Case Report

Thanatophoric dysplasia: a case report

Uruj Jahan, Astha Sharma*, Neena Gupta, Shruti Gupta, Fatima Usmani, Ankita Rajput

Department of Obstetrics and Gynaecology, G. S. V. M. Medical College, Kanpur, Uttar Pradesh, India

Received: 08 November 2018
Accepted: 13 December 2018

*Correspondence:
Dr. Astha Sharma,
E-mail: dr.sharmaastha@gmail.com

ABSTRACT

Thanatophoric Dysplasia (TD) is a congenital, sporadic and most lethal skeletal dysplasia caused by new mutation in FGFR3 gene. Authors report such a rare case of a term alive baby with dysmorphic features, born to an unbooked, 40 years old G3P30 with non-consanguineous marriage; admitted at 9 months of gestation to present hospital with complain of pain abdomen for 2 days. Patient delivered a term female baby of vaginally which had delayed cry after birth. Admitted in NICU immediately with respiratory distress. The baby looked dysmorphic and suggested TD as most likely diagnosis. The case is being reported for its rarity and for high importance of early booking and anomaly scan. Early diagnosis is important since it provides alternative options of termination of pregnancy when an affected foetus is detected.

Keywords: Dysmorphic features, Non-consanguinous, Thanatophoric dysplasia

INTRODUCTION

Thanatophoric Dysplasia (TD) is a congenital, sporadic and usually lethal skeletal dysplasia. Its incidence is 1 in 20000 to 50000 of live births. At birth it is characterized by micromyelia, small conical thorax, platyspondyly (flat vertebral bodies) and macrocephaly. It is caused by denovo autosomal mutation in the fibroblast growth factor receptor 3 (FGFR3) gene located on chromosome 4 p16.3. It has 2 subtypes and TD type I, being the most common subtype. The two subtypes can be differentiated by the skull shape and femur morphology. TD type I, the most common subtype, characterized by curved and short femur which is in a telephone receiver like configuration and no cloverleaf shaped skull. Also, the abdomen appears protuberant in comparison with the chest which is narrow and small. The fetuses with type II TD are reported to have cloverleaf skull which means a trilobed skull. The premature closure of coronal and lambdoid sutures is commonly seen with the cloverleaf skull. Other features common to both TD include small narrow thorax with horizontally placed short ribs, macrocephaly, large anterior fontanel, a small foramen magnum, distinctive facial features (frontal bossing, low nasal bridge, flat faces), severe platyspondyly, marked shortening and bowing of long bones, brachydactyly (short broad tubular bones in hands and feet), redundant skin folds along the limbs etc. Authors report one such rare case of an unbooked patient after delivery.

CASE REPORT

An unbooked 40 years old female; G3P30 with non-consanguineous marriage, with prior no antenatal visits; admitted to present hospital at full term in second stage of labour. There was no history of fever, rashes, spotting per vaginum, any drug intake, radiation exposure, family h/o congenital anomalous baby. She was not addicted to smoking, alcohol or any drug abuse. There was no past and family history of congenital abnormalities, diabetes mellitus, hypertension and thyroid dysfunction.
At the time of admission her vitals were within normal limits. There was mild pallor and oedema. There was no thyroid swelling or any significant lymphadenopathy. No abnormality detected on respiratory, CVS or CNS examination. P/A fundal height was 36 weeks with fetus in longitudinal lie, cephalic presentation fetal heart rate was 120/min with good uterine contraction. On P/V os fully dilated, cervix fully effaced, membranes absent and head at 0 station. Her routine blood investigations - complete blood count, blood sugar, blood group, S.TSH were within normal limits. HIV, HBSAG, HCV, VDRL were non-reactive. Patient delivered a term female baby vaginally which had delayed cry after birth, admitted in NICU immediately with respiratory distress, intubated and expired after 12 hours. Baby looks was dysmorphic, had macrocephaly with HC 42 cm. Face was coarse and edematous with frontal bossing, mid facial hypoplasia, depressed nasal bridge and short neck.

**DISCUSSION**

The term thanotrophic is derived from Greek word thanotopherus which means death bringing. This term was first described and used by Marotux for dwarf babies who died in 1st hour of life. Its incidence is 1 in 20000 to 50000 of live births. There are two subtypes with relative incidence: Type I-80% and Type II-20%. The two subtypes can be differentiated by the skull shape and femur morphology.

TD type I, the most common subtype, characterized by curved and short femur which is in a telephone receiver like configuration and no cloverleaf shaped skull. Also, the abdomen appears protuberant in comparison with the chest which is narrow and small.

The fetuses with type II TD are reported to have cloverleaf skull which means a trilobed skull. The premature closure of coronal and lambdoid sutures is commonly seen with the cloverleaf skull.

Other features common to both TD include small narrow thorax with horizontally placed short ribs, macrocephaly, large anterior fontanel, a small foramen magnum, distinctive facial features (frontal bossing, low nasal bridge, flat faces), severe platyspondyly, marked shortening and bowing of long bones, brachydactyly (short broad tubular bones in hands and feet), redundant skin folds along the limbs etc.

Affected individuals could not survive so disorder never passes to the next generation. Most of the fetuses with TD die In-utero.

The cause of death is due to respiratory insufficiency which may be secondary to the narrow chest cavity and hypoplastic lungs, brainstem compression by the narrow foramen magnum or a combination of both. Surviving neonate is almost always ventilatory dependent as occurred in present case.

Diagnosis is confirmed after autopsy by histopathology which shows disorganized chondrocyte columns, poor cellular proliferation, lateral overgrowth of metaphysis and increased vascularity of cartilages but unfortunately could not be done in present case as consent was not given by the parents.
Diagnostic tool

Although identification of a lethal skeletal dysplasia in the second trimester is often straightforward but establishing its specific diagnosis can be difficult. A three-dimensional ultrasound has an important role and description of external fetal morphology, the structure of fetal bones and the cranial sutures aids in the diagnosis of TD. Polyhydramnios in second and third trimester is common in both types. Occasional findings on both types are thickening of nuchal translucency in the 1st trimester, ventriculomegaly, agenesis of corpus callosum, cardiac defects and hydronephrosis. Prenatal diagnosis can be confirmed by molecular analysis of the mutation in FGFR3 gene extracted from fetal cells obtained by amniocentesis usually performed at 15-18 weeks of gestation or chronic villous sampling at about 10-12 weeks gestation.

Table 1: Review of cases of thanatophoric dysplasia reported earlier in literature from India.

<table>
<thead>
<tr>
<th>Author’s name</th>
<th>Age of baby/weight of baby</th>
<th>Diagnostic modalities</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tirumalasetti N</td>
<td>26 weeks/780g</td>
<td>Sonogram, radiograph and clinical features</td>
<td>Stillborn</td>
</tr>
<tr>
<td>Phatak SV et al</td>
<td>30 weeks</td>
<td>Radiograph and clinical features</td>
<td>Stillborn</td>
</tr>
<tr>
<td>Naveen NS et al</td>
<td>22 weeks</td>
<td>Sonogram and clinical features</td>
<td>Dead fetus</td>
</tr>
<tr>
<td>Lingappa HA et al</td>
<td>28 weeks/1.3kg</td>
<td>Clinical features and autopsy</td>
<td>Stillborn</td>
</tr>
<tr>
<td>Devangeri RS</td>
<td>20 weeks/400g</td>
<td>Clinical features, radiograph and autopsy</td>
<td>Stillborn</td>
</tr>
<tr>
<td>Gopal G et al</td>
<td>34 weeks/2.1kg</td>
<td>Clinical features, radiograph and autopsy</td>
<td>Live birth died 24 hours after birth</td>
</tr>
<tr>
<td>Kocherla K et al</td>
<td>26 weeks</td>
<td>Sonogram, radiograph and clinical features</td>
<td>Dead fetus</td>
</tr>
<tr>
<td>Sharma D et al</td>
<td>37 weeks 4 days</td>
<td>Clinical features</td>
<td>Still born</td>
</tr>
<tr>
<td>Hegade VP et al</td>
<td>30 weeks</td>
<td>Clinical features, radiograph, CT Scan and autopsy</td>
<td>Still born</td>
</tr>
<tr>
<td>Maratad DM et al</td>
<td>17 weeks</td>
<td>Sonogram, radiograph and clinical features</td>
<td>MTP</td>
</tr>
<tr>
<td>Durga R et al</td>
<td>26 weeks</td>
<td>Sonogram, radiograph and clinical features</td>
<td>MTP</td>
</tr>
<tr>
<td>Yuvraj MF et al</td>
<td>26 weeks/600g</td>
<td>Sonogram and clinical features</td>
<td>MTP</td>
</tr>
</tbody>
</table>

CONCLUSION

This case is being reported for its rarity and for high importance of early booking and anomaly scan. Good quality antenatal sonography can detect foetuses with features of TD in utero and further confirmation can be obtained by genetic sequencing and mutation analysis of FGFR3 gene. Early diagnosis of TD is important since it gives alternative options of termination of pregnancy when an affected foetus is detected.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES
