

Case Report and Review of a Pregnant Woman with Achondroplasia

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Abstract

Achondroplasia is the most common cause of short stature. It is diagnosed based on physical exam, radiology and confirmed with molecular testing. Achondroplastic women are fertile and can attain pregnancy. In this report, we describe the antepartum, intrapartum and postpartum course of an Achondroplastic pregnant women. We present here a case of a 31-year old primigravida, known Achondroplastic patient, who was taken care of in our prenatal clinic without any complications. She successfully delivered a healthy baby via cesarean delivery at 38 weeks. Achondroplastic pregnant women are at increased risk of certain cardiopulmonary complications and they potentially require cesarean section for delivering the baby.

Keywords

Achondroplasia, Achondroplastic

I. Introduction

The term Achondroplasia meaning “without cartilage formation” was first used in 1878 to distinguish this condition from rickets [1]. Achondroplasia is the most common skeletal dysplasia and is the most common form of dwarfism. It has a prevalence of 1 in 20,000 live births [2].

Achondroplasia is inherited in an autosomal dominant fashion, but approximately 80% of cases are the result of new (de novo) mutations

[1]. Its pathology is due to a gain-of-function mutation in Fibroblast Growth Factor Receptor 3 (FGFR3) gene on the distal short arm of chromosome 4. In about 98% of cases, a G to A point mutation at nucleotide 1138 of the FGFR3 gene (G1138A) causes a glycine to arginine substitution in amino acid 380 (p.Gly380Arg) in the transmembrane domain of the FGFR3 gene. This mutation permanently activates the FGFR3 receptor,

inhibiting chondrocyte proliferation, which ultimately leads to impaired endochondral bone formation, growth restriction, bone shortening, and other skeletal anomalies [2,3]. An individual with achondroplasia who has a reproductive partner with average stature is at 50% risk in each pregnancy of having a child with achondroplasia. When both parents have achondroplasia, the risk to their offspring of having average stature is 25%; of having achondroplasia is 50%; and of having homozygous achondroplasia (a lethal condition) is 25%. [3,4].

II. Case Report

We present here a case of 31 year old, Primigravida with Achondroplasia, who presented to prenatal care after spontaneous conception. She was 4 feet 2 inches (127 centimeters) and weighed 127 pounds. The father of the baby was of normal stature. She was at 24 weeks gestation when she presented for her first prenatal visit. Her initial laboratory work was normal, sonogram confirmed single live intrauterine pregnancy. She had uncomplicated prenatal care, regular fetal sonograms showed normal fetal development and growth. We involved a multidisciplinary team approach, which included an Obstetrician, Maternal fetal medicine specialist (MFM), Anesthesiologist and a Genetic counsellor. Along with her regular prenatal care, she was also seen

regularly by MFM for fetal growth and development sonograms. Anesthesiology was consulted for cardio-pulmonary evaluation and also for counselling on route of anesthesia administration for elective cesarean delivery. She also had genetic counselling by a certified genetic counsellor and was offered genetic testing, which she refused. The multidisciplinary team recommended delivery of the baby at 38 weeks of gestation via cesarean section and the patient and her family agreed to the plan. She also decided to undergo elective sterilization at the time of cesarean delivery.

Patient underwent elective cesarean delivery and bilateral tubal ligation at 38 weeks for cephalopelvic disproportion. She received general anesthesia prior to cesarean delivery.

Postoperative course was uneventful and her postpartum course was uncomplicated. She has regular postpartum visits with us without any complications.

III. Discussion

Achondroplasia is the most common type of dwarfism, it is characterized by disproportionate body habitus with short limbs, narrow trunk and slightly bigger head.

Clinical Characteristics of Achondroplasia.

- Disproportionate short stature
- Macrocephaly with frontal bossing
- Midface retrusion and depressed nasal bridge
- Rhizomelic (proximal) shortening of the arms with redundant skin folds on limbs
- Limitation of elbow extension
- Brachydactyly
- Trident configuration of the hands
- Genu varum (bow legs)
- Thoracolumbar kyphosis (principally in infancy)
- Exaggerated lumbar lordosis, which develops when walking begins

Radiological characteristics:

- Short, robust tubular bones
- Narrowing of the interpedicular distance of the caudal spine
- Round pelvis with square ilia and horizontal acetabula
- Narrow sacrosciatic notch
- Proximal femoral radiolucency
- Mild, generalized metaphyseal changes [5,6]

Diagnosis:

The diagnosis of achondroplasia is based upon clinical and radiographic findings but confirmed by molecular testing.

In the fetus, achondroplasia is suspected when shorter long bones and macrocephaly are present on the third-trimester ultrasound. The diagnosis is then confirmed by molecular genetic testing of fetal genomic DNA obtained by percutaneous umbilical blood sampling (PUBS). This invasive procedure presents a small but significant risk for both the fetus and mother. Therefore, non-invasive procedures like Next Generation Sequencing (NGS) using

circulating fetal DNA (cf-DNA) in maternal plasma are available. [7] NGS can accurately detect fetal achondroplasia, as well as other autosomal dominant mutations, without having an invasive procedure [7]. The diagnosis of achondroplasia should be suspected in the newborn with proximal shortening of the arms, large head, narrow chest, and short fingers. When there is clinical suspicion, radiographic features can confirm the diagnosis; neonatal radiographs will show square ilia and horizontal acetabula, narrow sacro sciatic notch, proximal radiolucency of the femurs, and generalized metaphyseal abnormalities.

Pregnancy with Achondroplasia

High-risk pregnancy - A high-risk pregnancy is one in which one or both parents have achondroplasia. Once the FGFR3 pathogenic variant has been identified in the affected parent or parents, prenatal testing for a pregnancy at increased risk and preimplantation genetic diagnosis are possible [Gooding et al 2002]. Noninvasive prenatal diagnosis using cell-free fetal DNA in maternal serum with high sensitivity and specificity is also available [7].

Low-risk pregnancy – Low risk pregnancy is one in which routine prenatal ultrasound examination may identify short fetal limbs and raise the possibility of achondroplasia in a

fetus not known to be at increased risk. Ultrasound findings of achondroplasia generally are not apparent until 24 weeks' gestation, although widening of the femoral diaphysis-metaphysis angle may allow earlier detection [Khalil et al 2016]. Chitty et al [2011] published the frequency of various ultrasonographic features in fetuses with achondroplasia, and Hatzaki et al [2011] used a combination of 3D ultrasonography and molecular analysis to enhance the diagnostic accuracy of FGFR3-related dysplasias[8].

Complications and concerns in pregnant women with Achondroplasia:

In a pregnant patient with Achondroplasia, cesarean delivery is required because of foreseeable dystocia due to cephalopelvic disproportion [10]. When the prenatal diagnosis of achondroplasia is made in a fetus of non-affected parents, consideration should be given to cesarean section. The reason for this is that the large head of achondroplasia might not fit easily through the normal sized pelvis, potentially leading to intracranial bleeding and secondary hydrocephalus. Most women with achondroplasia need general, rather than spinal or epidural, anesthesia to avoid problems related to spinal stenosis [11]. Appropriate precautions,

Achondroplastic pregnant women are also at increased risk for respiratory failure.

Kyphoscoliosis, as well as a small thoracic cage, lead to reduced lung capacity in these patients. Expansion of the thoracic circumference is further limited by the enlarged uterus of pregnancy. All of these factors together may result in respiratory distress during the third trimester, possibly requiring early delivery. For these reasons, a consultation with a pulmonologist is recommended in early pregnancy to avoid respiratory complications.

In patients with achondroplasia, kyphoscoliosis makes spinal anesthesia difficult and associated with neurological complications. [13] On the other hand, general anesthesia, with straightforward airway management, is safe and does not damage the cervical spine [13].

Cervical cord compression at the cervical medullary junction is also common and may require surgical decompression in infancy or early childhood. The best predictors of the need for decompression include; Lower limb hyper-reflexia and/or clonus, Central hypopnea (demonstrated by polysomnography) and foramen magnum measurements that are below the mean for

children with achondroplasia [9]. The need for decompression at the cervical medullary junction is an acute emergency in pregnancy, but is also rare.

Respiratory difficulties and breathing disorders in achondroplasia are thought to underlie the increased risk for sudden death in infants and children. Cardiovascular events are the main cause of mortality in adults. Cardiovascular complications like Hypertension, Metabolic Syndrome, Ischemic Heart Disease and stroke can occur due to Obstructive Sleep Apnea (OSA). Treatment of OSA with adenotonsillectomy and/or CPAP can improve respiratory abnormalities and decrease respiratory events, and for adults with OSA, can reduce the incidence of long-term complications [15].

Ghumman et al [2005] also reported the uncomplicated delivery of an unaffected baby to an achondroplastic dwarf under general anesthesia. Due to contracted pelvis, Cesarean section was also performed. Cevic and Colakoglu [2010] also described successful delivery of achondroplastic female by cesarian section and general anesthesia and highlighted the importance of the preoperative assessment.

IV. Conclusion

With this case report, we conclude that Achondroplastic pregnant women are at increased risk for having cardiopulmonary complications and need to be addressed appropriately. When the pregnant woman is of average stature and the fetus has achondroplasia, fetal macrocephaly may cause cephalopelvic disproportion, therefore delivery by cesarean section should be considered in such cases. Pregnant women with achondroplasia must always be delivered by cesarean section because of the small size of the pelvis and preferably under general anesthesia.

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