some are due to a G to C point mutation at nucleotide 1138.[2,3,4,5] These mutations lead to hyperctive protein, interfering in development of skeletal system which results in improper bone growth. Achondroplasia is usually associated with one normal copy of the fibroblast growth factor receptor 3 gene and one mutant copy.[6,7] Achondroplasia is diagnosed by the characterisitc clinical features and skeletal radiographs. The treatment modalities include surgical limb lengthening and growth hormone however the efficacy of both these modalities of treatment are variable.8Patients with achondroplasiaalthough seldom rarely reach the height of 5 feet, they usually have normal intelligence. The severity of the disease is determined by genetic predisposition like homozygosity or heterozygosity of the abnormal FGFR3.6, Prenatal diagnosis achondroplaisa includes ultrasound abnormalities like shortened long bones and abnormal skull, for which confirmation requires analysis of fetal material obtained following invasive procedures such as amniocentesis and chorionic villus sampling or newer modalities using cell-free fetal DNA (cffDNA) circulating in maternal blood using polymerase chain reaction (PCR) or newer techniques like next generation DNA sequencing (NGS).[10,11]

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