Thanatophoric Dysplasia in Newborn Twins: Case Report and Literature Review

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Abstract

Thanatophoric dysplasia (TD) is an osteochondrodysplasia always lethal in the neonatal period. The vast majority of cases are due to de novo mutations. It is divided into two types: a short curved femur characterizes type 1, while a straighter femur with clover leaf skull characterizes type 2. In thanatophoric dysplasia the limbs are very short. The rib cage is small. The vertebral bodies of the spine are greatly reduced in height with wide spaces between them. Autosomal dominant mutations in the fibroblast growth factor receptor 3 gene (FGFR3), which has been mapped to chromosome band 4p16.3, results in both subtypes. This condition has characteristic sonographic features that suggest the diagnosis prenatally. Thanatophoric fetuses usually die within the first 48 hours of life from pulmonary hypoplasia caused by a narrow thorax, leading to respiratory insufficiency. We reported twin dizygote cases of type 1 TD with similar findings adjusting with TD for the first time, along with a short review of the available literature.

Key words
Thanatophoric dysplasia, Newborn, Twins

Introduction

Thanatophoric Dysplasia (TD) is a congenital, sporadic, usually lethal skeletal dysplasia characterized by shortening of the limbs, small conical thorax, platyspondyly and macrocephaly .[1,2] Its incidence is 1 in 64,000 to 1 in 100,000 of live births. It was first described by Maroteaux et al in 1967.[3] The name of this dysplasia is derived from a Greek word 'Thanatophores' which means constantly bearing death.[4] Thanatophoric dysplasia is due to a lethal mutation (change) in the same gene that produces achondroplasia, a familiar and far more common form of short-limbed dwarfism that is compatible with life. The vast majority of cases are due to de novo mutations. To date, over 100 cases have been described. Thanatophoric fetuses usually die within the first 48 hours of life from pulmonary hypoplasia caused by a narrow thorax. Thanatophoric dysplasia (TD) is divided into two types: a short curved femur characterizes type 1, while a straighter femur with clover leaf skull characterizes type 2.[1]

In thanatophoric dysplasia the bones of the arms and legs are very short. The ribs are also extremely short. The vertebral bodies of the spine are greatly reduced in height with wide spaces between them. The rib cage is small, leading to respiratory insufficiency and often to death.[5]

This condition has characteristic sonographic features that suggest the diagnosis prenatally, although distinction from other short-limbed dysplasia syndromes may be difficult.[6] We report two cases of type 1 TD with typical imaging findings, along with a short review of the available literature.

Case report

Twin male neonates (gestational age approximately 37 weeks) were delivered by Caesarean section due to breech position and fetal bradycardia. Dichorionic and diamniotic twins were born with low Apgar scores (6-7) and amniotic fluid was meconial in both of them. The mother was from a rural area and did not have any antenatal ultrasonographic evaluation. She had three healthy female babies and this gestation occurred after clomiphene citrate consumption. Their weights were 2490 and 2260 grams, respectively. Twin two was hydropic and the findings were similar to the first one but succumbed due to severe respiratory distress and bradycardia within few hours. The second one was also ill and cyanotic. Respiratory distress was handled by mechanical ventilation. Height and head circumference was measured 35

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and 35.5 cm, respectively. The facies were coarse and edematous. Large head with wide anterior fontanel, small face, Short neck, narrow thorax, severe shortening of limbs with brachydactyly were the findings suggestive of Thanatophoric dysplasia and pulmonary hypoplasia was labeled as the most probable cause of the newborn's death on the second day (Figure 1).

The plain skiagram of the baby revealed a large sized skull with short base, and flat vertebral bodies. The thorax was narrow with horizontally placed ribs. The iliac bone was small. Both the humorous and femora revealed the 'telephone receiver appearances'. Brachydactyly with absence of the carpal and tarsal bones were noted on the x-rays (Figure 2).

Discussion

Thanatophoric Dysplasia is a condition of unknown etiology with the majority of case reports being sporadic. Some authors have reported a dominant gene mutation to be associated with this condition. Maternal Rubella infection has been proposed to be a probable etiological factor.[7]

Molecular analysis of the fibroblast growth factor III receptor gene (FGFR 3) in both subtypes suggests that this is a genetically homogenous disorder. This usually leads to in-utero death of the fetus; the longest survival however has been reported to be of 9 years.[8] Males are affected more than females. The case reported here was in male twins delivered by Caesarean section and remained alive for 48 hours only. Short limb dwarfism is usually of two types: type 1 presenting with polyhydramnios, macrocephaly, short limbs, narrow thoracic cage and curved short femur (the typical telephone receiver appearance) but without a clover leaf skull. Type 2 is characterized by short limbs, narrow thoracic cage, straight short femora, hydrocephalus, and clover leaf skull .[1,5] However the other reported varieties are Torrance, San-Diego, and Luton types. The present case belongs to type 1 with the 'telephone receiver appearances' of both the humerii and femora. The thorax was narrow with horizontally placed ribs along with brachydactyly. Dizygote twins with similar findings adjusting with TD are reported for the first time in this article.

Bowing of tubular bones may be explained by diminished mechanical stability. The perichondral spurs and linguiform endochondral growth plates result in 'Maple leaf like' contour of metaphyses of tubular bones and acetabular roof .[9]

Death usually occurs either as a result of conical thorax and pulmonary hypoplasia (as seen in the present cases) or due to cervical cord compression at a narrowed foramen magnum associated with posterior arch anomaly.[10]

Antenatal sonography in second trimester not only confirms the diagnosis but also differentiates it from the other non-lethal dysplasias. Three dimensional ultrasound is able to visualize the thickened redundant skin fold, limbs and craniofacial anomalies more clearly. Nevertheless X-ray examination must be performed after birth to confirm various findings which along with the autopsy diagnosis helps in counseling of the parents.[11]

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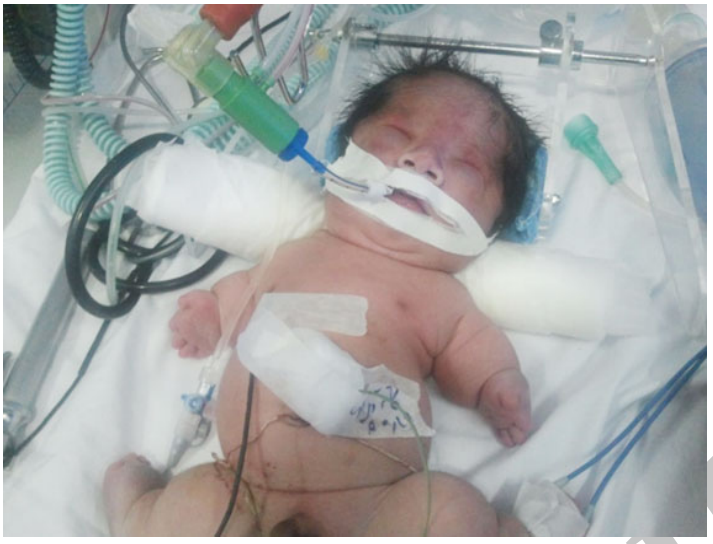
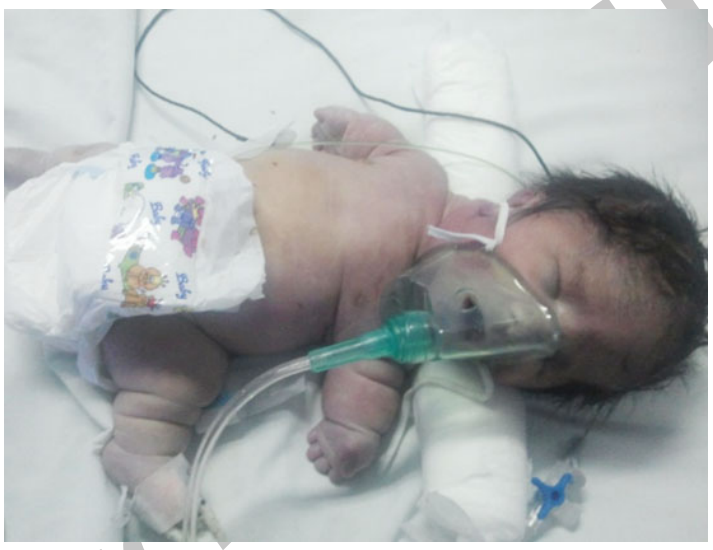
(Figure 1)





(Figure 2)