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Prenatal Ultrasonographic Detection of Thanatophoric Dysplasia: A Case Report

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Abstract: *Thanatophoric dysplasia is a rare osteochondrodysplasia classified in two types I and II, due to a mutation of the FGFR3 (fibroblast growth factor receptor 3) gene located on the short arm of chromosome 4. It is a rare lethal malformation for which early prenatal detection by obstetrical ultrasound allows to propose a therapeutic termination of the pregnancy to the pregnant woman in order to avoid any psychological and obstetrical trauma. We report the case of a 31-year-old woman, nulliparous, without any particular history in whom the ultrasound performed at the 31st week of amenorrhea allowed us to make the diagnosis of thanatophoric dysplasia type I in front of very evocative images of fetal dysmorphism. Because of the rarity of this condition we report this case of tanatophoric dysplasia with a brief review of the literature.*

Keywords: Thanatophoric dysplasia, Osteochondrodysplasia ,Antenatal diagnosis, obstetric ultrasound

Introduction:

Thanatophoric dysplasia (TD) or thanatophoric nanism is a rare and lethal neonatal osteochondrodysplasia [1]. Its incidence is estimated at 1.68-8.3 per 100,000 births [1]. It is due to a mutation in the Fibroblast growth factor receptor 3 (FGFR3) gene, located on the short arm of chromosome 4 [2]. TD is classified into two types (TD1 and TD2).

Clinically, it is manifested by a cloverleaf appearance of the skull in type II, a narrowing of the thoracic cage with consequent fetal lung hypoplasia, shortening of the limb bones with a curved aspect of the femurs in DT1 while they are straight in DT2. Settlement of the vertebral body with widening of the intervertebral spaces. Ultrasound, sometimes associated with radiography of the uterine contents, allows the antenatal diagnosis of DT.

We report a case of thanatophoric dysplasia diagnosed at 29 weeks of amenorrhea in a nulliparous patient by obstetrical ultrasound performed in our department and followed until birth.

Observation:

Mrs K.M 31 years old, without any notable pathological history or notion of consanguinity or known congenital malformation in the family. She consulted in our department for a decrease in active fetal movements at the 29 weeks of amenorrhea. The patient was not followed until then. The obstetrical ultrasound showed a monofetal pregnancy, a male fetus, the amniotic fluid was in normal quantity, we noted the presence of a macrocrania, a narrow thorax with a shortening of the femurs that are curved. The diagnosis of Thanatophoric dysplasia type 1 was then evoked. The patient and her partner were informed. The patient gave birth by vaginal delivery at 38 weeks gestation. The newborn was dwarfed, his height was 33 cm, his birth weight was 2900 g. The apgar at birth was 5/10, then 7/10 at the fifth minute. Died 30 minutes after birth in acute respiratory distress.

Discussion:

Thanatophoric dysplasia is a congenital skeletal dysplasia that was first described in 1967 by Maroteaux et al [3]. It is caused by activation of the FGFR3 gene located on the short arm of chromosome 4 leading to down-regulation of bone growth [2, 3]. Its inheritance is autosomal dominant , but almost all cases of TD occur in individuals with no family history of TD [4]. In our case, there was no family history of TD.

There are two types that are very similar in their clinical features but have distinct radiological characteristics and genetic mutations [3]. Type I accounts for 80% of cases and type II for 20% of cases. The two types can be differentiated by the morphology of the skull and femur [7, 8]. Type I, the most frequent, is characterized by a macrocrania, a short and curved femur . Fetuses with type II DT have a cloverleaf skull. Premature closure of the coronal and lambdoid sutures is often the cause of this skull deformity.

TD is the most common form of lethal osteochondrodysplasia [1]. Death occurs rapidly after birth, usually due to breathing disorders. However, cases reaching older ages or even adulthood exist, but remain marginal. The antenatal diagnosis of TD is based on the following ultrasonographic findings: a relatively narrow chest cavity, short, thick and curved tubular bones, especially those of the lower limbs, thickening of the soft parts of the extremities, a relatively large head with a frontal hump. A cloverleaf skull appearance can also be seen in type II.

Prenatal diagnosis can be confirmed by molecular analysis of the FGFR3 gene mutation extracted from fetal cells obtained by amniocentesis usually performed at 15-18 weeks of amenorrhea or by chorionic villus sampling at around 10-12 weeks of

amenorrhea [5].The risk of recurrence is not increased compared to that of the general population because it is a de novo mutation [3].

The main differential diagnosis of TD is achondroplasia. In achondroplasia, the shortening is greater than 80% of the average gestational age, whereas in TD it is 30-60%. The other two differential diagnoses are: osteogenesis imperfecta and achondrogenesis [9] . However, the presence of a characteristic "cloverleaf" head, the curved aspect of the femur, the narrowness of the thoracic cavity, responsible for a very high mortality, differentiates TD from other causes of micromelic nanism.

Postnatal autopsy of the affected fetus shows disorganized chondrocyte columns, low cell proliferation, lateral proliferation of the metaphyses and increased vascularization of the cartilage [6]. The autopsy to confirm the diagnosis histologically could not be performed in our case because consent was not given by the parents.

Conclusion:

Thanatophoric dysplasia is a lethal neonatal pathology. Its early prenatal diagnosis by ultrasound is imperative in order to propose a medical termination of pregnancy.The presence of a macrocrania, a curved femur, the narrowness of the thorax are the basic elements of the diagnosis and allow to differentiate it from other causes of micromelic nanism . The diagnosis of certainty is assured by molecular biology.

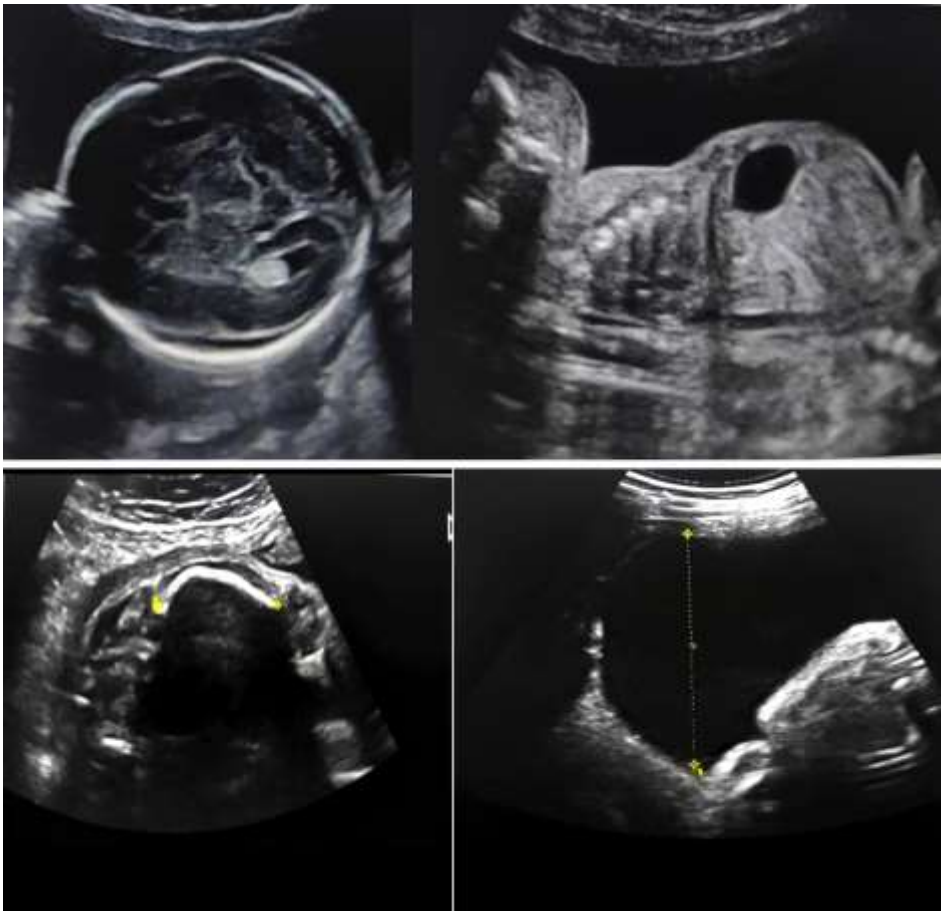

Figure 1: Ultrasound performed at 29 weeks of amenorrhea showing macrocephaly, shortening of the limbs, curved femur, prominence of the abdomen contrasting with a narrow thorax with presence of hydramnios

Figure 2: Delivery by vaginal route at 38 weeks of amenorrhea.
Photos of a dwarf newborn with the same characteristics as those described on the ultrasound. Died 30 min after birth

Figures:

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Figure 2: Delivery by vaginal route at 38 weeks of amenorrhea.
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