



Prenatal Diagnosis of Achondrogenesis Type 2 in the Early Second Trimester by using Three-Dimensional Computed Tomography

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Abstract

Achondrogenesis type 2 (ACG2) is a lethal skeletal disorder that is characterized by extremely short limbs with cupped and splayed metaphyses and poor vertebral body ossification. A 23-year-old Japanese woman (gravida 1, para 0) was referred to our hospital at 19 weeks and 0 days gestation with the fetus having severe shortening of the long bones. According to ultrasonographic examination, thanatophoric dysplasia type 1 or ACG2 was suspected. Therefore, we performed three-dimensional computed tomography (3D-CT) which showed the lack of ossification of the fetal vertebral bodies clearly. We diagnosed ACG2, and the parents decided on termination of the pregnancy. Here we report a case of ACG2 that was clearly identified with 3D-CT in the early second trimester.

Keywords: Achondrogenesis; Prenatal diagnosis; Three-dimensional computed tomography

Introduction

Achondrogenesis type 2 (ACG2) is a lethal disorder that presents with a large skull, very small and short limbs, and a lack of mineralization of most vertebral bodies. The pelvis has small iliac wings with absent ischia, pubic bones, and sacral elements. The extremities show severe rhizomelia and mesomelia with relative sparing of the hands [1]. It occurs in approximately 1 in 20,000 births and is caused by a dominant mutation in the type 2 collagen gene (COL2A1) [2]. However, it is difficult to diagnose it exactly, because there are more than 150 different classification in skeletal dysplasia disease, of which many are extremely rare [3,4].

Recent studies have suggested that three-dimensional computed tomography (3D-CT) is more accurate than ultrasound for prenatal diagnosis of skeletal dysplasia [5]. The morphology of the spine and pelvic bones is often inconspicuous on ultrasound, and an accurate diagnosis can be difficult using only ultrasound. On the other hand, 3D-CT can more precisely evaluate the skull, ribs, pelvic bones, vertebrae, and bone mineralization regardless of fetal position or amniotic fluid volume. Here we report a case of ACG2 that was clearly identified on 3D-CT in the early second trimester.

Case Presentation

A 23-year-old Japanese woman (gravida 1, para 0) was referred to our hospital at 19 weeks and 0 days gestation with the fetus having severe shortening of the long bones. She had no history of drug or alcohol abuse and no relevant family history. Additionally, she had no complication and any history of infection in the first of pregnancy. She had no screening of fetus by ultrasound scan from 11 weeks to 13 weeks. In 14 weeks gestation, her fetus was scanned only for measuring biparietal diameter. In 18 weeks gestation, severe shortening of the limbs was detected for the first time. In our hospital at 19 weeks gestation, ultrasonographic examination for the fetus revealed severe shortening of the limbs (-5.3 S.D.), a narrow thorax, nuchal translucency, and no cloverleaf skull deformity. When pressing the skull of the fetus with the ultrasound probe, the skull was not deformed. No heart defects or other obvious structural abnormalities were identified.

Based on these findings, thanatophoric dysplasia type 1 (TD1) or ACG2 was suspected. Therefore, we performed 3D-CT at 19 weeks of gestation. CT was performed with a multi-detector row CT unit (Aquillion ONE; Toshiba Medical Systems, Tokyo, Japan) with 3D adaptive iterative

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Figure 1: Prenatal three-dimensional computed tomography at 19 weeks of gestation. Thoracic, lumbar and sacral vertebral bodies had completely lack of mineralization (ossification). Absence of ischia and pubic bones were observed. Skull bone was proportionately large, thorax was small with short ribs. Micromyelia was seen in extremities. Long bones were almost normally modeled. (a) Frontal view (b) Lateral view.

dose reconstruction (AIDR3D). The data acquisition parameters were 64 X 0.5-mm detector collimation, a 0.5s rotation time, and exposure factors of 120 kV and 75 mAs. These figures clearly revealed a lack of ossification of the fetal vertebral bodies (Figure 1A and B). This characteristic confirmed the prenatal diagnosis of ACG2. The parents decided on termination of the pregnancy. We dilated the cervix by osmotic dilators, inserted gemeprost, and then delivered the fetus, weighing 282 g.

Radiological evaluation of the fetus after the delivery showed findings consistent with ACG2 (Figure 2a, b). It showed metaphyseal flaring and cupping of long bones, absence of talus and calcaneal ossification were observed more clearly than 3DCT. In addition, the molecular analysis of DNA obtained from placenta demonstrated mutation for a c.3427G>A transition (P.G1143S) in exon 40-54 of the COL2A1 gene.

Discussion

Our case demonstrates that, even in the early second trimester, ACG2 is characterized by a lack of vertebral body ossification. Moreover, 3D-CT contributed to a precise diagnosis of ACG2. Ossification occurs at a relatively early human gestational age: the clavicle and mandible are ossified by 8 weeks; the appendicular skeleton, ileum and scapula by 12 weeks; and the metacarpals and metatarsals by 12–16 weeks [6]. Secondary (epiphyseal) ossification centers can be seen by radiographs by 20 weeks gestation. Since bone is echodense by ultrasound, the fetal bone is relatively well visualized by two-dimensional ultrasound in the second trimester of pregnancy [7,8]. However, the morphology of the spine and pelvic bones is often inconspicuous on ultrasound. In previous studies, 33–88% of ACG2 cases were correctly diagnosed by ultrasonography in the prenatal period [9].

In this case, it was difficult to distinguish ACG2 from TD1. Both disorders are characterized by severe shortening of the limbs and a narrow thorax, but with ACG there is a lack of vertebral body ossification. However, the spine could not be clearly visualized in our case because the fetus was in the spine position. Accurate prenatal diagnosis allows physicians to provide appropriate counseling to families about perinatal lethality, consideration for focused molecular analysis, prediction of neonatal complications, recurrence risk, and maternal management [7]. In addition a timely specific prenatal diagnosis is important because of termination laws. In Japan, the

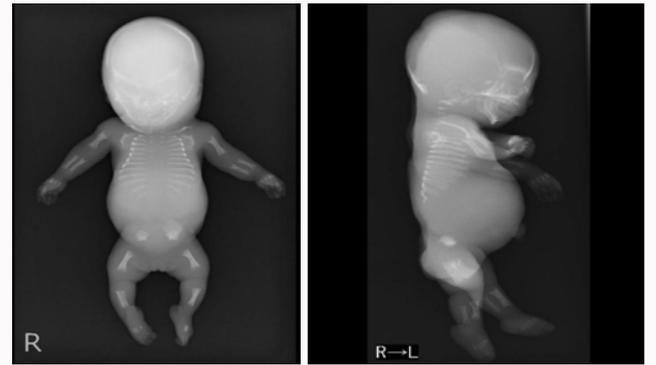


Figure 2: Radiograph in a stillborn infant. Showing extremely short femora and humeri with flares and cupped metaphyses. (a) frontal view (b) lateral view.

decision to terminate a pregnancy must be made by 22 weeks gestation. To allow time for patient counseling, we recommend making a diagnosis by 20 weeks of gestation.

Ultrasound examination is useful because it is minimally invasive and easy; however, the resolution depends on the fetus position and amniotic fluid volume. On the other hand, 3D-CT is able to provide a precise diagnosis even if there is almost no amniotic fluid [10]. Recent studies have suggested that 3D-CT is more accurate than ultrasound for prenatal diagnosis of skeletal dysplasia [5].

This case showed a precise prenatal diagnosis of ACG2 by using 3D-CT in the early second trimester. On the other hand, ACG2 was diagnosed by transvaginal ultrasound at 12 weeks by Soothill in 1993 [6]. The authors showed that the fetus had severe generalized subcutaneous edema and short limbs by ultrasound scanning. In addition, radiological evaluation of the fetus after termination showed marked limb shortening with flaring and cupping of the metaphyseal ends of the long bones and ribs but no rib fractures. Immunocytochemistry showed the presence of type 1 collagen. They diagnosed ACG2 by those findings. However, the fetus in that case clearly had ossification of the fetal vertebral bodies; therefore, that case might not conform to the current ACG2 [4]. Including molecular analysis, we considered the possibility of osteogenesis imperfecta. Except for the above-mentioned case report, our report is the first report of a precise prenatal diagnosis of ACG2 in the early second trimester.

This is the first report of a precise prenatal diagnosis of ACG2 using 3D-CT in the early second trimester. This case suggests that 3D-CT can provide additional and more accurate information to diagnose fetal ACG2.

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