CASE REPORT

Challenging Management for Pregnancy and Delivery in Women with Achondroplasia and Pesudoachondroplasia

Adityo Prabowo[1], Khanisyah Erza Gumilar[2]

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Abstract

Background: Achondroplasia is a rare genetic disease of bone growth with an incidence of 1:20,000 live births which is characterized by short stature disproportionate body, shortening of long bones, macrocephaly, and kyphoscoliosis. While pseudoachondroplasia is caused by an autosomal dominant mutation in the cartilage oligomeric matrix protein (COMP). Due to the rarity of this condition and its adverse impact on the obstetrical outcome, we find it interesting to report two cases of achondroplasia and pseudoachondroplasia with pregnancy.

Case description: The first case was a 24-year-old woman with achondroplasia (patient's height was 116 cm) primigravida, who was referred at her 36–37 weeks of gestation. Ultrasound examination of the fetus revealed micromelia skeletal dysplasia. At 37–38 weeks of gestation, the patient underwent a cesarean section under the subarachnoid block (SAB) regional anesthesia because of the complication of cephalopelvic disproportion (CPD). The baby had a relatively large head circumference, frontal bossing, disproportionate short limbs, and trident hand appearance which is pathognomonic of achondroplasia. The second case was a 26-year-old woman with pseudoachondroplasia (patient's height was 127 cm) multigravida with a history of one abortion, who was referred at her 35–36 weeks of gestation. The patient underwent elective cesarean section with SAB regional anesthesia and the baby looked physically not inheriting maternal abnormalities.

Conclusion: Achondroplasia increases maternal and fetal obstetric complications; thus, requiring prenatal counseling, comprehensive risk evaluation, and multidisciplinary team management of anesthesia, obstetrics, and neonatology.

Keywords: Achondroplasia, Autosomal dominant, Cartilage oligomeric matrix protein, Fibroblast growth factor receptor 3, Pregnancy, Pseudoachondroplasia, Short stature.

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Background

Achondroplasia is a type of dysplasia that causes disproportionate dwarfism (short stature) in humans with an incidence of 1 in 20,000 live births. This disease is caused by an autosomal dominant mutation in the fibroblast growth factor receptor 3 (FGFR3) gene. This mutation causes inhibition of chondrocyte proliferation which causes failure of endochondral formation, growth restriction occurs, bone shortening, trident hand, elbow flexion contracture, and other bone anomalies.[1] Pseudoachondroplasia is caused by autosomal dominant mutation in the COMP protein characterized by a normal body length at birth but the growth will slow down and result in short stature disproportionate without experiencing trident hand and elbow flexion contracture like achondroplasia. About 80% of cases are new mutations (*de novo*), the rest 20% are inherited from the parents.[2]

Mothers with achondroplasia/pseudoachondroplasia have disproportionate short stature, limited neck movement, risk of kyphoscoliosis/thoracal deformity, and risk of foramen magnum stenosis. In the normal pregnant women, physiological changes occur including a decrease in functional residual capacity (FRC) of about 20–30% or 400–700 mL.[3] This physiologic change is worsened by smaller thoracic cavity with decreased vital volume and restrictive lung disease in achondroplasia. These conditions will increase the risk of complications for the mother and fetus.[1]

Case Description

The first case was a 24-year-old woman primigravida with the diagnosis of achondroplasia (patient's height was 116 cm) (Fig. 1A). The patient was referred because of fetal skeletal dysplasia suspicious from ultrasonography. The patient was diagnosed at 28–29 weeks of gestation with skeletal dysplasia, the biometric length of bones corresponded to 23 weeks and the ribs were shorter. The patient was planned for elective cesarean section at 38–39 weeks of gestation due to CPD and achondroplasia. The patient gave birth via emergency cesarean delivery with SAB regional anesthesia; the baby was a female with a birth weight of 2500 gm, an appearance, pulse, grimace, activity, and resiratory (APGAR) score of 7-8 and fetal signs of achondroplasia were found (Fig. 1B). The patient underwent intracesarean IUD insertion. During and after surgery, the patient had no complications. In this case, the baby also inherited maternal abnormalities and found frontal bossing, trident hand (Fig. 1C), and disproportionate short stature.

The second case was a 26-year-old woman with multigravida, with a history of one abortion. The patient was referred to the hospital because of a narrow pelvis (patient's height was 127 cm) (Fig. 2A). The patient was planned for elective cesarean section at 38–39

[1,2]Department of Obstetrics and Gynaecology, Airlangga University, Surabaya, East Java, Indonesia

Corresponding Author: Adityo Prabowo, Department of Obstetrics and Gynaecology, Airlangga University, Surabaya, East Java, Indonesia, Phone: +62 81216162621, e-mail: adityop92@gmail.com

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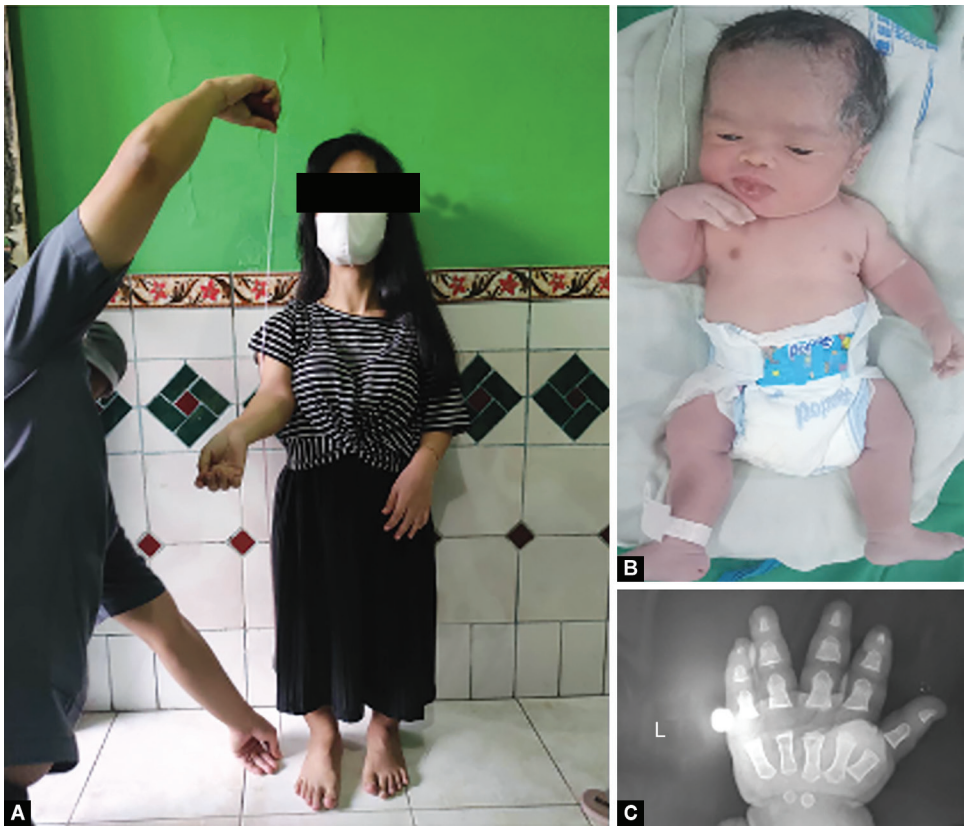

Figs 1A to C: (A) Achondroplasia mother; (B) Achondroplasia baby; (C) "Trident hand" (bone age photo at 1-month-old baby)

Figs 2A and B: (A) Pseudoachondroplasia mother; (B) Normal baby

weeks of gestation due to CPD and maternal pseudoachondroplasia. From the ultrasound examination, there was no discrepancy in fetal bone size with an estimated fetal weight of 2300 gm. The patient gave birth by cesarean delivery with SAB regional anesthesia the baby was born a boy with a birth weight of 2400 gm, with an APGAR score of 8–9, and there were no congenital abnormalities or signs of pseudoachondroplasia (Fig. 2B). The patient underwent tubectomy and after surgery the patient had no complications.

Discussion

Pregnant woman with achondroplasia/pseudoachondroplasia will usually have a narrower thorax cavity, and the condition of pregnancy (especially in the third trimester), has the potential to cause declining lung function rapidly. The larger the size of the uterus will push the diaphragm up and can cause respiratory distress in pregnant women and fetal hypoxemia at any time. Therefore, the risk of preterm delivery in this case also increases. The older gestational age can also worsen kyphoscoliosis of the mother and leg shape disorder that the patient has had since the beginning because the burden of pregnancy is getting heavier. The maternal presence of a narrow pelvis causes CPD and often affects the mode of delivery by cesarean section.

Patients with achondroplasia/pseudoachondroplasia have a short nasopharynx, maxillary hypoplasia, short cervical spine, macroglossia, and instability of the atlanto–axial joint, sometimes with tracheomalacia, making visual access for intubation under general anesthesia difficult. In both cases, regional anesthesia was preferred although it has the potential difficulty to identify the patient's interspinous space. However, this decision is supported by minimal abnormalities in the vertebrae in the two cases discussed above. Therefore, preoperative managements urge the involvement examination of a multidisciplinary team including pulmonology, cardiology, neurology, neonatology, and anesthesiology are needed. Pregnant women with achondroplasia can continue their pregnancy to the near term with good monitoring and preparation for complications that may arise. There is a risk that the disease is inherited in an autosomal dominant manner, so there is a possibility that the fetus will have skeletal dysplasia, macrocephaly, polyhydramnios, and fetal distress.[4]

The diagnosis in both patients (maternal) are assessed through a medical history, physical examination, and orthopedist consultation. Since birth, the first maternal had a disproportionate

short stature, without the history of fractures, goiter, malnutrition, and mental retardation. Patient has characteristics of frontal bossing, trident hand, and flexion contracture elbow. Unfortunately, the patient has never had an orthopedist examination since childhood. The risk factor for this achondroplasia is old paternal age, where the spermatogenesis of men aged over 36 years has the opportunity of *de novo* DNA mutation.[2] The second case (maternal), it was found that the history of the mother's body length at birth was not clearly known, but with increasing age, a disproportionate short stature was found on physical examination, but without frontal bossing, trident hand, and elbow flexion contracture which are characteristics of achondroplasia. From orthopedics, she was diagnosed with pseudoachondroplasia. Body disproportion that occurs in achondroplasia was confirmed by the value of the upper to lower segment (US/LS) ratio which is higher than the normal US/LS curve value according to age (in both cases, above 1.6 years).[1]

It is important to evaluate the fetus and make genetic counseling to the family about the prognosis of the fetus. The fetus should be evaluated for the characteristics related to the possibility of achondroplasia.[3] Suspicion of bone dysplasia is investigated out by detailed examination of the following long bones: Femur, humerus, ulna, radius, tibia, fibula, and chest circumference (usually shortened). It is necessary to find out the following from ultrasound: A sign of fragile bones to rule out osteogenesis imperfecta, a sign of hydrops fetalis to rule out the diagnosis of achondrogenesis (lethal), and extremely narrow thorax to rule out tanatophoric dysplasia (lethal). Measurement of ratio femur length/abdominal circumference (FL/AC) or thoracic circumference/AC (TC/AC) are very important to determine the fetal prognosis. The prognosis become worst when the ratio FL/AC was below 0.16 and TC/AC was below 0.8. Our first case data of FL/AC was 0.17 and TC/AC was 0.81, so the achondroplasia baby still has good prognosis.

Doppler imaging examination also important to rule out the differential diagnosis of fetal growth restriction. For achondroplasia diagnosis in first case, operator found the signs such as frontal bossing on the skull, hypoplasia of the midface bone, saddle nose, macrocephaly, small fingers, and trident hand. Other congenital screenings should be evaluated such as vertebrae, anal, cardiac, trachea, esophagus, and renal (VACTER). Confirmation of prenatal diagnosis in suspected of achondroplasia is by molecular tests (FGFR3 mutations) on chorionic villus sampling (CVS) samples carried out at 11–13 weeks of gestation or amniocentesis at 15 weeks of gestation.[1] However, unfortunately, this examination cannot be carried out due to limited facilities and patients arriving late in pregnancy.

Conclusion

Achondroplasia increase maternal and fetal obstetric complications; thus, requiring prenatal counseling, comprehensive risk evaluation, and multidisciplinary team management of anesthesia, obstetrics, and neonatology.

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Orcid

Adityo Prabowo https://orcid.org/0000-0002-7010-2681
Khanisyah Erza Gumilar https://orcid.org/0000-0002-5050-2370

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