

## Thanatophoric Dysplasia: A Lethal Birth Defect, Case Report

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**Abstract :** Thanatophoric dysplasia, the most common of the congenital lethal skeletal dysplasias occurs sporadically. It is characterized by short limbs, small conical thorax, platyspondyly and macrocephaly. The affected fetus usually dies within the first 48 hours of life because of pulmonary hypoplasia. Medical Termination of Pregnancy was done in a primigravida diagnosed with Thanatophoric dysplasia at 20 weeks of gestation. The fetus was born with a narrow thorax, macrocephaly and short curved femurs characteristic of type 1 of the Thanatophoric dysplasia.

**Keywords:** dwarfism, dysplasia, lethal, skeletal, thanatophoric

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### I. Introduction

Thanatophoric dwarfism (TD) literally meaning death seeking dwarf is the most common form of lethal bone dysplasia with a prevalence of 1 in 10,000[1]. TD is characterized by severe shortening of the limbs, a narrow thorax, macrocephaly, and a normal trunk length. There are two types- type 1 and 2, both autosomal dominant. Type 1 is associated with curved femurs in the fetus while 'clover leaf' skull is typical of type 2. In this report we describe one case of thanatophoric dwarfism type 1. The rarity of this disorder and its low prevalence prompted us to report this case.

### II. Case Report

A 20 year old primigravida, healthy, non-consanguineously married woman was brought to the hospital at 20 weeks of gestation for antenatal evaluation. The pregnancy was reported uneventful. There was no family history of genetic disorders or any other relevant past history. Three dimensional ultrasound examination showed a single live fetus, and amniotic fluid was adequate. Biparietal diameter of the fetus was corresponding to 20 weeks and 2 days of gestation with short bowed tubular bones of both upper and lower extremities. Both the femurs showed telephone handle appearance. The thoracic cavity was small and narrow. With these findings, diagnosis of thanatophoric dwarf was made. Medical termination of pregnancy was performed at 20 weeks of gestation.

On examination, the fetus (male) was weighing 400 grams. There was macrocephaly, frontal bossing, depressed nasal bridge, chest was funnel shaped and face appeared small. Both the upper and lower limbs were grossly shortened and brachydactyly was present. Femurs were curved (telephone receiver femurs). Abdomen was protruded. The placenta was found to be normal.

The macrocranium with no clover-leaf shaped skull, and the "telephone receiver" femurs makes the differential diagnosis between type 1 and 2, this case being a type 1 thanatophoric dysplasia. However, religious and cultural beliefs were a hindrance to further autopsy and radiological examination.

### III. Discussion

The name thanatophoric dysplasia is derived from the Greek thanatophoros, meaning death bearing. It was first described by Maroteaux et al in 1967[2]. Thanatophoric dwarfism presents with extreme shortness of limbs, bowing of long bones of the extremities, short thorax, protruded abdomen and excessive subcutaneous fat and skin creases. The skull is disproportionately large compared to facial dimensions with frontal bossing, enlarged fontanelle, depressed nasal bridge and prominent eyes. Hydramnios is frequent. Characteristic radiologic findings include excessive shortening of the long bones, disproportionate thorax with short ribs and malformed pelvis, with flat spiculated acetabulum[3].

Polyhydroamnios in the late second and third trimesters is common in both types. Occasional findings in both types are thickening of nuchal translucency in the first trimester, ventriculomegaly, agenesis of the corpus callosum, cardiac defects and hydronephrosis[4].

TD is caused by specific autosomal dominant mutations in the gene that codifies for the Fibroblast Growth Factor Receptor (FGR3). The mutations constitutively activate the tyrosine kinase activity of the receptor. As normally FGR3 is a negative regulator of bone growth, the gain-of-function mutations allow the

activated receptor to send negative signals within the cells of the cartilage (chondrocytes), thus leading to the generalized disorganization of endochondral ossification at the bone growth plate[5].

It is possible to recognize short limbs in fetuses beginning as early as 13 weeks of gestation, when femur length can be routinely measured on ultrasound. Thus sensitivity of ultrasound in this regard is high as shown by Weldner et al[3]. Recently, cephalometric analysis by ultrasound is used for prenatal diagnosis of TD. All long bones should be examined to determine distal versus proximal limb shortening. The two conditions which present a difficulty in diagnosis are osteogenesis imperfecta and achondroplasia. Osteogenesis imperfecta is suggested by fractured limbs or ribs, while achondroplasia is characterized by fewer than three ossification centres per spinal segment, long bones are not curved and a family history of dwarfism makes differentiation possible.

Prenatal diagnosis of TD is performed by analysis of DNA (FGFR3 sequences) extracted from fetal cells obtained by amniocentesis usually performed at 15-18 weeks gestation or chorionic villus sampling at about 10-12 weeks gestation.

Early neonatal death in TD is due to reduced thoracic dimensions causing pulmonary hypoplasia. Malformations and potentially significant neuroaxial injury, principally at the level of the atlas vertebrae may also contribute to the death. Though, some reports of patients with TD surviving the neonatal period have been documented recently.

Management concerns are limited to extreme life support measures for the newborn. In the rare cases of long-term survival, the management consists of treatment of manifestations: respiratory support (tracheostomy, ventilation), medication to control seizures, shunt placement when hydrocephaly is identified, suboccipital decompression for relief of craniocervical junction constriction, hearing aids when hearing loss is identified and orthopaedic evaluation upon the development of joint contractures or joint hypermobility.

Surgical intervention by decompressions of brain stem in small foramen magnum has allowed prolonged survival in some of these cases.

Recurrence risk of TD is not significantly increased over that of the general population. Germ line mosaicism in healthy parents, although not previously reported, remains a theoretical possibility.



**4. FIGURE: FETUS WITH THANATOPHORIC DWARFISM TYPE 1**

#### **IV. Conclusion**

Three dimensional ultrasound proves to be the gold standard for diagnosing and differentiating among the different skeletal dysplasias, as early as 13 weeks of gestation. Cephalometric analysis on ultrasound helps in detecting the craniofacial and limb deformities. Where the affected parent consents, termination of pregnancy can be offered, when a case of Thanatophoric Dysplasia is diagnosed. Post-natal radiological examination and detailed autopsy is essential to precisely identify the type of skeletal dysplasia, which is paramount for proper genetic counselling.

### **References**

- [1]. Chandrasekharan N, Bhide A. Fetal Dysmorphology. in: Bhide A, Arulkumaran S, Damanio KK, Daftary SN(Eds.), Practical Guide to HIGH-RISK PREGNANCY & DELIVERY, A South Asian Perspective. 4 (India, Reed Elsevier India Private Limited, 2015) p22.
- [2]. Abdulkadir AY, Isyahr K, Dare A, Abdullahi SG, Idies SK, Tabari AM, Prenatal Third trimester Sonographic Behaviour of a Thanatophoric Dwarfs., Journal of Prenatal Medicine 2008, 2(4), 42-46.
- [3]. Kulkarni ML, Sureshkumar C, Venkataramana V, Koshy S, Bhagyavathi M, Reddy GS, Journal of Indian Paediatrics 1994, 31, 1405-1410.
- [4]. Liboi E, Lievens PM-J, Thanatophoric dysplasia, Orphanet encyclopedia, September 2004.
- [5]. Mos C, Medical Ultrasonography 2009,11(2), 37-43.