Thanatophoric dysplasia. A two case report.

Călin Moș

University of Oradea, Faculty of Medicine and Pharmacy, România

Abstract

Thanatophoric dysplasia (TD) is one of the most common lethal neonatal skeletal dysplasias that occurs in 1 of 15,000-40,000 births. This cases reports present the prenatal sonographic diagnoses of one case of TD type I (TD1) and one case of TD type II (TD2). Both fetuses were characterized by macrocephaly, short limbs, a narrow thoracic cage and micromelia. At 32 weeks’ of gestation, the TD1 had a “telephone receiver” femurs, but without a cloverleaf skull. At 18 weeks of gestation the TD2 fetus was characterized by a more straight short femur and a cloverleaf skull. Three-dimensional ultrasound was able to enhance the visualization of craniofacial and limb deformities associated with TD.

Key words: thanatophoric dysplasia, lethal bone dysplasia, ultrasound, prenatal diagnosis

Rezumat

Displazia tanatoforică (TD) este una dintre cele mai comune displazii scheletice neonatale, cu incidența de 1 caz la 15.000-40.000 de nașteri. În acestă prezentare prezentăm un caz de displazie tanatoforică tip I (TD1) și un caz de displazie tanatoforică tip II (TD2). Ambii fetoși au avut un aspect ecografic caracterizat de macrocefalie, micromelia și torace hipoplazic. La 32 de săptămâni, morfologia fătului cu TD1 a fost caracterizată de un femur în formă de receptor de telefon, dar fără o deformare a craniului în formă de trifoi. La 18 săptămâni de amenoree fătul cu TD2 a avut un femur mai drept și un craniu deformat în trifoi. Utilizarea ecografiei tridimensionale crește posibilitățile de vizualizare a malformațiilor craniofaciale și ale membrelor asociate cu TD.

Cuvinte cheie: displazia tanatoforică, displazie osoasă letală, ecografie, diagnostic prenatal

Case 1. Thanatophoric dysplasia type I

A 30 years old pregnant woman had presented for a routine ultrasound scan at 32 weeks of gestation. Five years ago the first pregnancy was normal. There was no family history of genetic disorders or any other relevant obstetrical past history. The previous nine week scan was normal.

At 32 weeks a new ultrasound examination demonstrated an abnormal fetal biometry and morphology. The following sonographic features were found: macrocranium (fig 1) with frontal bossing, midface hypoplasia with flattened nasal bridge, severe micromelia, with short and curved femurs (“telephone receiver” femurs) (fig 2, fig 3), normal trunk length but...
hypoplastic and narrow thorax with short ribs, protuberant abdomen (fig 4), hypertelorism, platyspondyly (flat vertebral bodies) (fig 5, fig 6), thick, redundant skin folds, short-fingered hands (fig 7), polyhydramnios (fig 8). All these findings suggested with confidence the diagnosis of thanatophoric dysplasia.
The macrocranium with no cloverleaf-shaped skull, and the "telephone receiver" femurs makes the differential diagnosis between type I and type II, this case being a type I thanatophoric dysplasia.

The placenta was thick with some hypoechoic and irregular structures with an hyperechoic rim. These lesions represent ischemic-thrombotic destructions of the placenta (intervillous thrombosis) (fig 8)

Fig 8. Hypoechoic lesions with echogenic and irregular crenated borders sugestive for intervillous trombosis

Doppler sonography was also normal on the uterine, umbilicals and cerebrals vessels. Ductus venosus flow was also normal with a positive a wave (fig 9). The anatomy of the heart was normal, but on Doppler examination an abnormal ventricular filling was identified (E/A ~1 at mitral valve and E/A >1 at tricuspid valve) (fig 10)

Fig 10. Abnormal right ventricular filling E/A>1(inversion between early and late diastolic peaks of mitral inflow)

After caesarian delivery the diagnosis of thanatophoric dysplasia tip I was confirmed by radiologic and anatomopathologic reports (fig 11, fig 12).

Fig 11. The anteroposterior radiogram shows macrocranium, micromelia, narrow thorax, protuberant abdomen, normal mineralization of the bones, severe platyspondyly
Case 2. Thanatophoric dysplasia type II (TD 2)

A 26 years old pregnant woman, 18 week and 1 day of gestation, presented for fetal morphology ultrasound examination. First pregnancy, 3 years before, was normal. She had no spontaneous abortion, with the exception of one abortion on demand. No family history of congenital abnormalities was present.

Ultrasound examination revealed a large fetal head with abnormalities of the skull (cloverleaf-shaped skull) (fig 13, fig 14), micromelia (the upper limb bones are tubular, thickened, very short and straight, the femur was small in length but almost straight) (fig 15-20), platyspondilia, normal length thorax but obviously narrowed in relation to the pelvis (fig 19), and hypoplasia of the middle face (fig 21).

Cloverleaf-shaped skull and straight line femur confirmed the diagnostic of TD 1.

Also, a relatively small heart with cardiac axis deviated to the left but with no evidence of cardiac abnormalities was found (fig 22). Doppler ultrasonography was normal for umbilical arteries, venous ductus, fetal aorta, atrioventricular valves and middle cerebral artery (fig 23, fig 24).
Fig 16. Humerus very short (corresponds to 14 weeks 5 days)

Fig 17. Very short tibia bones (correspond to 14 weeks 4 days)

Fig 18. Narrow thorax and large abdomen

Fig 19. 3D maximum mode rendering. Normal length trunk, but hypoplastic thorax and ribs, platyspondyly, vertebral bodies very well seen with good mineralization, limbs bones very short but the femur straighter than in TD1

Fig 20. Severe micromelia of the upper limbs bones . The bones are tubular, thickened, short and straight

Fig 21. 3D surface rendering of the foetal head demonstrating macrocrania, frontal bossing and midface hypoplasia with flattened nasal bridge
Discusstions

The name thanatophoric dysplasia derived from the Greek *thanatophoros*, meaning *death bearing*. It occurs in 0.24 to 0.69 out of 10,000 births [1,2,3].

It is a lethal skeletal disorder characterized by a large head with prominent forehead bowed (frontal bossing), middle face hypoplasia with depressed nasal bridge, very short long bones (micromelia), flat vertebral bodies (platyspondyly), narrow chest with short ribs and a normal length trunk [4,5].

This dysplasia has two types, differentiated by the skull shape and the femur morphology.

Type I (80%) is characterized particularly by the femur shape which is in a telephone receiver like configuration and no cloverleaf shaped skull [6].

Type II (20%) differs from type I especially by the cloverleaf-shaped skull, the femur that is straighter than those found in type I and the vertebral bodies that are a little taller than in type I [7,8].

At the fetuses with skeletal dysplasia, three dimensional ultrasound has an important role in the descriptions of the external fetal morphology, the structure of the fetal bones and the cranial sutures [9,10,11].

Polyhydramnios in the late second and third trimesters is common on both types. Occasional findings on both types are thickening of nuchal translucency in the first trimester, ventriculomegaly, agenesis of the corpus callosum, cardiac defects and hydronephrosis [12-20].

Thanatophoric dysplasia is always lethal, due to the severe pulmonary and thoracic hypoplasia. Both types are due to de novo mutations and the recurrence risk is very low [21].

The differential diagnosis was made with others skeletal dysplasia with micromelia like acondrogenesis (bones demineralization that are most marked in the calvarium and vertebral bodies, shortened trunk length), homozygous acondroplasia (both parents are affected by the heterozygous acondroplasia), osteogenesis imperfecta type II (generalized hypomineralisation of the bones, especially the calvarium which is compressible, multiple bones fractures), congenital hypophosphatasia (has practically similar to osteogenesis imperfecta), and diastrophic dysplasia (fixed abducted thumb, clubfoot).

References


