Spine Abnormality in a Fetus at 21 Weeks of Gestation

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Section 2 – Answer

Case description

A 29-year-old pregnant woman, 2 gravida 1 para (one cesarean section 3 years ago, mother of a healthy child) was sent to our hospital at 13 weeks of gestation because of the personal history of Type 1 diabetes mellitus. First trimester combined screening revealed reduced risk for aneuploidies: trisomy 21 (1:13,809), 18 (1:2282), and 13 (1:1733). The ultrasound (US) showed a live fetus with a cephalocaudal length of 54.7 mm (gestational age of 12 weeks), nuchal translucency of 1.6 mm (below 95th centile for gestational age), and the presence of nasal bone. Fetal echo anatomy was normal. The second-trimester ultrasonography, performed at 21 weeks and 5 days of gestation, showed a live fetus had a head circumference of 189.9 mm and a biparietal diameter of 53.4 mm, both in the 50th centile for gestational age. The skull had a normal shape with no intracranial abnormalities, and the face had no apparent dysmorphism. The evaluation of the fetal facial profile showed nasal bone hypoplasia (4.4 mm) [Figure 1]. Cross-section view of the neck had nuchal edema (6.5 mm) [Figure 2]. The evaluation of the thorax and abdomen had no apparent abnormalities. The sagittal section of the spine showed signs of deviation with an apparent hemivertebra and thoracolumbar scoliosis [Figures 3 and 4]. The limbs and extremities had normal structure; long bones were short for gestational age with a humerus of 29.2 mm, radius of 24.8 mm, ulna of 27.5 mm, femur of 29.3 mm, tibia of 24.6 mm, and fibula of 25.4 mm, all below the 5th centile for the gestational age [Figure 5]. No bone fractures were identified.

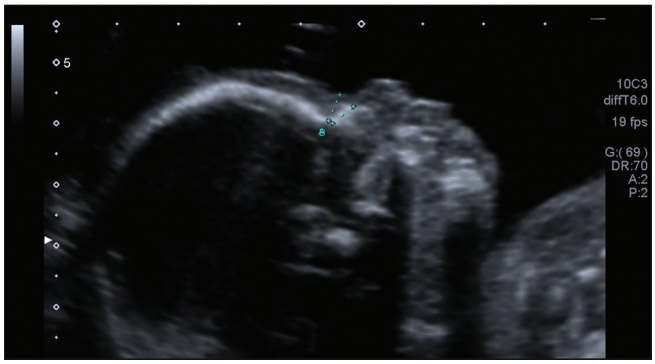

Figure 1: Ultrasound: Fetal facial profile showing nasal bone hypoplasia

Interpretation

The US findings included severe shortening of the long bones and abnormalities in the sagittal section of the fetus spine. Before establishing a diagnosis, it is important to consider other pathologies that present with shortening of the long bones such as aneuploidies (primarily Down syndrome), fetal growth restriction, and skeletal dysplasias.[1] However, in this case, the presence of thoracic hemivertebra and thoracolumbar scoliosis combined with shortening of the long bones was highly suggestive of severe skeletal dysplasia.

After the US the patient was referred to our prenatal diagnosis department for prenatal counseling and further investigation.

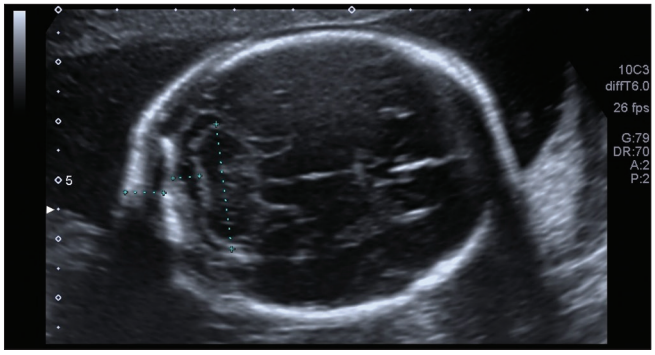

Figure 2: Ultrasound: Cross-section view of the neck showing nuchal edema

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Received: 10-03-2020 **Revised:** 15-04-2020 **Accepted:** 05-05-2020 **Available Online:** 15-08-2020

Access this article online

Quick Response Code:

Website: www.jmuonline.org

DOI: 10.4103/JMU.JMU_36_20

How to cite this article: Miranda C, Coelho D, Pereira E, Rosmaninho A, Furtado JM. Spine abnormality in a fetus at 21 weeks of gestation. J Med Ultrasound 2021;29:144-6.

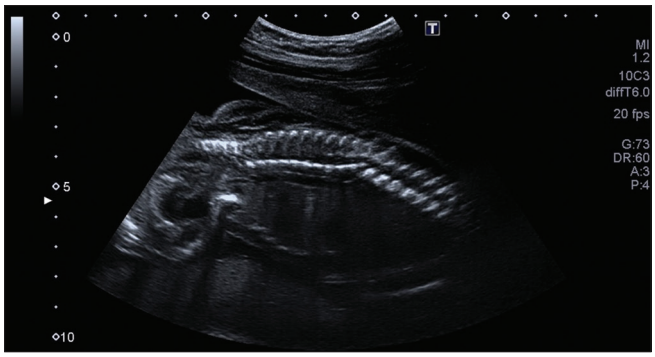

Figure 3: Ultrasound: Sagittal section of the spine showing deviation with an apparent hemivertebra

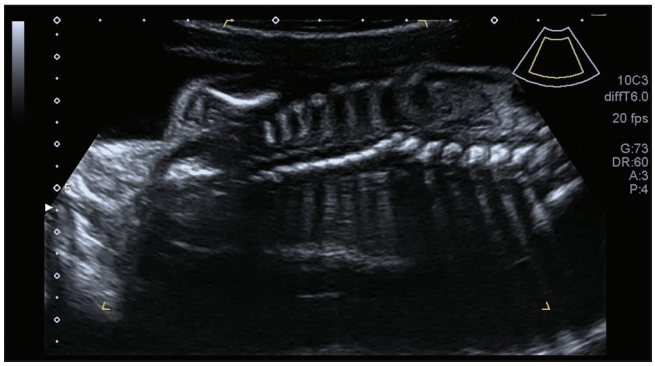

Figure 4: Ultrasound: Sagittal section of the spine showing deviation with an apparent hemivertebra

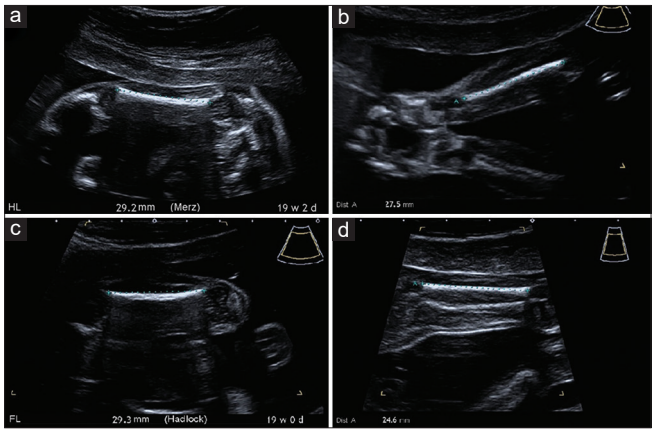

Figure 5: Ultrasound: Shortening of the long bones (below 5th centile). No apparent abnormalities (a-humerus; b-ulna; c-femur; d-tibia)

She underwent amniocentesis and molecular study for skeletal dysplasias. The patient remained under surveillance in the prenatal diagnosis department while awaiting results. Cytogenetic analysis revealed a karyotype 46, XY and skeletal dysplasias obtained at 28 weeks of gestation detected a c. 1138A > G (p. K2006R) mutation in the COL1A2 gene and a c.6017A > G (p.K2006R) mutation in the FLNB gene. At that time, the US showed a fetus with short, long bones, apparent hemivertebra in the last two thoracic vertebrae, and severe thoracolumbar vertebral scoliosis; no fractures were identified. After discussing the clinical case and its prognosis in a multidisciplinary appointment with geneticists and pediatrics, the couple's request for termination of pregnancy was accepted. The embryofetopathological study revealed a fetus with osteopenia, long bone deformities with signs of fracture, bluish eye sclerae, and ossification defects in the skull. These alterations were compatible with the clinical diagnosis of osteogenesis imperfecta (OI). The couple's subsequent genetic study revealed a heterozygous carrier with a mutation in the COL1A2 gene and a heterozygous carrier with a mutation in the FLNB gene.

Skeletal dysplasias are a large, heterogeneous group of conditions involving bone growth and formation. Several different skeletal dysplasias have been identified, but only a few are lethal in the prenatal period. The overall prevalence of skeletal dysplasias during pregnancy is 7.5/10,000 US-screened pregnancies. They are primarily caused by genetic variants but may be related to extrinsic causes, including drugs and maternal diseases such as poorly controlled diabetes mellitus and autoimmune diseases.[1] Skeletal dysplasias begin to manifest in the early stages of fetal development and diagnostic accuracy is critical, as it will significantly affect parental counseling regarding pregnancy prognosis and follow-up. The three most common lethal skeletal dysplasias are thanatophoric dysplasia, OI Type 2, and achondrogenesis.[1,2]

OI is one of the most common skeletal dysplasia with an estimated incidence of approximately 1 per 20,000 births. It comprises a group of rare hereditary connective tissue disorders associated with anomalous bone density.[3] The clinical spectrum is wide, and there are at least nine recognized forms of OI, designated Type I to Type IX, with overlapping characteristic features.[3,4] Clinical manifestations of OI include osteopenia, excess or atypical fractures, short stature, scoliosis, blue sclerae, and hearing loss.[3,5] Type I is the mildest form and Type II is the most severe. Most cases of OI are caused by dominant, autosomal mutations genes encoding the alpha 1 and alpha 2 chains of Type I collagen (COL1A1 and COL1A2).[5-7]

Prenatal diagnosis of skeletal dysplasia is based primarily on fetal US findings, especially in the second trimester. The suspicion of theses diagnoses should be raised in the presence of shortening of the long bones or qualitative bone abnormality.[1,2] Invasive procedures to obtain fetal cells for a specific molecular analysis can confirm the diagnosis in some cases. Once the diagnosis is performed, the couple should be counseled and given options by a multidisciplinary team.[1,4,7]

Declaration of patient consent

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

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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