Picture Stories

Thanatophoric dysplasia

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Background

Thanatophoric dysplasia (TD) was first described in 1967, the Greek term "thanatophoros" (death bringing) emphasising the lethal nature of the disorder[1]. It has an incidence of 1/20,000 to 1/50,000 live births[2]. There are two types. Type 1 has curved long bones with flat vertebral bodies[1]. Type 2 characteristically has straight femurs with tall vertebral bodies and clover leaf skull[1,2]. We present a neonate born with type 1 TD.

Case report

A term baby, weighing 2500g, was born to a 36-year-old mother after four years of secondary subfertility. The parents were non-consanguineous and the first pregnancy was a first trimester miscarriage. There was no family history of early neonatal deaths or skeletal dysplasia. The pregnancy was uneventful and mother was not on any medications. Routine antenatal ultrasonography during the second trimester revealed a short femur, polyhydramnios and suspected skeletal dysplasia and parents were counselled. The baby boy was delivered by elective caesarean section. Apgar scores were 3 and 8 at 1 and 5 minutes respectively.

The weight was on -2SD, the length was 37 cm (well below the -3SD) and the occipito-frontal circumference was 36 cm (75th centile). There was marked frontal bossing with large anterior and posterior fontanelles. The nasal bridge was flat and ears were low set. The limbs were remarkably short both proximally and distally with redundant skin. The fingers were short. There was narrow thorax with protuberant abdomen (Figure 1).

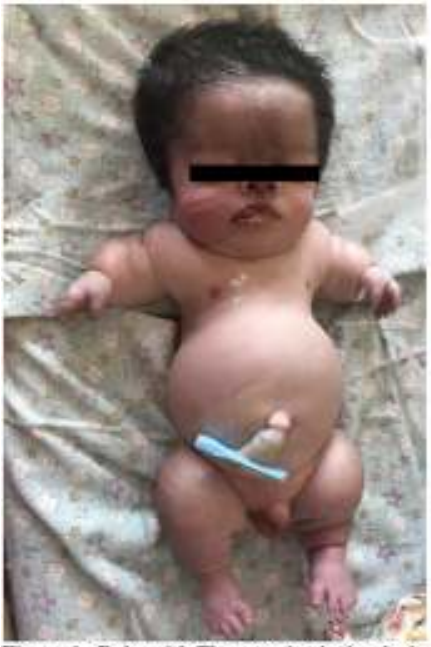

Figure 1: ***Baby with Thanatophoric dysplasia***
**Permission given by parents to publish photograph*

There were no cardiac murmurs. The skeletal radiograph revealed the characteristic telephone receiver shape femora and short long bones with flat vertebrae (Figure 2). Uniform reticular granular appearance of the lungs were also noted.

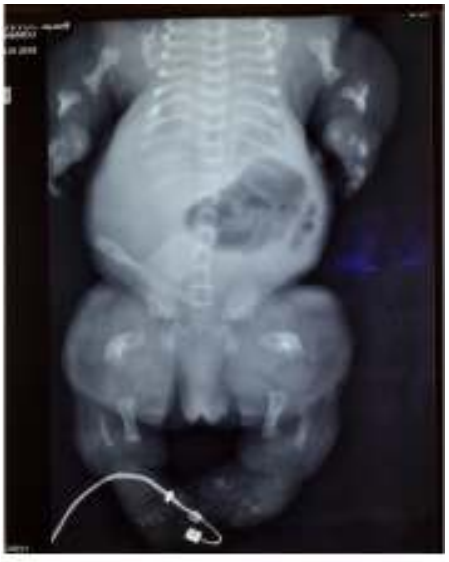

Figure 2: *X-ray showing characteristic telephone receiver appearance of femur*

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The baby had severe respiratory distress since birth due to underlying lung hypoplasia. Baby expired at 7 hours of age. The autopsy revealed no structural abnormalities of the internal organs.

Discussion

TD has an autosomal dominant inheritance pattern[1-4]. Gain of function mutation of fibroblast growth factor 3 (FGFR3) gene on chromosome 4p 16.3 is responsible for skeletal dysplasias including TD[4,5,6]. FGFR3 is a negative regulator of bone growth and mutation results in negative effect on chondrocytes leading to the skeletal abnormalities and cerebral cortical malformations[2,4]. However, most cases of TD are due to new mutations in the FGFR3 gene[1,3] and no family history may be elicited. Males and females are equally affected[2].

Even though most skeletal dysplasias can be diagnosed with antenatal ultrasonography, definitive diagnosis of TD can be difficult[2]. Most of the features may be appreciated during the antenatal scan[2]. The infants are severely growth retarded with an average length of 40 cm[1]. The limbs are markedly short with sausage like fingers[1]. The characteristic feature of type 1TD is the short femur with typical curvature like a telephone receiver[2-4]. The cranium is large with an average circumference of 37 cm[1]. The foramen magnum is small and the base of the skull is short[1]. Other craniofacial characteristics are full forehead, depressed nasal bridge and small facies, giving rise to a "boxer's face" appearance. The thorax is narrow with short ribs, giving rise to the appearance of "champagne bottle cork"[1,4,5]. This causes pulmonary hypoplasia and severe respiratory distress at birth. The skin appears thick due to extreme redundancy[5]. The spine is short with platyspondyly and relatively wide intervertebral space[1]. The scapulae are small and square shaped. Abnormalities of the pelvis are short iliac bones and flat acetabulum[1,5].

Nervous system defects are megalencephaly, temporal lobe hypoplasia, hydrocephalus, brain stem hypoplasia, encephalocoele and maldevelopment of inferior olivary nucleus[1]. There is severe intellectual impairment in the few survivors[1]. Other occasional abnormalities are atrial septal defect, patent ductus arteriosus, hydronephrosis, horseshoe kidney, radioulnar synostosis, imperforate anus and soft tissue syndactyly of fingers and toes[1]. Presence of cloverleaf skull and straight femur differentiates type 2 TD from type 1 TD. Approximately, 20% of the affected infants show clover leaf skull due to craniosynostosis[5]. During the antenatal period, polyhydramnios and feeble fetal activity are frequent[1]. Infants who are affected with the disease die in utero or soon after birth partly due to lung hypoplasia[1]. Rarely, survival beyond the neonatal period has been reported[1-3].

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