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A Rare Case Report of Thanatophoric Dysplasia-Type 1

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***Abstract*:** *Thanatophoric dysplasia Type I is a rare form of neonatal lethal skeletal dysplasia. Here we report a 25 years old gravid womenwho came to our department for routineanamolyscan .Anamoly scan at 18 weeks showed features of short limbs,curved femur,hydrocephalus and narrow thorax.According to these findings we suspected diagnosis of thanatophoric dysplasia. Further radiological investigtion was performed with fetal MRI for complete assessment. Due to lethality of the skeletal dysplasia the fetus was aborted. Subsequently abortus was radiographically examined, before fetal autopsy.*

Key words: *Thanatophoric dysplasia Type I,skeletal dysplasia,Anamoly scan ,narrow thorax, curved femur*

I. Introduction

Thanatophoric dysplasia (TD) type 1 is a form of lethal osteochondrodysplasia which occurs sporadically and as a result of new autosomal dominant mutation.[1].It was first described in 1967 by Maroteaux and Lamy. The name TD is derived from a Greek word which means "Death bearing"[2]. The reported incidence is about 1 in 60,000 births.[3] Affected neonate shows marked underdevelopment of the skeleton and short limb dwarfism.[4] The anomaly results due to mutations of fibroblast growth factor receptor 3 gene (FGFR3) leading to the introduction of a new cysteine residuein various locations of the extramembranous segment of the receptor[1].Diagnosis of this condition is made by ultrasonography usually in the second trimester[4].We report one such rare case encountered in our department

II. Case Report

A 25 years old primigravida came for routine anamoly scan to our department .Anamoly scan was done, fetus was 18 weeks gestation.Ultrasound examination revealed an abnormal fetal morphology – Ventriculomegaly,short fetal limbs,curved femur,normal trunk length with narrow thorax and protuberant abdomen.According to these findings we suspected diagnosis of Thanatophoric dysplasia.On detailed clinical history there was no family history of genetic disorders or any significant past history but the couples had first degree consanguineous marriage .Fetal MRI was done to look for additional findings .Then the patient was advised termination of pregnancy.The fetus was examined,on inspection fetus had large head ,depressed nasal bridge,low set malformed ear,short neck,small thoracic cage,protuberant abdomen and short limbs .Post-partum radiograph showed relative macrocephaly,frontal bossing narrow chest,short horizontal ribs,small scapulae,,flattened vertebral bodies throughout the axial skeleton,curved appendicular bones typically femur have a "telephone handle" bowing and hypoplastic iliac bone.The histologic changes in the growth plate show diminished proliferation of chondrocytes and poor columinization in the zone of proliferation.The gross pathological features correlate with the radiological findings

III. Ultrasound Findings

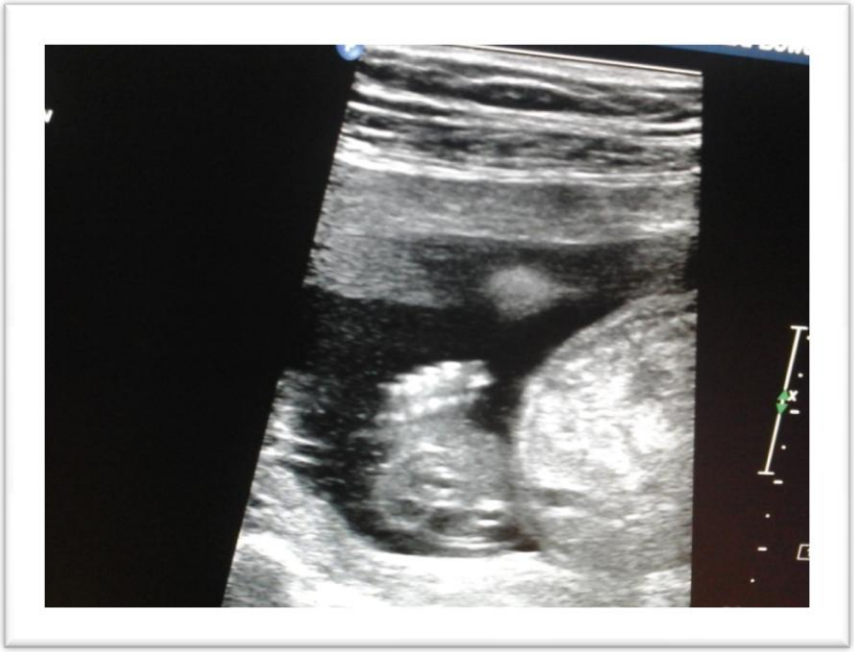


Fig:1-Ultrasonography showing Short lower Limb

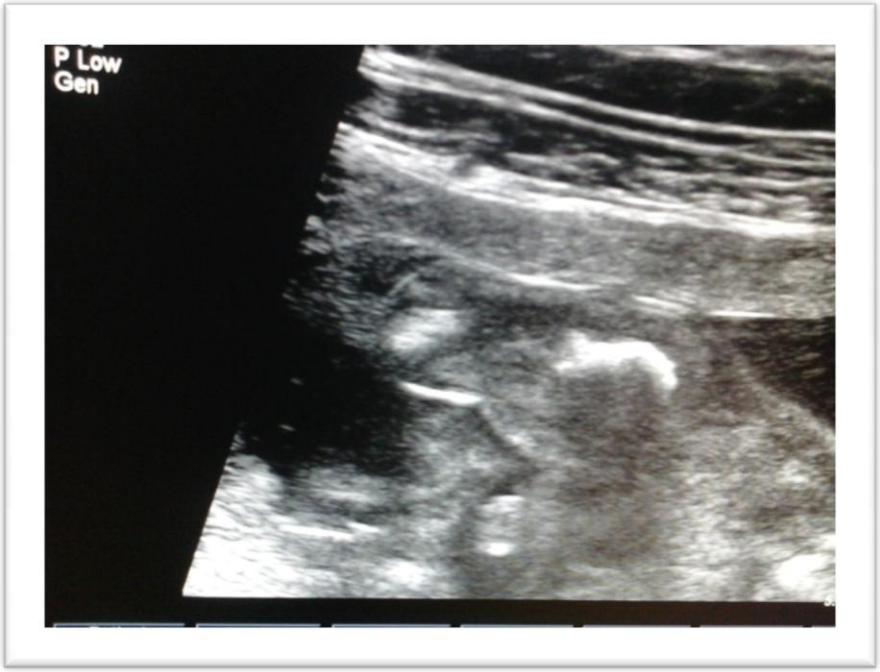


Fig 2:Telephone Handle Femur Appearance

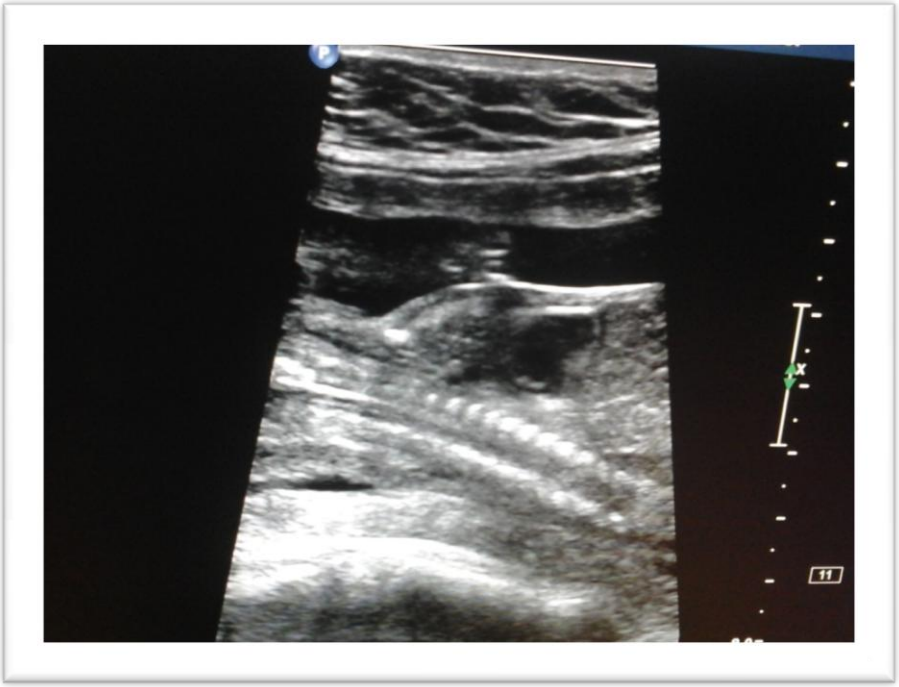


Fig 3: Narrow thoracic cavity- Bell shaped

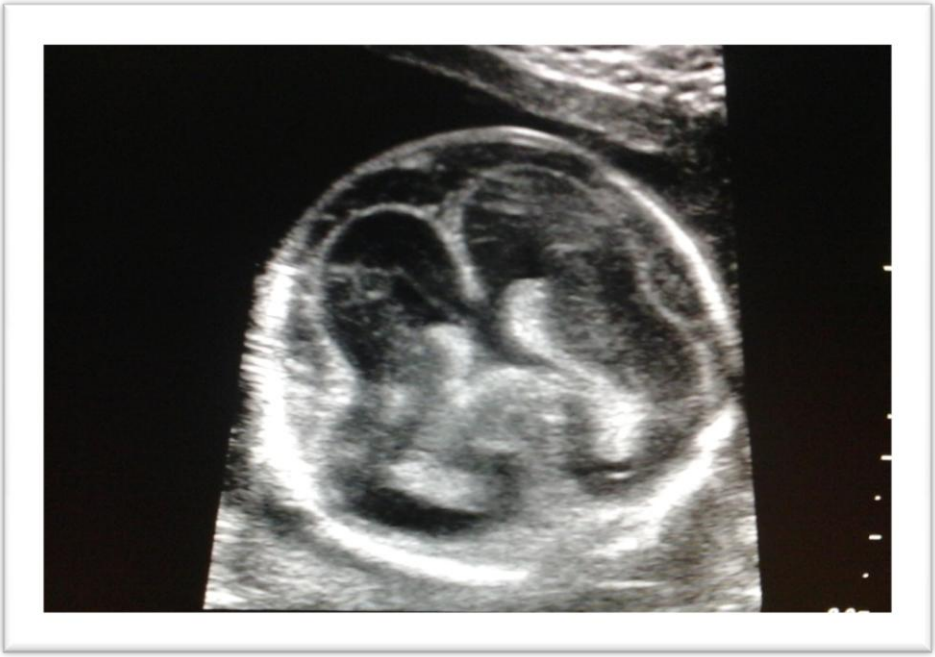
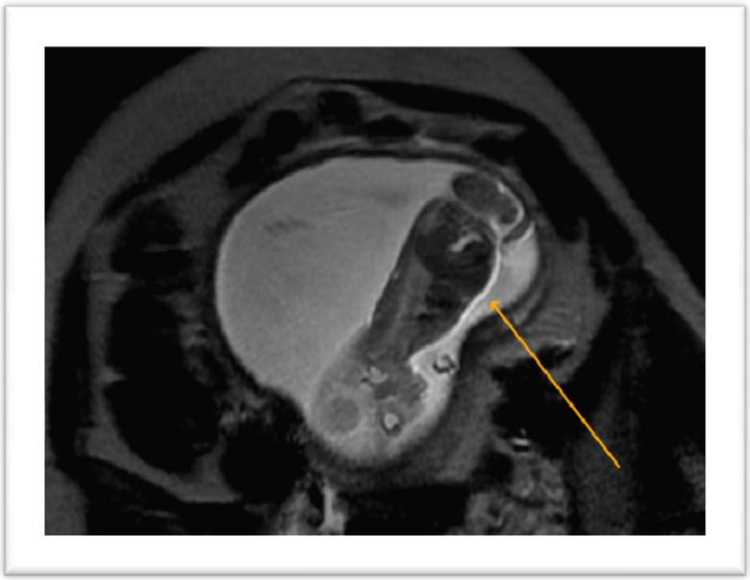
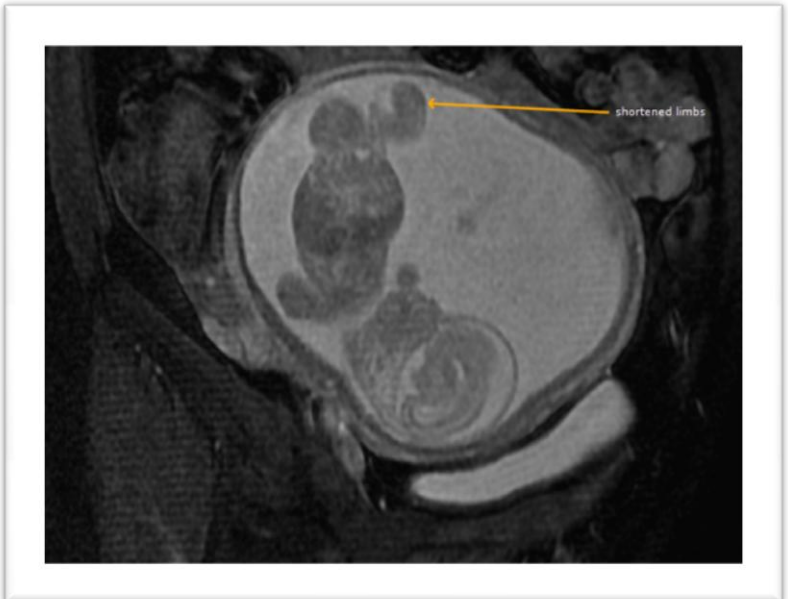


Fig 4-Dilated lateral ventricles

MRI FINDINGS

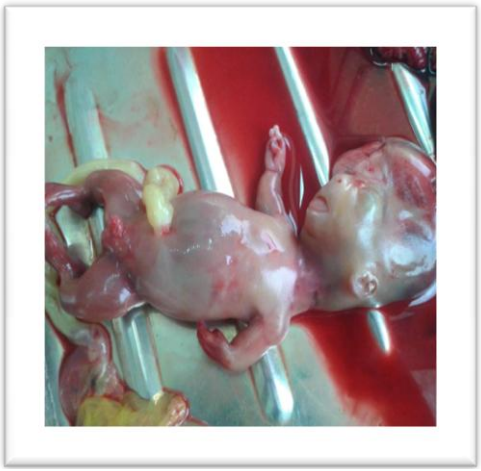


(a)

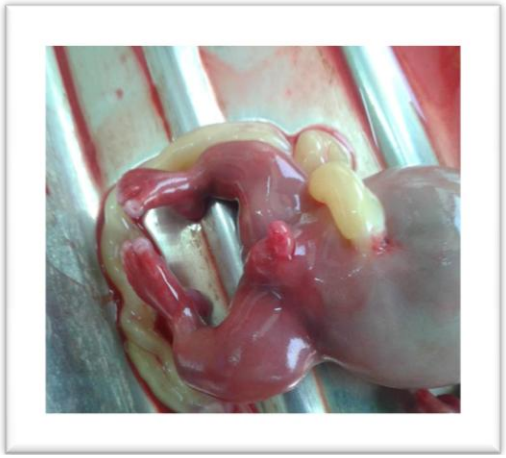


(b)

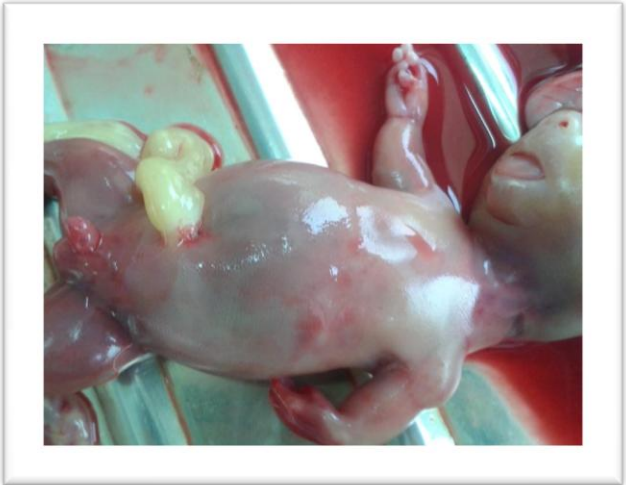
Fig 5-Fetal MRI showingnarrow thorax with normal trunk length (a) and short limbs (b)



(a)



(b)



(c)

Fig 6-Aborted fetus showinglarge head,depressed nasal bridge, low set malformed ear (a),short lower limbs (b) and short neck,small thoracic cage,protuberant abdomen and short upper limbs

IV. Post Mortem Radiographic Findings

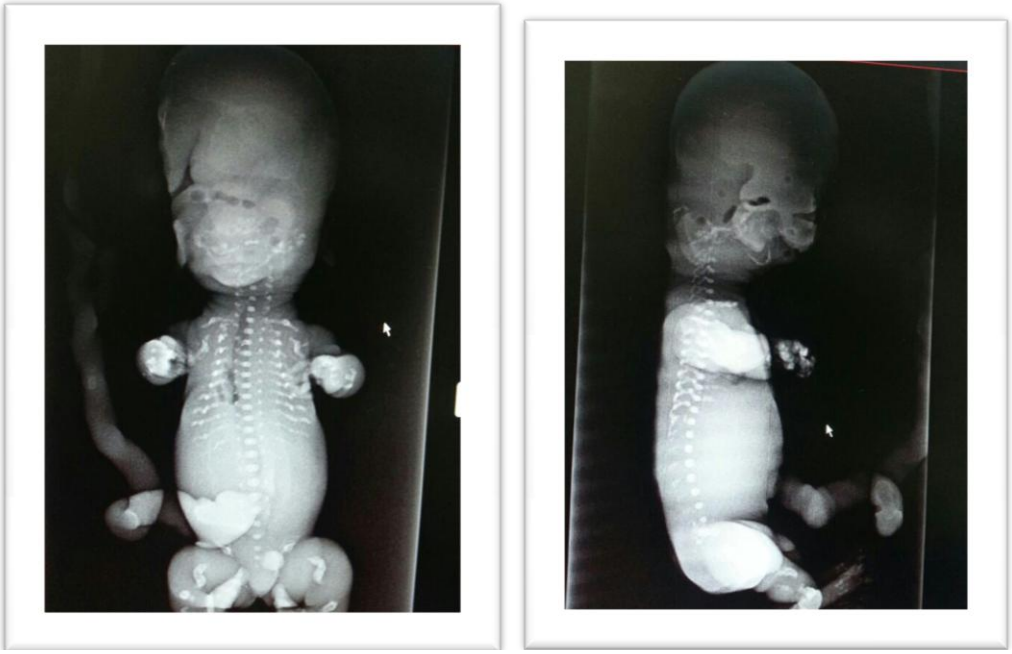


Fig 7-Post mortem radiographic findings showing relatively large head ,shortened Limbs ,telephone handle femur appearance ,small thoracic cage, small horizontal ribs ,small scapula and hypoplastic iliac bone,frontal bossing and flattened vertebral bodies**.**

V. Discussion And Conclusion

Thanatophoric dysplasia is characterized by abnormalities of head, face, thorax and skeletal system. Abnormalities of the head include megacephaly, occasionally with 'clover - leaf shaped' skull known as " kleesblattschödel". In the face, excess skin usually yields a 'boxer's face' appearance with frontal bossing and depressed nasal bridge. The abdomen is protuberant. The thorax is classically bell-shaped which is similar to 'champagne bottle cork' and results in pulmonary hypoplasia. The ribs are hypoplastic and the long bones of the extremities are short and curved. The proximal portions of the limbs are small giving a 'rhizomelic appearance'. The vertebrae are flattened with diminution of inter-vertebral spaces.[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 telephone receiver like configuration and no clover leaf 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]

As the name thanatophoric or "death-bearing" suggests, the condition is frequently lethal in-utero or shortly after birth. The cause of death is respiratory failure that occurs shortly after birth. Respiratory insufficiency may be secondary to the narrow chest cavity and hypoplastic lungs, brain stem compression by the narrow foramen magnum or a combination of both. Surviving individuals can only live to early childhood and only with intensive medical support. The prolonged suffering is not limited to the neonate concerned but also to the parents as the surviving neonate is almost always ventilator-dependent and mentally deficient[9]

The counseling part of management is very important in this disease, especially to the parents of the affected children. Without proper genetic counseling, most families having had a fetus with TD would be too worried to have further pregnancy. Since the majority of cases of TD occur sporadically, it is important to counsel that the recurrence risk is low for only one previously affected fetus and that the extended family members of the proband are not at increased risk. A general empiric recurrence risk for this entity was estimated at only 2%. To relieve the parental anxiety in such low risk couple, prenatal ultrasound examination may be offered in subsequent pregnancies to identify features suggestive of TD, such as macrocephaly, vertebral ossification defect, bowed femori,micromelia, and small thorax with protuberant abdomen. If indicated, amniocentesis may be offered and the diagnosis may be done by molecular analysis.[9]

Differentiation of TD from other forms of dwarfism, such as Achondroplasia and Diastrophic Dysplasia of the family of osteochondrodysplasia can be difficult. In TD, shortening of long bones, the appearance of skull, the presence of spinal curvature and the narrowing of spinal canal have similar configuration as that of achondroplasia.

However, the most important difference between these entities is that, TD is characterized by severe shortening of ribs, restricted lung volume and severe respiratory distress that leads to death within a few hours after birth. In TD, the vertebral bodies are flat and underdeveloped, whereas, in typical form of achondroplasia, the vertebral bodies are square and Cuboid. [10]

The morphological features in the present case were consistent with those of Type I Thanatophoric dysplasia. Thus Knowledge of this entity is essential for correct diagnosis as imaging plays a key role in evaluation of such rare entities, thus helping further management. The radiological features were appreciated post autopsy.

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