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Lethal Short Limb Dwarfism: Thanatophoric Dysplasia- Type I

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A 30-year-old, mother, delivered a 2.6 kg term female child by caesarean section, in view of brow presentation and failure of induction of labor. Antenatal ultrasound of mother at 5th and 7th month had detected a fetus with short curved limbs and small chest, with a suspicion of achondroplasia. At birth, the neonate was noted to have dysmorphic features, macrocephaly, midfacial hypoplasia, depressed nasal bridge, low set ears, short limbs, short narrow thorax with lumbar lordosis [Table/Fig-1&2]. Radiological survey of the child clinched the diagnosis of Thanatophoric Dysplasia (TD) Type I [Table/Fig-3]. Echocardiography screening revealed atrial septal defect, ventricular septal defect and patent ductus arteriosus with severe pulmonary hypertension.

Skeletal dysplasias constitute a heterogeneous group of bone growth disorders resulting in abnormal shape and size of the skeleton. TD is the most common lethal osteochondrodysplasias with a prevalence of 1:20,000 to 1:40,000 births [1]. It is characterized by marked underdeveloped skeleton and short-limb dwarfism. The term 'thanatophoric' derived from the Greek word "thanatophorus", means "death bringing" and was first described by Maroteux [1-3]. TD is caused by activation of FGFR3 gene located on the short arm of chromosome 4 leading to negative regulation of bone growth [1,2]. The activation of FGFR3 in a majority is due to denovo mutations.

There are two clinical types of TD which closely resemble in their clinical features; however have distinct radiological features and genetic mutations [3]. In Type I TD, the amino acid arginine, at 248 position, is substituted by cystine and in Type II TD the lysine at 650 position is replaced by Glutamate in most cases [1]. Type 1, the more commonly encountered form is characterized by a normal-shaped skull and curved (telephone receiver shaped) long bones, especially seen in femur bone, whereas type II is associated with a cloverleaf-shaped skull and straight femurs [1-3].

The phenotypic features of TD range from severe shortening of limbs, macrocephaly, frontal bossing, wide fontanel's, cloverleaf skull, prominent eyes, to long narrow bell shaped thorax resulting in pulmonary hypoplasia [3]. Radiological features are short, cupped and anteriorly splayed ribs with severe hypoplasia of pelvic bones, short and flared femur with medial spike (telephone receiver shaped in Type I), large calvarium with short base and small foramen magnum, cloverleaf skull and thin flat vertebrae. The pelvis characteristically shows decreased vertical height and increased horizontal width of iliac bones with flat acetabulae [2]. The diagnostic sonographic criteria are severe rhizomelic-micromelia with bowing of long bones [3]. The metaphyseal ends can have a thorn like projection secondary to prominent ossification resulting in 'Maple leaf like' contour of metaphysis of tubular bones.

The close differential diagnoses of TD, includes osteogenesis imperfecta type II and III, which is characterized by fracture of long bones and achondrogenesis characterized by extreme hypomineralization. Other rarer differentials include achondroplasia, perinatal hypophosphatemia, campomelic dysplasia and hypochondrogenesis [3].

Prognosis for TD is grim, with stillbirths or deaths occurring during early neonatal period because of respiratory failure due to lung hypoplasia or brain stem compression due to underlying hydrocephalus [3]. Postnatal treatment involves life-support measures, parental counselling and provision-of-comfort care for the newborn [2].

Prenatal diagnosis and genetic counselling can be done with the help of antenatal ultrasonography and/or molecular studies, especially for fetuses with short limbs. Early and timely detection of lethal forms on antenatal scans will help in obstetricians and parents to take decision regarding option of medical termination of pregnancy [1, 3].

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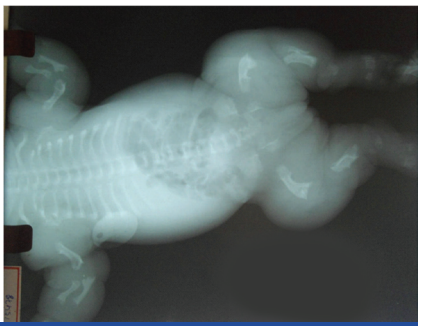

[Table/Fig-1]: Reveals frontal bossing, depressed nasal bridge, prominent eyes, short neck, short and narrow thorax, short limbs **[Table/Fig-2]:** Lateral view of the neonate shows large head, short neck, prominent forehead, low set ears and lumbar lordosis **[Table/Fig-3]:** X Ray- Skeletal Survey : Skeletal Survey shows short bowed long bones with bullous end, short ribs, narrow thorax, handle bar appearance of clavicle, vertebral bodies short end superiorly & inferiorly, dysplastic acetabuli with flat acetabular roof, small iliac bones and telephone reciever appearance of femurs

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