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**CASE REPORT****Thanatophoric Dysplasia**

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**Abstract**

**Objective:** Report a case of thanatophoric dysplasia

**Method:** Case report

**Result:** Case of a 25-year-old woman, with a diagnosis of gravid preterm G4P2A1H2 31-32 weeks + polyhydramnios + fetal hydrops, a single intrauterine live fetus with thanatophoric dysplasia. On ultrasound examination found fetal biometry; BPD: 7.78 cm, FL: 3.58 cm, HL: 3.11 cm, AC: 30.90 cm, HC: 28.48 cm AFI: 33.27 cm, a frontal bossing (+) picture appears, claver leaf skull (+) and micromelia (proximal, distal, phalanges). The ultrasound examination suggested Severe skeletal dysplasia (thanatophoric dysplasia), polyhydramnios, + single intrauterine live fetus + SC 1x scars. Then an amniocentesis is performed and results are obtained. Chromosome analysis is carried out using the G-banding technique. Chromosomes have been studied from 20 cells from 3 different cell culture preparations and obtained the number of chromosomes in each cell studied is 46, XY which means the number of chromosomes 46 pieces with fetal sex chromosome XY. Mosaic chromosome abnormalities generally occur due to non-disjunction in the mitotic phase after conception. At 33-34 weeks gestation, an infant was born by SC with birth weight: 1900 g, baby's length: 31 cm, A / S 2/3.

**Conclusion :** Thanatophoric dysplasia is a "lethal" skeletal dysplasia. A careful prenatal examination is needed in the diagnosis and termination of pregnancy.

**Keywords:** Thanatophoric dysplasia, prenatal diagnosis

**INTRODUCTION**

Thanatophoric dysplasia (TD) is the most common form of "lethal" skeletal dysplasia in the neonatal period. The term thanatophoric, comes from the Greek terminology "thanatophorus", which means "innate death" or "bearing death".<sup>1</sup>

Thanatophoric dysplasia is a form of severe skeletal disorder characterized by very short limbs and excessive skin on the arms and legs. Prominent phenotypic features of this condition include short ribs, chest constriction, enlargement of the head, underdeveloped lungs, and protruding and wide-spaced eyes.<sup>1</sup>

FGFR3 is part of the tyrosine kinase receptor group. Usually, FGFR3 is a negative regulator of bone growth. Mutations in thanatophoric dysplasia that encode FGFR3 cause an increase in function, sending negative signals to cartilage cells. This occurs when ligand bonds in chondrocytes induce homodimerization and heterodimerization receptors. This in turn

activates the function of tyrosine kinase, which then potentiates a number of effects on cell growth and differentiation

## CASE REPORT

A female patient reported 25 th diagnosis with fetal abnormalities. From the history it was found that there were complaints of low back pain radiating into the placenta. There were no signs of labor in this patient. First day of last menstrual period (LMP) obtained on 1<sup>st</sup> July 2018 with EDD 8<sup>th</sup> April 2019. The patient had ANC at the midwife 2 times (at 3 and 4 months of gestation), and only controls the obstetrician once at 7.5 months gestation.

The patient is in her fourth pregnancy with a history of caesarean section in the first pregnancy, spontaneous labor in the second pregnancy, and curettage in the third pregnancy.

From the physical examination, the general condition of the patient is moderate; composmentis cooperative awareness; BP 120/80 mmHg; Pulse 82 x / min; RR 24 x / min. From the obstetric examination, the abdomen appears to be distended exceeds the gestational age, the fundus has a distance of four fingers below the xypoid process with head presentation. The height of the fundus is 29 cm. "His" was negative and FHR 160-166 x / min. From the genital examination, no vaginal bleeding was found.

Laboratory results show within normal limits. Hb = 11.1 gr / dl; Leukocytes = 12,500 / mm<sup>3</sup>; Ht 35%; Platelets 220,000 / mm<sup>3</sup>. USG examination obtained BPD = 9.97 cm; AC = 29.68 cm; HC = 32.81 cm; FL = 1.48 cm; AFI; 36.75 cm; SDAU = 3.01 cm. Frontal bossing, clover leaf skull and micromelia were found (in proximal, distal, phalanges).





Patients diagnosed with gravid preterm G4P2A1H2 31-32 weeks + Suspected Thanatophorik Dysplasia + Polyhydramnios + SC 2x. The patient is planned for 2 weeks more control and amniosynthesis.

## DISCUSSION

A case of Thanatophoric dysplasia (TD) has been reported. The diagnosis is made by careful antenatal ultrasound examination. Based on the ultrasound examination obtained BPD = 9.97 cm; AC = 29.68 cm; HC = 32.81 cm; FL = 1.48 cm; AFI; 36.75 cm; SDAU = 3.01 cm. Frontal bossing, clover leaf skull and micromelia were found (in proximal, distal, phalanges).

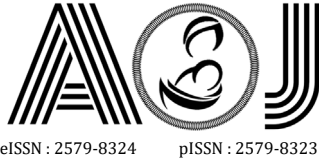
Thanatophoric dysplasia (TD) is the most common form of "lethal" skeletal dysplasia in the neonatal period. The term thanatophoric, comes from the Greek terminology "thanatophorus", which means "innate death" or "bearing death".<sup>1</sup>

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arms and legs. Prominent phenotypic features of this condition include short ribs, chest constriction, enlargement of the head, underdeveloped lungs, and protruding and wide-spaced eyes.<sup>1</sup>

Postnatal radiography and additional imaging studies can reveal irregular metaphysis of long bones and shortening of rhisomelic bones. These studies can also reveal platyspondyly, wide intervetebral distances, enlargement of the skull and small foramen magnum, brain stem compression, hydrocephalus, temporal lobe malformations, brainstem hypoplasia, or abnormal neuronal migration. Histological evaluation of long bone structure can show a disorder of endochondral ossification.

Mosaic chromosome abnormalities generally occur due to non-disjunction in the mitotic phase after conception. Abnormalities caused by gene and / or DNA abnormalities cannot be diagnosed with this technique. In this case, DNA analysis should be examined from fetal cells obtained from amniocentesis, usually done at 15-18 weeks of pregnancy, or chorionic villus sampling around 10-12 weeks of gestational age. Gene mutations that encode FGFR3 on the



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short arm of chromosome 4 (4p16.3) are the cause of TD I and TD II. For TD I, a series of mutations have been identified; R248C \*, Y373C \*, S249C, G370C, S371C. The most common mutation (\*) of 60-80% of TD I. For TD II a one-point mutation in the FGFR3 (K650E) gene has been identified from all TDII analyzed.<sup>3,6,7,8</sup>

Most babies with TD will die within the first few hours or days of life due to secondary respiratory insufficiency due to decreased thoracic capacity or brain stem compression. The focus of newborn management is limited to life support. In rare cases, namely to maintain long-term survival, management can include: respiratory support (tracheostomy, ventilation), drugs to control seizures, shunts in hydrocephalus, suboccipital decompression to eliminate craniocervical constriction, hearing aids when hearing loss is identified and orthopedic evaluation for the management of joint contractures.

Postnatal radiological examination can also be a basis for diagnosis of TD, and the examination can be found: Rhizomelic shortening of long bones, irregular metaphysis of long bones, platyspondyly, small foramen magnum with brain stem compression, CNS abnormalities including temporal lobe malformations including longitudinal lobe malformations, hydrocephalus, brain stem hypoplasia, neuronal migration abnormalities and bent femur bones - shaped like the old-fashioned telephone receivers (TDI).<sup>1,2,11</sup>

## CONCLUSION

Thanatophoric dysplasia (TD) is the most common form of "lethal" skeletal dysplasia in the neonatal period. A careful prenatal examination is needed in the diagnosis and termination of pregnancy. The reported case is a TD I case based on prenatal ultrasound findings and postnatal physical examination although in this case there was no examination of the FGFR3 gene analysis.

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