Case report:

Antenatal diagnosis of achondroplasia

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ABSTRACT:
We report a interesting case of antenatal diagnosis of achondrpoplasia in a young multigravida who presented with term pregnancy for routine ultrasound assessment which revealed a single, live intrauterine fetus with a discrepancy between femur length (FL) and biparietal diameter (BPD), narrowing of the interpeduncular distance. The diagnosis of achondroplasia was made with a sonological skeletal survey and findings were correlated with radiological skeletal survey after the baby was delivered.

KEY WORDS: Achondroplasia, Chondrodystrophia fetalis, Chondrodystrophic dwarfism, Micromelia

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INTRODUCTION:

"Dyplasia" means abnormal development. "Achondroplasia" refers to the abnormal development of cartilage ("chondro")[1]**.** It may be inherited by autosomal dominant gene, however most cases appear as spontaneous mutations. Radiographs of the skull, spine, pelvis and extremities reveal the characteristic features[2]. Achondroplasia is one of the most common forms of short limb dwarfism. It is usually suspected during ultrasound because of shortened long bones[3]. Antenatal ultrasound demonstrates a progressive discrepancy between femur length and biparietal diameter during the third trimester of pregegnancy[4].

CASE REPORT:

A twenty six year old multi gravida attended our department for antenatal ultrasound evaluation with the history of amenorrhea for 37 weeks. No ultrasound examination had been done earlier. The mother was asymptomatic and did not have any complaints. The ultrasound revealed a viable intrauterine fetus with femur and humerus length corresponding to 28 weeks of gestation and adnominal and head circumference corresponding to 37 weeks. The father's age was 28 years and there was no history of consanguinity. However grand father had an abnormally short stature. Complete antenatal sonological assessment revealed mildly enlarged calvarium, hypoplastic nasal bridge, disproportionate shortening of limbs with widened ends (Figure 1) and narrowing of the interpeduncular distance from proximal to distal in L1-L5, which are the characteristic features of achondroplasia. The parents were informed about the outcome of pregnancy and its prognosis.

A live, full term, appropriate for gestational age male baby with a birth weight of 2.5 kg was delivered by caesarean section. On clinical examination baby had a large head, normal trunk with rhizomelic shortening with bumping around the limb joints (Figure 2). Systemic examination was normal.
Radiological skeletal survey of the newborn demonstrated a mildly enlarged calvarium with frontal bossing, squared inferior ends of scapula, bullet

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shaped flattened vertebrae, broad and short pelvis, squared ileum, small sacrosciatic notch, horizontal acetabular roof, short long bones with metaphyseal widening, findings were consistent with achondroplasia (Figures 3a and 3b) The father denied for further evaluation which could have helped to evaluate the skull base in more detail. The parents were explained properly about the status and sequelae.

DISCUSSION:

The skeletal dysplasias are a heterogeneous group of disorders characterized by intrinsic abnormalities in the growth and/or remodeling of cartilage and bone, Achondroplasia, the most common of all skeletal dysplasias implies absent cartilage formation, was first used by Parrot in 1878[5] and It is the most common type of short-limb disproportionate dwarfism, the extremity involvement is rhizomelic, with the arms and thighs more severely involved than the forearms, legs, hands, and feet. Achondroplasia affects about 1 in every 40,000 children. Eighty percent of all "little people" have achondroplasia.

According to genetic basis[6] single gene mapped to the short arm of the fourth chromosome (band 4p16.3) is responsible for achondroplasia and is transmitted as an autosomal dominant trait. At least 80% of cases result from a random new mutation. In sporadic cases, a paternal age older than 36 years is common.

Molecular basis[7] Mutation in FGFR3 is responsible for achondroplasia, hypochondroplasia, and thanatophoric dysplasia. It may be inherited in a homozygous (lethal) or heterozygous (non-lethal) manner. Heterozygous A is the most common non-lethal dysplasia (R1), incidence being ~1 out of 26000.

Achondroplasia is evident at birth as a disproportionate short-limb dwarfing condition; our patient also had disproportionate short-limb dwarfism. Diagnosis is made based on physical examination and skeletal radiographic findings. Clinically patient has rhizomelic shortening of long bones, large cranium with frontal bossing, flattening of the nasal bridge protuberant abdomen, prominent buttock, thoracolumber kyphosis, lumbar hyperlordosis, characteristic rolling gait**,** Trident hand. Since the features are very characteristic a careful observation would lead to diagnoses of this rare condition. People with chondroplasia are normal except for their physical appearance most obvious being their stature[8].

Previously considered a diagnosis of the third trimester, recent studies have shown that a second trimester diagnosis is possible. There is a progressive discrepancy between femur length and biparietal diameter during the third trimester of pregnancy. With the femur length falling below the first percentile when compared to biparietal diameter [9,10,11] .This may occur as early as 21 weeks or as late as 27 weeks' gestational age. It is important to recognize the pattern of BPD measurement greater than expected for gestational age in association with FL measurement less than expected, in combination with average abdominal circumference measurements as suggestive of heterozygous A, in order to avoid the mistake of simply taking the mean of the three values.

In cases where both the parents are heterozygous achondroplastic, fetal USG can help to differentiate between normal, heterozygous and homozygous achondroplasia. Fetuses with FL below the third percentile compared with BPD at 17 weeks' BPD age, and with progressive shortening over the following 6 weeks, have homozygous A, where as those in whom a FL decrease occurs between 17 and 23 weeks' BPD age have heterozygous achondroplasia [9].

Heterozygous achondroplasia is associated with normal or near-normal femur lengths until 20-24 weeks of pregnancy. Thereafter, the growth rate of the femur decreases. Hence, ultrasonography may not be useful for diagnosing achondroplasia in the first half of the pregnancy. Later in the pregnancy, ultrasonography can detect short-limb dysplasia. However, differentiation among various skeletal dysplasias is difficult. Ultrasound can be used in the neonate to detect ventricle size and other abnormalities. Radiographs of the skull, spine, pelvis and extremities reveal the characteristic features[2]. Narrowing of the spinal canal is the pathologic hallmark of achondroplasia[12]**.** Skull radiograph demonstrates a large cranium, frontal bossing, small nasal bones, small skull base, stenotic foramen magnum. A lumbar spine reveals platyspondyly with posterior scalloping, distinct narrowing on the interpedicular distances from proximal to distal in L1-L5, thick and short pediicles. exagerrated lumbar lordosis, bullet shaped vertebrae due to angular kyphosis at thora-

columbar junction The pelvis is typically broad and short, and the ilium has a square appearance. The sacrosciatic notch is short, and the acetabular roof is horizontal. The pelvis assumes a characteristic "Champagne glass" appearance. The ribs are short; scapulae may be squared inferiorly with shallow glenoids. There is symmetric shortening of the long bones, with proximal portions being most affected. The bones ends are often splayed, with metaphyseal cupping. The distal femoral physes have an inverted-V (Chevron) shaped configuration. The ulna and tibia are often shorter than radius and fibula. Tubular bones of hands and feet are short and thick. The humerus is markedly shortened. The fingers are of same length, with separation of middle and ring fingers (Trident hand)[13,12].

Our case had a large head, squared inferior ends of scapula; bullet shaped flattened vertebrae, broad and short pelvis, squared ileum, small sacrosciatic notch, horizontal acetabular roof which are the typical imaging features of achondroplasia.

Computed Tomography can be used to measure size of the foramen magnum, spinal canal and develop a 3-dimensional image of the rib cage, which can be used to calculate lung volumes and can substantiate a successful surgical chest expansion[14]. Magnetic resonance imaging can be helpful to evaluate the symptoms associated with foramen magnum stenosis, to establish the cause of neurocranial enlargement for preoperative evaluation of lumbar spinal stenosis[15].

Plasma can be analyzed for the FGFR3 mutation in the mother when a short-limb skeletal dysplasia is diagnosed prenatally on ultrasound[16].This can be confirmatory for achondroplasia and can help the family to make educated decisions. DNA testing can be performed when both of the parents are affected. Infants with affected genes from both the parents (double homozygous) are either stillborn or die shortly after birth. In our case plasma analysis for the FGFR3 mutation in the mother would not have been possible firstly; due to non availability of these investigations in our hospital secondly it was term a pregnancy.

The important differential diagnosis of achondroplasia has been confused with other dwarfing dysplasia like mucoppolysaccharidosis, trisomy and spondyloepiphyseal dysplasia. However, careful biochemical and radiographic evaluation of these individuals should readily reveal the proper diagnosis[12].

CONCLUSION:

To summarize achondroplasia can be diagnosed before birth by fetal ultrasound or after birth by complete medical history and physical examination as it was possible in our case. DNA testing is now available before birth to confirm fetal ultrasound findings for parents who are at increased risk for having a child with achondroplasia.

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