Thanatophoric Dysplasia : Antenatal Diagnosis

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Introduction

Skeletal dysplasias constitute a heterogeneous group of bone growth disorders resulting in abnormal shape and size of the skeleton. The existing classification is complicated because many are referred to by eponyms. Thanatophoric dysplasia is the most common form of skeletal dysplasia that is lethal in neonatal period. The term thanatophoric derives from the Greek word “thanatophorus” which means “death bringing”. Characteristics of thanatophoric dysplasia include severe shortening of the limbs, a narrow thorax, macrocephaly and a normal trunk length. We present a case of thanatophoric dysplasia diagnosed antenatally on ultrasound.

Case Report

A 26 year old second gravida lady presented for regular antenatal ultrasound at 20 weeks of gestation. The antenatal ultrasound of foetus showed length of femur, tibia and humerus corresponding to 15 weeks of gestation (Fig.1). However the biparietal diameter and abdominal circumference were corresponding to 20 weeks of gestation. The head was large with dilatation of lateral and third ventricles suggestive of hydrocephalus. The anteroposterior diameter of chest was small. The amniotic fluid index was normal. Based on these findings a diagnosis of a lethal bony dysplasia likely thanatophoric dysplasia was offered. The parents were counselled for termination of pregnancy. The post abortion radiograph of specimen showed short humerii, femorii, forearm bones and tibiae with metaphyseal flaring. The head was large, the chest was bell shaped. The vertebrae showed H-shaped platyspondyly. The ribs were short and the scapulae were small. There was reduced height of iliac bones with increased horizontal width. The acetabulae were flat (Fig. 2).

Discussion

Thanatophoric dysplasia has a reported incidence between 1/6000 and 1/17,000 births [1]. Its prevalence in United States is 1 per 10,000-35,000 live births. Both sexes are equally affected. There is no particularly

predisposed population and recurrence risk is sporadic. The genetic basis is thought to be due to new autosomal dominant mutation affecting different functional domains of FGFR3 gene. It is proposed by some authors that hypochondroplasia, achondroplasia and thanatophoric dysplasias are different ends of the FGFR 3 mutation with hypochondroplasia being mildest and thanatophoric dysplasia the most severe form [2]. In all these entities there is disorder of endochondral ossification with decreased or absent chondrocytes [3]. Thanatophoric dysplasia is divided into two clinically defined subtypes. Type 1 the most common subtype, is characterized by a normal-shaped skull and curved long bones which are shaped like a telephone receiver. The femurs are most affected. It is most often associated with severe platyspondyly. However in Type 2 there is cloverleaf-shaped skull and femurs as well as other long bones are straight. It is less commonly associated with platyspondyly. Some clinical overlap exists between the two subtypes. The vast majority of cases are due to de-novo mutations.

This being a lethal dysplasia, stillbirth or death during neonatal life occurs due to respiratory failure. The diagnosis is easily made in second trimester when mother presents with polyhydramnios, though in our case the amniotic fluid index was within normal limits. Barbara

Fig. 1 : Antenatal ultrasound showing short long bones in (b) tibia corresponding to approx 15 weeks of gestation as compared to normal length of tibia (a) at 20 weeks of gestation.

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Fig. 2 : Kidigram showing short long bones, narrow chest and large skull and H-shaped platyspondyly.

et al [4] suggested that the accurate antenatal diagnosis of skeletal dysplasia is difficult though the antenatal prediction of lethality can be accurate. The sonographic criteria suggesting diagnosis of thanatophoric dysplasia are severe rhizomelic micromelia with bowing, length of limbs being less than third percentile for gestational age. A hypoplastic thorax can be indicated by cardiac circumference greater than 60% of the thoracic circumference. The normal abdomen may appear protuberant in comparison with hypoplastic thorax. The skin appears thick sonographically due to extreme redundancy and may prevent normal movement and positioning of limbs causing them to be oriented at right angles to the body. The skull can appear trilobed especially in coronal view. This is often seen in Type II variety. The presence of bulging in the temporal location and bilateral involvement are clues to pick up this diagnosis on sonography. Ventriculomegaly as seen in our case, agenesis of the corpus callosum, cardiac anomalies, renal anomalies and radioulnar synostosis are occasionally associated and have been reported by various authors.

The radiographic features include large calvarium as compared to skull base. Approximately 20% of affected skull show cloverleaf skull due to primary craniosynostosis. The chest is bell-shaped with

decreased anterior-posterior diameter as seen in our case. Generally the ribs are short, horizontal with flaring of the anterior ends. The scapulae are small. The long bones are short and the femora characteristically shows telephone-like configuration. The metaphyseal ends can have a thorn like projection. The spine characteristically shows platyspondyly and H or U configuration of the vertebrae on anteroposterior film due to normal size pedicles of the flattened vertebrae.

The height of the intervertebral disc space is upto four times greater than adjacent vertebrae. There may be decreased interpedicular distance in the mid lumbar region. The pelvis characteristically shows decreased vertical height of iliac bones with increased horizontal width. The acetabulae are flat [5].

The differential diagnosis includes osteogenesis imperfecta type II which is characterized by fracture of long bones and achondrogenesis characterised by extreme hypomineralisation. Other rarer differential diagnosis includes camptomelic dwarfism, chondrodysplasia puncta and severe hypophosphatasia.

No database or registry exists in India to give an actual insight into the problem of congenital malformation and their prenatal diagnosis. It is important to integrate a network of diagnostic testing for proper and early diagnosis of bony dysplasia. Close liaison between geneticists, radiologists, pediatric surgeons, pediatricians and obstetricians is a must for prenatal diagnosis and management of fetal malformations.

Conflicts of Interest

None identified

References

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