American Journal of Medical Case Reports, 2016, Vol. 4, No. 1, 35-37
Available online at http://pubs.sciepub.com/ajmcr/4/1/10

DOI:10.12691/ajmcr-4-1-10

A Rare Case of Thanatophoric Dysplasia

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Abstract This case is presented for its rarity in the presentation of this dreaded skeletal dysplasia and it is important to differentiate this skeletal dysplasia from others due to overlapping appearance of features with other dysplasia.

Keywords: *skeletal dysplasia, thanatophoric dysplasia*

Cite This Article: Durga. R, and T.K Renuka Devi, "A Rare Case of Thanatophoric Dysplasia." *American Journal of Medical Case Reports*, vol. 4, no. 1 (2016): 35-37. doi: 10.12691/ajmcr-4-1-10.

1. Introduction

Thanatophoric dysplasia is a rare form of skeletal dysplasia that is lethal in the neonatal period. The word "Thanatophorus" derives from a Greek word which means "death bearing" or "death bringing". This case is published for its rarity in presentation and also it's a unique autosomal dominant disorder which can occur even with normal parents..

2. Case Report

Unbooked 31 years old Mrs.R G4P2L2A1 reported to us at 26 weeks of gestation with LMP:30/12/2011, EDD:6/10/2012.Attended OP with H/O 7 months amenorrhea and over distension of abdomen compared to her previous pregnancies. She is RH negative and she was given anti D after her previous two deliveries and one abortion. She had regular periods and she had a non consanguineous marriage. This was her fourth pregnancy and her previous three pregnancies were uneventful with healthy children and Anti D was given after each pregnancy. Her past history and family history were uneventful.

On general examination her BMI was found to be 22.3.Her vitals were stable and systemic examination was clinically normal. On examination, uterus was 8 weeks bigger than the period of amenorrhea corresponds to 34 weeks gestation, tense, nontender, no contractions, hydramnios present with breech presentation and fetal heart sounds were heard. On per vaginal examination, Cervix was uneffaced, posteriorly placed,os closed and breech was felt. Hence clinically it was G4 breech with hydramnios.

In view of breech presentation with hydramnios antenatal ultrasound was done to rule out anomalies. The Antenatal ultrasonogram showed following features:

1. Grossly dilated lateral ventricles and third ventricles due to which biparietal and head circumference could not measured.

2. Brain tissue was pushed to the periphery by dilated ventricles and floating falxcerebri and tentorium cerebelli seen, known as "dangling choroid".

3. Abdominal circumference of 223mm corresponding to 26 weeks and 5 days.

4. Femur length of 30 mm corresponding to 19 weeks 2 days.35% shortening of limbs than the expected limb length for that gestational age. All long bones were shortened.

5. The other features were depressed nasal bridge, protuberant abdomen and polyhydramnios.

6. The fetal movements and the fetal heart sounds were present.

Thus, the ultrasonogram showed single live intrauterine gestation corresponding to 26-27 weeks with multiple congenital anomalies.

As per the criteria for antenatal ultrasound in the Medscape article dated february12, 2014,9/11 features for thanatophoric dysplasia were present in this fetus. Hence the diagnosis of thanatophoric dysplasia was made.

Based on the ultrasonic findings the parents were counseled about the multiple congenital anomalies and its incompatibility with life. After obtaining their consent, medical termination of pregnancy was performed by medical methods using oral and pervaginal misoprostol tablets. The parents were refusing for genetic testing despite counseling. The mother was found to be depressed after termination and was sent for psychiatric counseling and prescribed with certain antidepressants and now she is on regular follow up doing well.

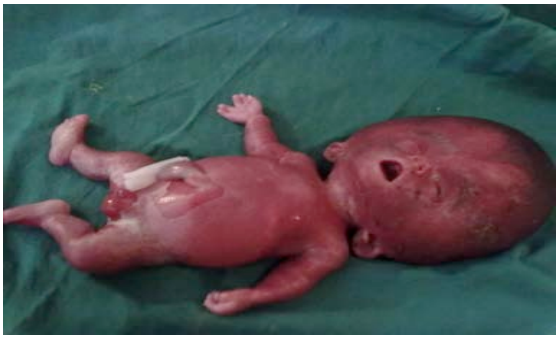

Figure 1. Fetus after termination

The terminated fetus showed following features:
a). cleft in the frontal bone.
b)Hydrocephalous.
c) Depressed nasal bridge and short proximal limbs
d) Low set ears.
d).Hydrocephalous.

2.1. Individual Anomalies were Photographed

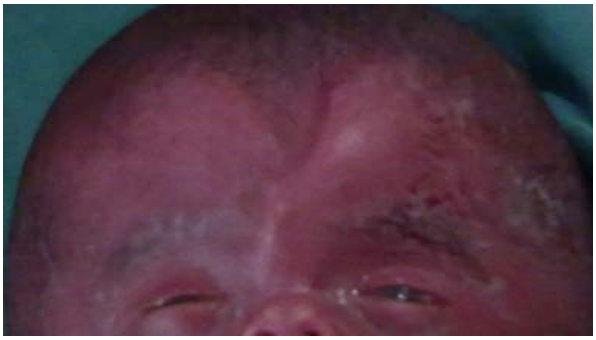

Figure 2(a). Clover leaf skull

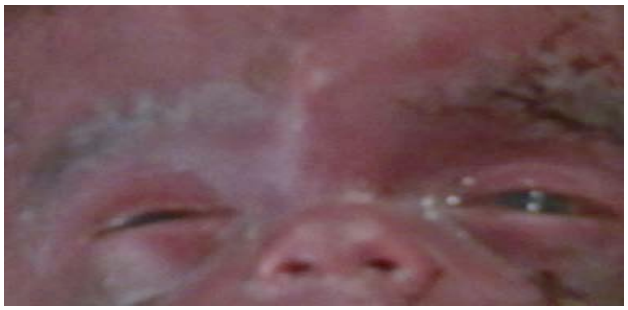

Figure 2(b). Depressed nasal bridge

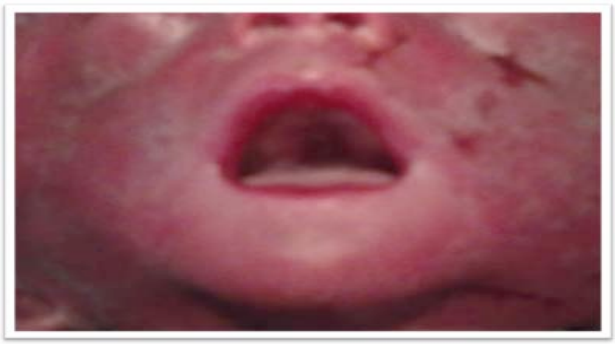

Figure 2(C). Higharched palate

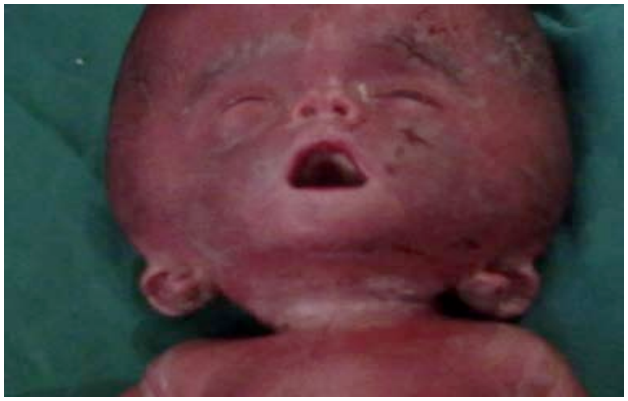

Figure 2(d). Lowsetears

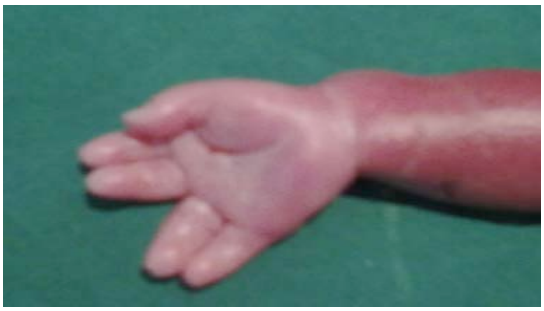

Figure 2(e). Trident hand configuration

Morphological Features of the terminated fetus exactly tallied with the image of thanatophoric dysplasia fetus from the textbook of diagnostic ultrasound.

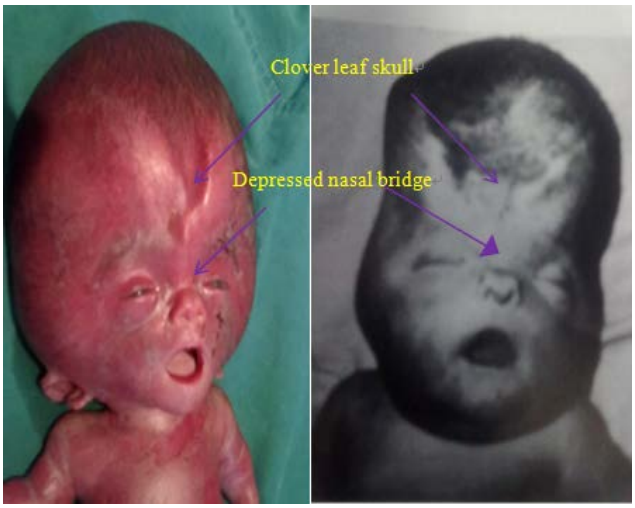

Figure 3. (a)Terminated fetus, (b) Thanatophoric dysplasia fetus

The similar features in both the photographs has been marked.

X ray was taken for the terminated fetus to rule out anomalies & skeletal dyplasias and has been compared with the Radiograph of thanatophoric dysplasia fetus.

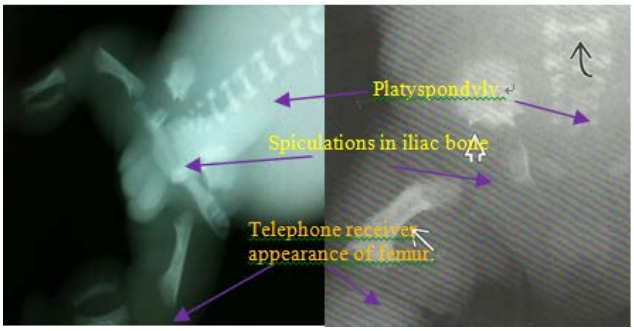

Figure 4. (a). X ray of terminated fetus, (b) Radiograph of Thanatofetus

The characteristic anomalies in the radiograph: Femur: Telephone receiver appearance. Spiculations in the iliac bone. Vertebra: Plate like platyspondyly.

2.2. Differential Diagnoses

Thanatophoric dysplasia.

Other differentials were excluded:

In Achondroplasia:Many children live past the neonatal period, in contrast to this fetus and features like spinal and foot deformities were absent in this fetus.

Hypophospatasia: In this condition, the bones will be under mineralised and marrow space will be obliterated. In this fetus well mineralised bones and prominent marrow space was found.

In Osteogenesis imperfecta multiple bone fractures and blue sclera will be seen, which were absent in this fetus.

In Asphyxiating thoracic dystrophy (jeune syndrome) Narrow thorax with micromelia is the most specific manifestation which were absent in this fetus.

Saddan: It is a severe achondroplasia with acanthosis nigricans. It is lethal in the late neonatal period in contrast to this fetus.

Hence, the probable diagnosis goes in favour of thanatophoric dysplasia.

3. Discussion

Thanatophoric dysplasia is a very rare skeletal dysplasia with a global incidence of 1 in 50,000 and Indian incidence of 1 in 100000. Male and female were equally affected in this condition. This is lethal in the neonatal period, however survival beyond the neonatal period is rarely reported. Thanatophoric dysplasia is an autosomal dominant disorder with missense mutation in fibroblast growth factor receptor 3(FGFR3) which has been mapped on chromosome 4p16.3 [2,4].

3.1. Types:

There are two types of thanatophoric dysplasia based on appearance of long bones and skull.

Type 1 is the commonest with the curved long bones(shaped like a telephone receiver) with normal skull.

Type 2 is associated with clover leaf shaped skull and straight femur.

There may be clinical overlap between these two types as in this case [4].

3.2. Pathogenesis

Upregulation of FGFR3 which is the receptor for the death of cartilage cells, sending negative signals to the chondrocytes and interfere with terminal chondrocyte differentiation. Thanatophoric dysplasia is always due to new dominant mutation and genetic empirical risk of inheritance and recurrence is only 2%.Thus,it can occur even with the normal siblings and parents.

3.3. Key Ultrasonographic Findings: [1,3]

- **Growth deficiency with limb length of less than 5%(by 20 weeks of Gestation age)**
- **Ventriculomegaly**
- **Macrocephaly**
- Cloverleaf shaped skull or Kleeblattschadel
- Well ossified skull and spine
- **Platyspondyly**
- **Micromelia**
- **Bowed femur**
- Narrow chest cavity with shortened ribs
- **Polyhydramnios.**

The ultrasonic finding in bold letters were found in this fetus.

3.4. Physical findings: [4]

- Severe growth deficiency.
- Generalised Shypotonia.
- Macrocephalic head.
- Flat facies with low nasal bridge.
- Clover leaf shaped skull.
- Narrow bell shaped thorax.
- Protuberant abdomen.
- Marked shortened limbs (micromelia).
- Brachydactyly with trident hand configuration.

3.5. Prognosis

Newborns in thanatophoric dysplasia are stillborn or die shortly after birth. Death in the neonatal period is due to severe respiratory insufficiency from reduced thoracic capacity or hypoplastic lungs or respiratory failure from brainstem compression [4].

4. Conclusion

This case is published for its rarity and for highlighting the importance of early booking and anomaly scan ,early booking in this case would have prevented unnecessary mental agony to the mother for bearing a congenitally anomalous child. This is a unique autosomal dominant disorder in contrast to other autosomal dominant disorders which occurs in each generation, this is due to a new empirical gene mutation which can occur only in the affected offspring even with normal parents. Thus, anomaly scan becomes mandatory to detect anomalies in this disorder [4].

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