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CASE REPORT

THANATOPHORIC DYSPLASIA IN THE NEWBORN

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ABSTRACT: Thanatophoric dysplasia (TD) is the most common, congenital, sporadic, usually lethal osteochondrodysplasia. TD has two subtypes: TD1 and TD2. Marked shortening of limbs (micromelia), bell shaped thorax and platyspondyly are the hallmarks of both subtypes. Clover leaf skull is a characteristic feature of TD type 2. De novo mutations in the fibroblast growth factor receptor 3 gene (FBFR3) results in this disorder. In most cases TD can be diagnosed by antenatal sonography. We report a neonate with Thanatophoric dysplasia.

KEYWORDS: Clover leaf skull, congenital, micromelia, platyspondyly, Thanatophoric dysplasia.

INTRODUCTION: Thanatophoric dysplasia (TD) is a sporadic, usually lethal skeletal dysplasia characterized by marked shortening of limbs, small conical thorax, platyspondyly and macrocephaly.[1, 2] Its incidence varies from 0.29 to 0.69 for every 10000 live births.[3] TD is derived from the Greek word "Thanatophores" which means constantly death bearing.[4]TD is due to a lethal mutation in the same gene that causes achondroplasia, a familiar and far more common form of short limbed dwarfism this is compatible with life.[5] The presence of dysmorphic facies, micromelia, macrocephaly and protruberant abdomen led us to the diagnosis of TD.

CASE REPORT: A two hour old male baby was referred to the outborn NICU of our institution, with the complaints of the baby not having cried immediately after birth and being dysmorphic with respiratory distress. This baby was the second born to a non-consanguineously married couple. The first child was a four year female and was apparently healthy. During this pregnancy the mother was neither registered nor immunized against tetanus. She did not undergo regular antenatal check-ups.

Only one antenatal scan was done prior to the delivery. Mother developed signs of severe pregnancy induced hypertension at around 34 weeks of gestation and was hospitalized. Antenatal scan done prior to delivery showed polyhydramnios with an anomalous baby having short limbs and hydrocephalus. Baby was delivered by emergency LSCS at a private hospital. Baby did not cry immediately after birth, was resuscitated and referred to us for further management. On examination, baby weighed 2100 grams, looked dysmorphic and general condition was poor. There were signs of decompensated shock, central and peripheral cyanosis, tachypnea with increased work of breathing and oxygen saturation with 12 lts of hood box oxygen was 70-75%. Baby was euglycemic, hypothermic and had poor cry and activity. Baby's length was only 36 cms with US: LS ratio of 2.5:1.

There was macrocephaly (hydrocephalus with head circumference of 42 cm), anterior and posterior fontanelle were wide open with sutural separation (Fig. 1). Baby had a coarse and edematous facies with frontal bossing, mid facial hypoplasia, hypertelorism with prominent eyes, depressed nasal bridge, low set ears and high arched palate. Neck was short, upper and lower limbs were shortened (rhizomelic dwarf) with short stubby fingers and deep skin creases (Fig. 2). Thorax was narrow and bell shaped and abdomen was protruberant (Fig. 1). Spine was normal. Baby had

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bilateral decreased air entry and cardiac examination was normal. Moro's and other newborn reflexes (sucking/rooting etc.) were depressed. With the characteristic facial features and skeletal anomalies we came to a diagnosis of TD.

On investigation, baby's septic screen was negative. Infantogram showed large sized skill with short base, small face, flat vertebral bodies (platyspondyly), typical "bicycle handle appearance" of clavicles, while both the humerii and femora revealed "telephone receiver handle" appearance. Thorax was narrow with horizontally placed ribs and widened costochondral junctions. Brachydactyly with absence of carpal and tarsal bones were also noted on the infantogram (Fig 3). Baby was managed with mechanical ventilation and other supportive measures as per unit protocol. However, the general condition did not improve and baby succumbed on day 2 of NICU stay. On autopsy the findings were suggestive of TD and pulmonary hypoplasia was labeled as the most probable cause of death.

DISCUSSION: Thanatophoric dysplasia or dwarfism (TD) literally meaning death bearing dwarf is the most common form of lethal skeletal/bone dysplasia characterized by severe micromelia and skeletal malformations.[6] It was first described by Maroteauax et al. in 1967.[7] At present, TD is divided into two clinically defined subtypes: TD type 1 and 2 with some clinical overlap between the two subtypes.[6] Autosomal dominant mutations in the fibroblast growth factor receptor 3 (FGFR3) gene, which has been mapped to chromosome band 4p16.3, results in both subtypes. The vast majority of cases are due to de novo mutations. Males are more affected than females. Mutation in the FGFR3 gene results in impaired enchondral ossification, which is more prominent towards the peripheries of the metaphysis leading to tongue shaped osseous cones directed towards the epiphyses. The perichondral spurs and linguiform enchondral growth plates results in "maple leaf" like contour of the metaphysis of tubular bones.[8]

CLINICAL FEATURES: TD is usually of two phenotypic subtypes. Type 1 (80% of cases) presents with polyhydramnios, macrocephaly, short limbs, narrow thoracic cage and curved short humerii and femora (the typical telephone receiver handle appearance).

Type 2 (20% of cases) is also characterized by similar features as type 1, but in addition it also has clover leaf skull, hydrocephalus and femora are short and straight. Kyphosis and scoliosis have also been observed. Acanthosis nigricans, cerebral anomalies including that of the temporal gyri, hippocampus and neuroglial heterotropias may also be seen in few cases.[1, 9]

Radiological features in a neonate with TD include cloverleaf skull, small narrow thorax with horizontally placed ribs, small scapulae, severe platyspondyly (decreased height of vertebral bodies), horizontal acetabular roofs, small sacroiliac notches, marked shortening and bowing of long bones with telephone receiver appearance, irregular metaphysis and short broad tubular bones in hands and feet.[10]

Differential diagnosis of TD includes homozygous achondroplasia, achondrogenesis, captomelic dwarfism, chondrodysplasia punctata, severe hypophosphatasia and severe osteogenesis imperfecta.[6] The presence of a characteristic cloverleaf skull with telephone receiver appearance of humerii and femora with platyspondyly differentiates TD from the other causes of severe short stature.

MANAGEMENT: Most of the fetuses with TD die in utero. Of the few fetuses which are born alive, succumb in the early neonatal period. Narrow thorax with severe pulmonary hypoplasia and pulmonary hypertension is a major cause of death in these neonates. Infrequently cervical cord compression at a narrowed foramen magnum associated with posterior arch anomaly may be the cause of death.[8]

ANTENATAL DIAGNOSIS: Prenatal sonography in the second trimester may reveal polyhydramnios with the classical skeletal features like cloverleaf skull, bell shaped thorax, micromelia, broadened and flattened ribs, ovoid vertebral bodies and pulmonary hypoplasia. Amniocentesis and/or chorionic villus sampling may be done to confirm the mutation in the FGFR3 gene.[6, 9]

PROGNOSIS: TD is uniformly lethal either in utero or in the early neonatal period. The longest survival however has been reported to be of 9 years.[11]

PREVENTION: Since majority of the cases of TD occur sporadically, parents with only one previously affected fetus the recurrence risk in subsequent pregnancies is low. A general empiric recurrence risk for TD is estimated as 2%. In most cases ultrasonography in the second trimester should suffice for the diagnosis of TD in utero. If indicated amniocentesis and/or chorionic villus sampling may be offered and the diagnosis may be confirmed by molecular analysis of the mutation in FGFR3 gene.[12]

CONCLUSION: TD is a congenital, sporadic, autosomal dominant skeletal dysplasia which is usually lethal. Cloverleaf skull, micromelia, narrow thorax and platyspondyly are the hallmarks of TD. Good quality antenatal sonography will detect fetuses with features of TD. Prenatal diagnosis and genetic counseling helps parents make intelligent decisions with regard to the continuation and outcome of pregnancy.

REFERENCES:

1. Chang TK, Wang Y, Liu AM, Tung JC. Thanatophoric dysplasia type 1. Acta Pediatr Taiwan 2001; 42 (1): 39-41.
2. Sandkrist L. Thanatophoric dysplasia. A report of three cases. Acta Pathol Microbiol Immunol Scand A 1983; 91 (5):335-341.
3. Calin Mos. Thanatophoric Dysplasia. A two case report. Medical Ultrasonography 2009; 11 (2):37-43.
4. Young RS, Pocharzetsky R, Leonicas JC, Wexley H. Thanatophoric dwarfism and cloverleaf skull (Kleeblastscadel). Radiology 1973; 106:403-405.
5. Shahin Mafinezhad, Yasaman Bozorgnia, Reza Gharaee. Thanatophoric Dysplasia in newborn twins: Case report and literature review. Iranian Journal of Neonatology 2012; 1(3):1-4.
6. Kulkarni ML, Sureshkumar C, Venkataramana V, Samuel Koshy, Bhagyavathi M, Shekar Reddy. Thanatophoric Dysplasia. Indian Pediatr 1994; 31: 1405-1410.
7. Maroteaux P, Lamy B, Robert JM. Le nanisme thanatophore. Presse Med 1967;75: 2519-2524.
8. Ashish Verma, Suyash Mohan, Sunil Kumar. Thanatophoric Dysplasia: Case Report and Review of Literature. Journal of Clinical and Diagnostic Research 2007;1(4):308-311.

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9. Chen CP, Chern SR, Stuh JC, Wang W, Yeh LP, Chang TY et al. Prenatal diagnosis and genetic analysis of type 1 and 2 thanatophoric dysplasia. Prenat Diag 2001; 21: 89-95.
10. Weber M, Johannisson T, Thompson M, Rehder H, Neithard FU. Thanatophoric dysplasia type 1: new radiologic, morphologic and histological aspects towards the exact definitions of the disorder. J Pediatr Orthop B 1998; 7:1-9.
11. Baker KM, Oslon DS, Harding CO, Pauli RM. Long term survival in typical thanatophoric dysplasia type 1. Am J Med Genetics 1997; 70: 427-436.
12. Naveen NS, Murlimanju, Vishal Kumar, Thejodhar Pulakunta, Jeeyar H. Thanatophoric Dysplasia: A Rare Entity. Oman Med J 2001; 26(3):196-197.

Figure 1

Figure 1: Showing (i) Short stature with extremely short limbs with stubby fingers and deep skin creases (ii) macrocephaly (iii) bell shaped narrow thorax (iv) protruberant abdomen and (v) low set ears.

Figure 2

Figure 2: Showing (i) coarse edematous facies (ii) frontal bossing (iii) depressed nasal bridge (iv) hypertelorism (v) prominent eyes (vi) short neck.

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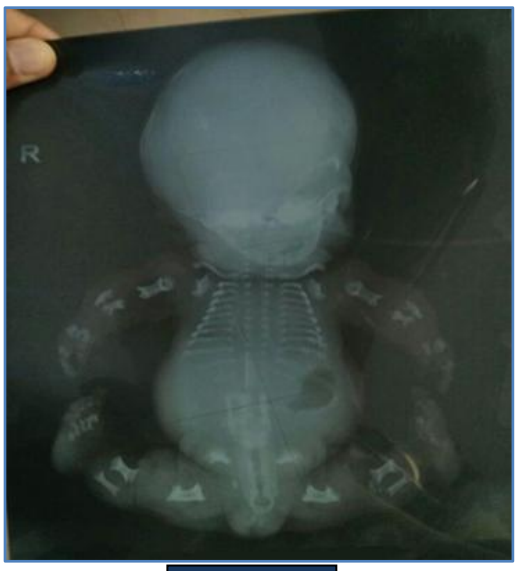

Figure 3

Figure 3: Radiograph showing (i) large skull with narrow base (ii) horizontally placed ribs (iii) flattened vertebral bodies (iv) bicycle handle appearance of both clavicles (v) characteristic telephone receiver appearance of both humerii and femora

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