# Skeletal Defect at Mid-trimester Ultrasound Scan

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## Section 2 - Answer

### Case Description

A 25-year-old primigravida was sent to the hospital due to gestational diabetes. First trimester ultrasound (US) scan and combined screening revealed reduced risk for aneuploidies as follows: trisomy 21 (1: 16,185), 18, and 13 (1: 100,000), pregnancy-associated plasma protein A = 3 MoM, free beta-human chorionic gonadotropin = 0.92 MoM, and a nuchal translucency of 2.8 mm (above the 95$^{th}$ centile for gestational age). At the mid-trimester US, the amniotic fluid was slightly increased, the fetus had a head circumference (203 mm), and a biparietal diameter (55.8 mm) above the 95$^{th}$ centile [Figure 1]. The skull had a frontoparietal narrowing ("lemon" sign) [Figure 2], with no apparent intracranial abnormalities. There were an increased cardiothoracic ratio and a clear disproportion between the thoracic and the abdominal diameter ("keel-shaped" or "bell-shaped" trunk) suggesting shortening of the ribs [Figures 3 and 4]. There was an obvious shortening of the long bones below the 5$^{th}$ centile, including the humerus (16.6 mm), ulna (19 mm) [Figure 5], femur (9 mm) [Figure 6], and fibula (16.5 mm); both the femur and humerus had a slight curvature (telephone receiver shape) [Figure 7]. Face, lungs, heart, abdomen, genitalia, and spine were normal.

### Interpretation

These US findings suggested a severe and isolated shortening of the long bones, restricting fetal growth, and were highly suggestive of severe skeletal dysplasia.

Skeletal defects are a heterogeneous group of malformations which are found in nearly 1 in 4000 births. Osteochondrodysplasias, defects of cartilage or bone growth, and development are one of the main groups of these pathologies. Some of these entities are thought to be caused by mutations on the fibroblast growth factor receptor 3 (FGFr3) gene located at the short arm of chromosome 4, namely, achondroplasia, hypochondroplasia, and thanatophoric dysplasia (types I and II).[1,2]

The patient was referred to our prenatal diagnosis department for antenatal counseling and further investigation. At 21 weeks, the patient underwent amniocentesis and at 21 weeks and 2 days pregnancy was terminated.

The postabortion radiographic study confirmed the US findings [Figures 8 and 9]. The fetus had a decreased body size compared to the head, and a small chest compared to the abdomen. It also confirmed the presence of shortening of the long bones of the limbs and the ribs. The cytogenetic examination revealed a karyotype 46 XY and molecular study by Array-cGH for skeletal dysplasias detected a G (p.Tyr373Cys)-c. 1118A mutation in the FGFr3 gene in heterozygosity, consistent with the phenotype of thanatophoric dysplasia type I.

Thanatophoric dysplasia is the most common lethal skeletal dysplasia, found in 1 in 10,000-1 in 50,000 births. Its name derives from ancient Greek, meaning death-bearing, as it is almost always incompatible with life (there are some rare case reports of survivors) and the characteristic features are severe shortening of the limbs with several skinfolds, narrow thorax (with consequent increased cardiothoracic ratio), normal or large belly, and prominent forehead (ending up as disproportional abdomen compared to the thorax).[3] Classically, it is divided into two types. In type I, which is sporadic, the femurs are typically curved ("telephone receiver like") and are not often associated with cloverleaf skull. In type II, which is autosomal recessive, the femurs are straight, and the skull is typically cloverleaf shaped. Type I is

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**Received:** 28-12-2017 **Accepted:** 29-03-2018 **Available Online:** 25-05-2018

Access this article online

Quick Response Code:

Website: www.jmuonline.org

DOI: 10.4103/JMU.JMU_45_18



**How to cite this article:** Brandao P, Soares E, Estevinho C, Freixo M, Portela-Carvalho AS, Ferreira MJ. Skeletal defect at mid-trimester ultrasound scan. J Med Ultrasound 2018;26:171-3.

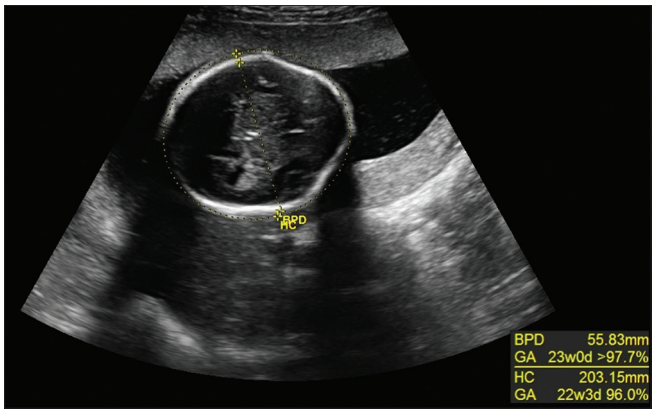


**Figure 1:** Ultrasound: Fetal head circumference and a biparietal diameter above the 95th centile

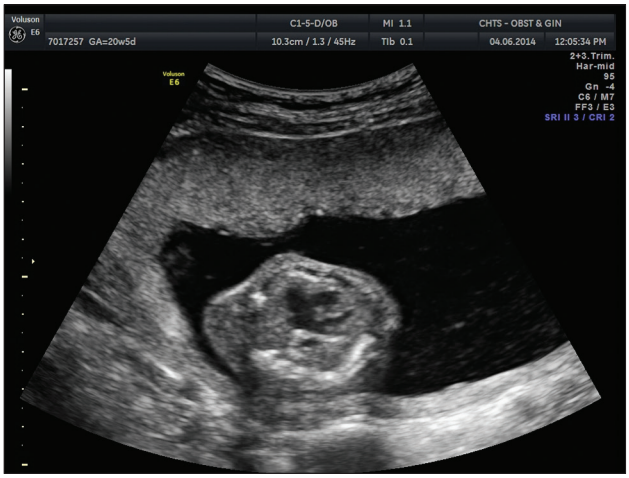


**Figure 3:** Ultrasound: Increased cardiothoracic ratio due to shortening of the ribs and consequent narrowed thorax

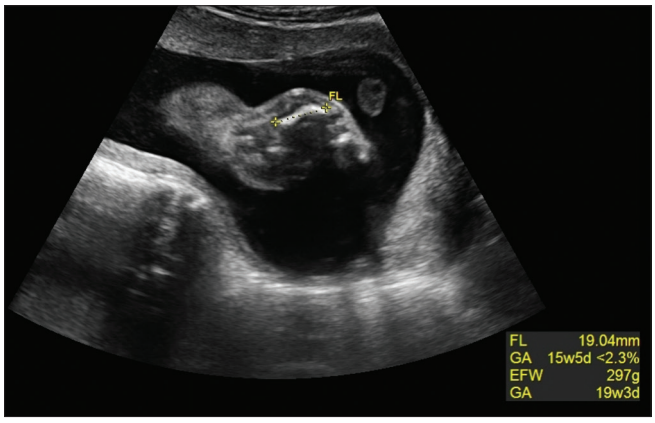


**Figure 5:** Ultrasound: Short ulna (below the 5th centile)

thought to be caused by several mutations of the FGFr3 gene, but type II is thought to be caused by a unique mutation.[4]

Usually, skeletal dysplasias may be diagnosed by US during the mid-trimester scan.[5,6] The most common feature to raise suspicion of these diagnoses is the shortening of the long bones,

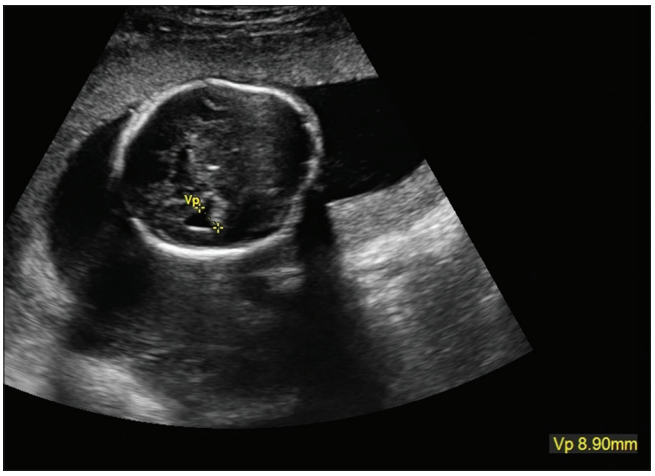


**Figure 2:** Ultrasound: Frontoparietal narrowing ("lemon sign") of the cranium. No intracranial abnormalities

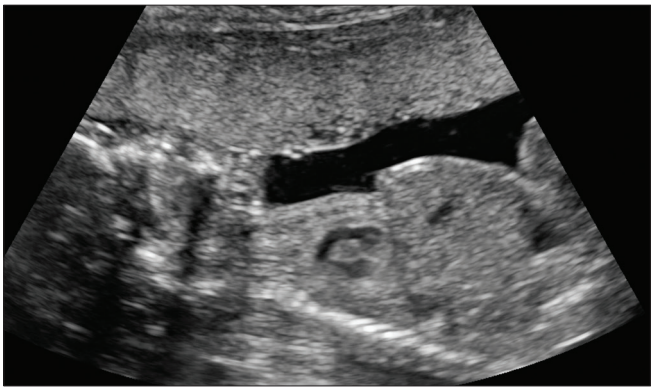

**Figure 4:** Ultrasound: Disproportion between the thoracic and the abdominal diameter - "keel" or "bell" trunk shape

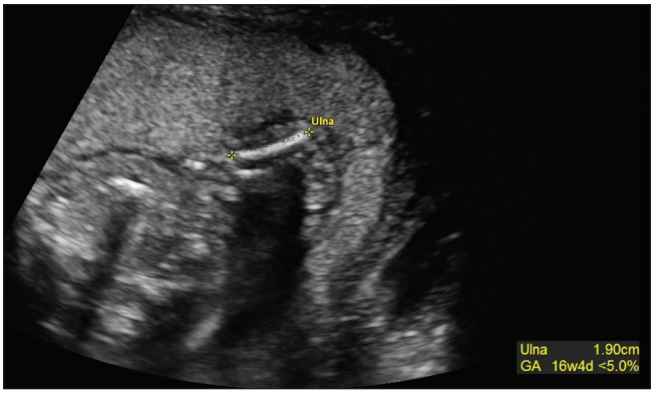


**Figure 6:** Ultrasound: Short and curved femur (below the 5th centile)

which is common to all of them. The differential diagnosis between them may not be easy, as their specific features may not be present, or may be subtle.[7,8]

As a conclusion, in the presence of shortened and bowed fetal long bones, thanatophoric dysplasia should always be ruled out. These fetuses have growth and movement restriction, as well as limited neonatal respiratory capacity, the reason why it is considered a

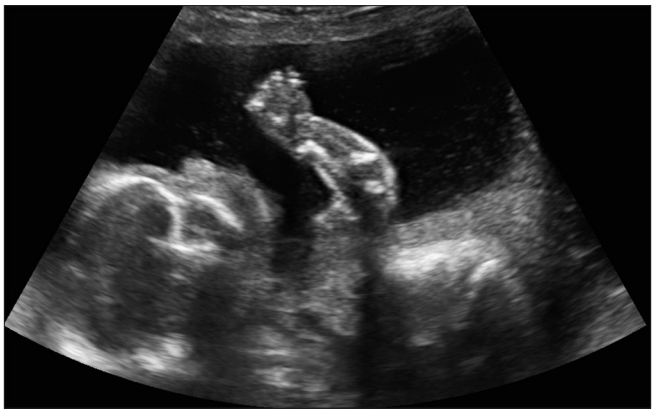

**Figure 7:** Ultrasound: Fetal arm with short long bones

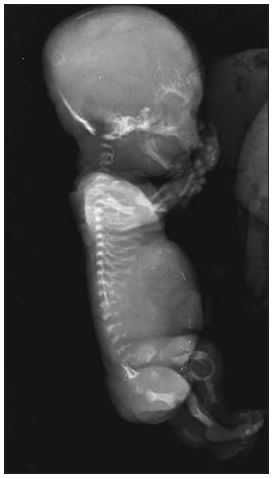

**Figure 9:** Profile postabortion X-ray of the fetus: small long bones, narrowed thorax due to shortened ribs

fatal condition. Suspecting this condition during mid-trimester scan is of utmost importance, to allow prenatal diagnosis which may be subsequently confirmed using Array-CGH analysis.

This case highlights the importance of routine examination of the long bones during the mid-trimester scan.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

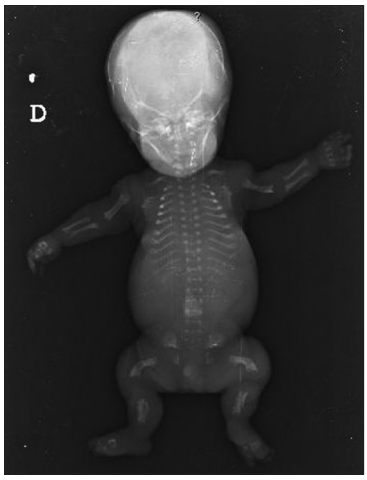


**Figure 8:** Anteroposterior postabortion X-ray of the fetus: shortened limbs with bowed bones and flared irregular metaphyses

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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