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Research Paper

Lethal Osteochondrodysplasia- Thanatophoric Dysplasia – A Case Report

Medical Science

KEYWORDS : Thanatophoric dysplasia, Fibroblast growth factor receptor 3, TIFFA scan, skeletal dysplasia.

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ABSTRACT

Thanatophoric dysplasia is one of the most common forms of neonatal lethal skeletal dysplasias. It is diagnosed usually by routine ultrasound examination or TIFFA scan in the second trimester itself. Further molecular analysis also confirms the diagnosis and aids in the counseling in the prenatal period as well as for subsequent pregnancies.

Introduction:

Constitutional diseases of bone or Osteochondrodysplasias have been classified into four groups based on the presence or absence of associated abnormalities in the axial skeleton and bone mineralization. As a group they are not uncommon, though each of these individual entities is rare. Thanatophoric dysplasia, a term derived from Greek word meaning "death bearing" falls into the category of Osteochondrodysplasias with defects in tubular bones and / or axial skeleton. It is characterized by the presence of macrocrania, micromelia (short limbs), narrow bell shaped thorax, platyspondyly (flat vertebral bodies), vertically shortened ilia, telephone receiver like short curved femora and clover leaf skull. It is often diagnosed by routine ultrasound examination in the second trimester, like most of the other skeletal dysplasias.

Case report:

A 27 year old second gravida with 28 weeks gestation was admitted to the hospital with a complaint of loss of fetal movements. History revealed that she had regular antenatal checkups. Ultrasound showed a dead male fetus with short upper and lower limbs, protruded abdomen and hydrocephalus. Labor was induced and the fetus was sent for examination. There was no history of consanguinity and the first child was healthy.

Suspecting a skeletal dysplasia detailed skeletal survey was done, which revealed macrocrania, micromelia (short limbs), narrow bell shaped thorax, platyspondyly (flat vertebral bodies), vertically shortened ilia, telephone receiver like short curved femora and metaphyseal flaring of long bones.

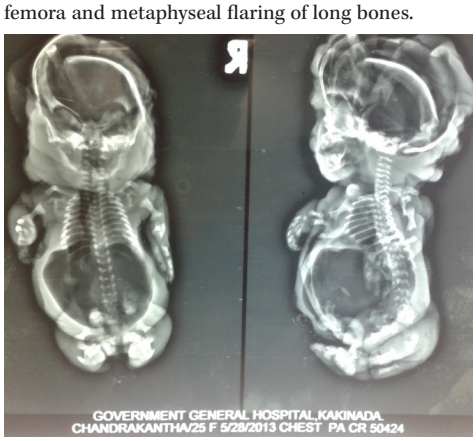


Figure-1- Infantogram showing shortened humeri, bowed femora and platyspondyly.

Figure -1.

External examination of the fetus showed a large head, frontal bossing, depressed nasal bridge, narrow thorax, Rhizomelic (proximal) type of short limbs and bowed femora. On fetal biometry all the parameters were fitting for a "short for gestational age' fetus except for crown rump length. Internal examination revealed no detectable abnormality.



Figure-2 – Fetus showing large head, protruded abdomen and short limbs with bowed legs

Histopathological examination of long bones,ribs and vertebra showed retarded and disorganized physeal growth zone. There was a horizontally oriented band of fibrosis at the periphery of the epiphysis with normal resting cartilage.

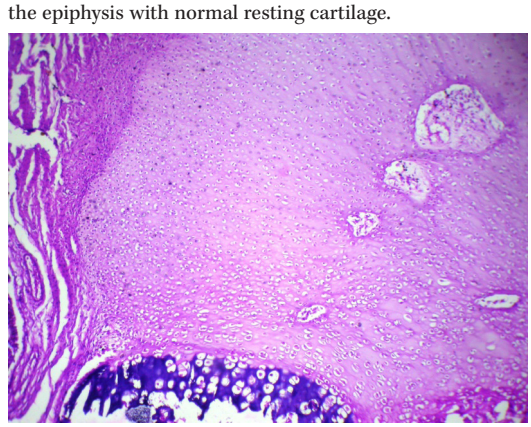


Figure-3- Section from physeal end of long bone showing disordered growth plate with peripheral fibrosis.

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Correlating the radiological, clinical and histopathological findings, the fetus was diagnosed to have Thanatophoric dysplasia-Type 1.

Discussion:

Osteochondrodysplasias or constitutional disorders of bone are classified into five groups based on molecular defects and into four groups based on the involvement of tubular bones & or axial skeleton, abnormal bone density and defective mineralization.

Thanaotophoric dysplasia (TD/ Type1 TD) falls into the sub -category of "Non-short trunk osteochondrodysplasias with platyspondyly" under the category of "Osteochondrodysplasias with defects of tubular bones and /or axial skeleton".[2] It is characterized by marked shortening of the limbs, narrow bell shaped thorax, large head with frontal bossing, platyspondyly and a normal trunk length. Also present are bowed femora and sometimes cloverleaf (trilobed) skull. Thanotophoric dysplasia with clover leaf skull (Type II-TD), another subcategory differs from Type I-TD in that it is always associated with cloverleaf skull and straight femora [2,3].

The incidence of TD is 1:20,000 to 1:50, 000 births. The causative factor identified is mutations in the FGFR 3 gene located on the short arm of chromosome 4 resulting in decreased apoptosis [1]. Thanatophoric dysplasia is the most common and frequently occuring form of neonatal lethal skeletal dysplasia. [2,4]. These mutations occur in an autosomal dominant pattern [2, 5].

Thanatophoric dysplasia is mainly diagnosed by routine prenatal ultrasound examination and sometimes by chorionic villous biopsy at 10 – 12 weeks of gestation or fetal DNA analysis at 15 – 18 weeks of gestation [4]. TD is frequently lethal before or immediately after birth. The cause of death after birth is mainly due to hypoplastic lungs.

Because of their occurrence as sporadic mutations, the risk of recurrence in future pregnancies is significantly low i.e. only 2%. This should be explained to the parents as a part of counseling and they should be followed up with TIFFA scan in the second trimester in subsequent pregnancies to alleviate the anxiety of the parents [6].

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