Thanatophoric Dysplasia

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Abstract

Thanatophoric Dysplasia (TD) is a severe skeletal dysplasia that is lethal in the neonatal period. There are two defined TD subtypes which have been classified clinically. The incidence is approximately 1/20,000 to 1/50,000. Type I TD being more frequent than Type II. Most individuals with TD die within the first few hours.This condition has characteristic sonographic features detected antenatally by midgestation, although distinction from other short-limbed dysplasia syndromes may be difficult. We report a case of type I TD with typical clinico-radiological features who succumbed within one hour of life.

Key words: Thanatophoric dysplasia; kleeblattschaedel; cloverleaf skull; lethal skeletal dysplasia.

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Introduction

Thanatophoric Dysplasia (TD) is a severe skeletal dysplasia that is lethal in the neonatal period. It was first described by Maroteaux et al in 1967[1]. The name of this dysplasia is derived from a Greek word 'Thanatophores' which means constantly bearing death. The incidence is approximately 1/20,000 to 1/50,000[2].Most individuals with TD die within the first few hours or days of life. The case highlights the importance of awareness of such condition which can be detected by antenatally for necessary counselling, the condition being mostly fatal.

The Case

A 23 years old second gravida pregnant mother was transferred from a peripheral hospital with antenatal diagnosis of a skeletal dysplasia for management at a tertiary care centre. Antenatal ultrasound at 31 weeks period of gestation suggested severe micromelia and corresponding mean age by femur length was only 14 weeks 5 days. Occipito-frontal circumference (OFC) and abdominal circumference corresponded to 35 weeks 5 days and 30 weeks respectively. Other sonographic features included clover leaf deformity, polyhydramnios and small thorax with pulmonary hypopasia. She delivered a baby at 34 weeks period of gestation by vaginal delivery. Baby had dysmorphic features (Fig 1) which included short limbs (upper limbs not reaching the umbilicus), macrocephaly, hypertelorism, flat nasal bridge, prominent occiput, low set ears, long forehead with mid facial hypoplasia, clover shaped skull, short neck, trident hand with brachydactyly, small bell shaped thorax and protuberant abdomen. On anthropometric examination length was 34 cm and weight of 2.18 kg. OFC was 35 cm and chest circumference of 26 cm, Upper segment: Lower segment ratio (US: LS) 3.6:1. Segmental length of upper as well as lower extremity was same; 4 cm each. Radiograph of baby showed short humerii, femorii, forearm bones and tibiae with metaphyseal flaring. Clavicles showed the typical 'bicycle handle appearance' while both the humerii and femora revealed the 'telephone receiver appearances'. The thorax was narrow with horizontally placed ribs with small scapulae. Medial acetabular spur was noted in pelvis bilaterally, with hypoplastic iliac bones.

Baby did not cry at birth and had poor respiratory efforts. Baby succumbed to this rare and lethal form of disease within first hour of life.

Fig 1: Characteristic dysmorphism of Thanatophopric Dysplasia with macrocephaly, hypertelorism, flat nasal bridge, low set ears, long forehead with mid facial hypoplasia, cloverleaf shaped skull, short neck, short limbs, trident hand, small bell shaped thorax and protuberant abdomen.

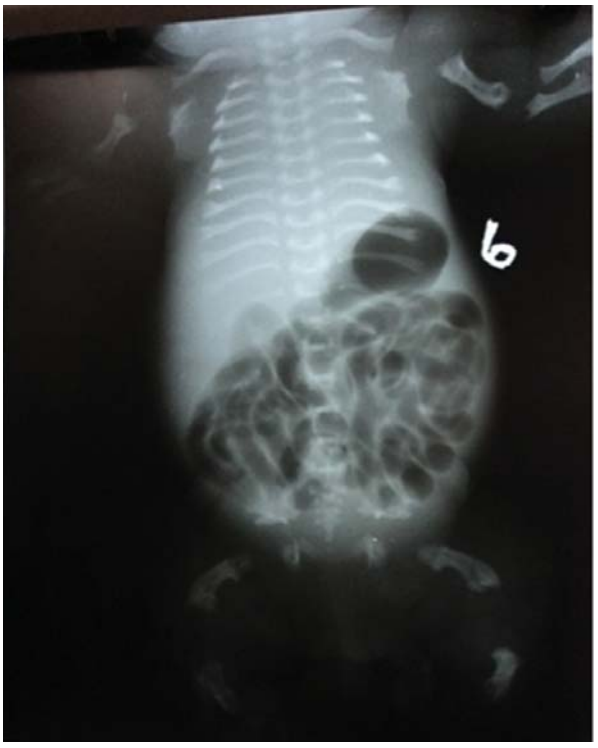

Fig 2: Showing typical X-ray appearances of skeletal abnormalities related to clavicle, thorax, vertebrae, humerii, and femora in a case of Thanatophoric Dysplasia. (Consent from family obtained)**.** Long bones are short with '*telephone receiver appearance*' of humerii and femorii and '*bicycle handle appearance*' of the clavicles. Narrow thorax with horizontally placed ribs, small scapulae and hypoplastic iliac bones are also prominent

Discussion

Thanatophoric Dysplasia (TD) is the most common lethal skeletal dysplasia presenting in the neonatal period. TD is characterized by severe shortening of the limbs, a narrow thorax, macrocephaly, and a normal trunk length. TD is of two clinically defined subtypes: Type I and Type II, the latter being more frequent. Type I is characterized by micromelia with bowed femurs and, occasionally, by the presence of cloverleaf skull deformity of varying severity and Type II babies have micromelia with straight femurs and a moderate to severe cloverleaf skull deformity. The term 'clover leaf skull' has been used synonymously to Kleeblattschlader syndrome[3]. Type I is characterized by bowed femurs; affected children have a cloverleaf skull sometimes. Type II always presents with a cloverleaf skull and the neonates have straight femurs.

The aetiologyof this disease remains unknown with the majority of case reports being sporadic. Most individuals with TD die within the first few hours or days of life by respiratory insufficiency secondary to reduced thoracic capacity or compression of the brainstem[4]. The case reported here was a male baby delivered by vaginal delivery and remained alive for less than an hour. Males are affected more than females. The majority of cases are due to de novo mutations. 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. Antenatal diagnosis is performed by analysis of DNA (*FGFR3* sequences) extracted from foetal cells obtained by amniocentesis/ chorionic villus sampling done at appropriate time.

Antenatal sonography in second trimester not only confirms the diagnosis but also differentiates it from the other non-lethaldysplasias. The sonographic criteria suggesting diagnosis of thanatophoric dysplasia are severe rhizomelic micromelia with bowing; length of limbs should be less than third percentile for gestational age. A hypoplastic thorax may be indicated by cardiac circumference greater than 60% of the thoracic circumference[4]. The skull may appear trilobed on a coronal view. The normal abdomen may appear protuberant in comparison with hypoplastic thorax. The differential diagnosis includes osteogenesis imperfecta type II which is characterized by fracture of long bones and achondrogenesis characterised by extreme hypomineralisation[6]. Other rarer conditions include camptomelic dwarfism, chondrodysplasia puncta and severe hypophosphatasia. In this lethal disease, recurrence risk is not significantly increased over that of the general population. The antenatal management

whether to terminate or continue is basically directed by parental desire after genetic counselling. The option of termination of the pregnancy, if feasible, should always be considered, the ailment being mostly fatal

Conclusion

Thanatophoric Dysplasia (TD) with typical clinico-radiological features is a severe skeletal dysplasia that is lethal in the neonatal period due to significant dysplasia of the thoracic cavity, leading to pulmonary hypoplasia and brain stem compression. By raising awareness of such rare as well as fatal condition, antenatal diagnostic accuracy can be enhanced which will help in genetic counselling and successful continuation of pregnancy.

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