ORIGINAL RESEARCH PAPER

Obstetrics & Gynaecology

A RARE CASE REPORT OF THANATOPHORIC DYSPLASIA

KEY WORDS:

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ABSTRACT

Thanatophoric Dysplasia (TD) is a congenital and sporadic skeletal dysplasia, the most lethal of its kind, caused by new mutations in the FGFR3 gene.This report describes a 30-year-old primigravida patient with six months of amenorrhea. A targeted imaging for fetal anomaly (TIFFA) scan revealed an anomalous fetus with features suggestive of TD, a rare and lethal condition. With informed consent, the pregnancy was terminated, and the dysmorphic appearance of the fetus confirmed TD as the likely diagnosis. This case highlights the rarity of TD and underscores the importance of early prenatal care and anomaly scans. Early diagnosis is crucial as it provides the option of pregnancy termination when an affected fetus is detected.

INTRODUCTION:

Its Greek term "Thanatophoric" the word coined by Pierie Maroteunx & his coworkers. Its lethal form of dwarfism, FGFR3 gene mutation, autosomal dominant inheritance, pathologically diminished proliferation of chondrocytes and poor columnization of zone of proliferation. Incidence is 1 in 20000 to 50000 live births.

CASE REPORT:

A 30 year old patient, primi with history of 6 months of amenorrhea, came for antenatal visit for the first time . Prior antenatal visits done in PHC.Patient was 24-week period of gestation as per the dating scan.. Antenatal profile was done and was normal. General examination was uneventful. On per abdomen examination, uterus corresponds to 22-24-week gestational period, relaxed, FHR heard on auscultation.

Other Systemic examination : CVS/RS/ CNS- normal.

Investigations :

Hb- 12gm% TC- 10200 PL-2.211/mm; BG -B positive ; UR - Normal; Serology - Non reactive Coagulation profile- normal; RBS -85mg/ dl TSH- 2.05 microgram/dl;

On USG: A single live intrauterine fetus of 24 week of gestation with features of suggestive of Thanatophoric Dysplasia type 1.

Placenta-fundal posterior grade 2, AFI- 15 cm, EFW-600 gm
With features of
- macrocephaly with small cranial bone, (fig 1)
-narrow thorax noted with curved ribs, mild cardiomegaly ,
- fetal long bone of hands & legs are short & curved, (fig 2)
- b/l club foot and club hand.

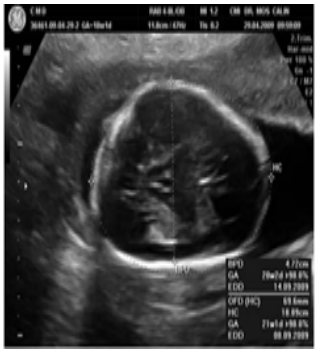

FIGURE 1

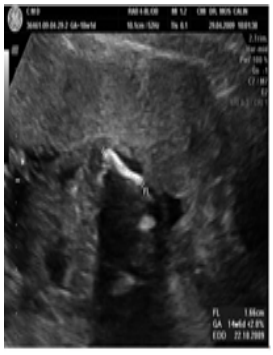

FIGURE 2

MANAGEMENT:

The couple is counselled about the diagnosis and its prognosis and need for termination. Termination of pregnancy was done by T.Mifepristone 200 mg p/o , followed by foleys induction next day. Folleys expelled after 12 hours,followed by delivering a fresh dead male fetus with placenta in toto, birth weight of 800 gm. Breast binding was advised and Tab Cabergoline 0.25mg two doses 12 hrs apart was given.

GROSS EXAMINATION:

(fig 3) Baby had macrocephally with hc- 20 cm. anterior & posterior fontanelles were wide open & sutures were separated.cFace was coarse & edematous with frontal bossing, mid facial hypoplasia, depressed nasal bridge, low set of ears& short neck.

- Upper & lower limbs shortened with short stubby fingers& deep skin creases
- Thorax was narrow but abdomen was protuberant. Spine was normal.
- With facial features & sketal abnormalities the diagnosis of thantophoric dysplasia type 1 was made.
- Infantogram was done, showing short femur and humerus . (fig 4)
- Fetal autopsy was not done as patient did not give the consent.

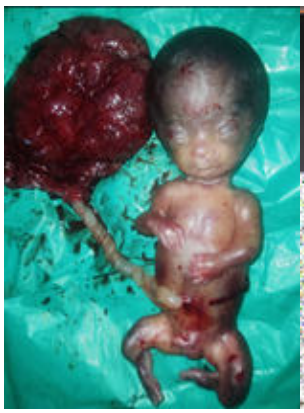

FIGURE 3

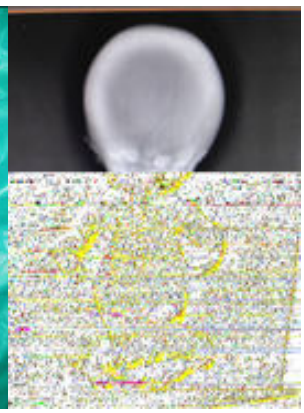

FIGURE 4

DISCUSSION:

Thanatophoric Dysplasia (TD) is a congenital, sporadic and usually lethal skeletal dysplasia at birth characterized by micromelia, small conical thorax, platyspondyly (flat vertebral bodies) and macrocephaly. TD is caused by de novo autosomal dominant mutations in the fibroblast growth factor receptor 3 (FGFR3)gene, which has been mapped to chromosome band 4p16.3. Fibroblast growth factors which are associated with cell growth, bind to the FGFR3 receptor and activates a signal transduction pathway that regulates

endochondral ossification by inhibition of cell division and stimulation of cell maturation and differentiation. Mutations in the FGFR3 gene give rise to activation of the receptor in the absence of growth factors, thus causing abnormal long bone development . It has been recently proposed that mutated FGFR3 induces premature exit of proliferative cells from the cell cycle and their differentiation into pre hypertrophic chondrocytes thus ascribing to the defective differentiation of chondrocytes the main cause of long bone growth defects in TD I There are two subtypes, which are differentiated by the skull shape and femur morphology.[3]

Type I - 80% , most common, characterized by curved and short femur, telephone receiver like configuration and no cloverleaf shaped skull , abdomen is protrubent compare to narrow chest.

Type II - 20%, have cloverleaf skull (trilobed skull) due to premature closure of coronal and lambdoid suture.

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, brachydactly (short broad tubular bones in hands and feet), redundant skin folds along the limbs.[4]

Prenatal diagnosis can be confirmed by molecular analysis of the mutation in FGFR3 gene extracted from fetal cells obtained by amniocentesis or chorionic villous sampling. Chromosomal analysis and DNA molecular testing for FGFR3 can be done in suspected cases of TD but it was not cost effective in our case because almost all cases of TD are caused by new mutation in the FGFR3 gene and occur in people with no history of the disorder in their family. Affected individuals never survive so disorder never passes to next generation. Recurrence risk is also not increased over that of the general population as it is a de novo mutation.[4]

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, brain stem compression by the narrow foramen magnum or a combination of both. Surviving neonate is almost always ventilator dependent and mentally deficient.[5]

Postnatal autopsy of the affected fetus shows disorganized chondrocytes columns, poor cellular proliferation, lateral overgrowth of metaphysis, and increased vascularity of cartilage . Autopsy to confirm the diagnosis by histopathology could not be performed in our case as consent was not given by the parents.

Differential diagnosis of TD includes homozygous achondroplasia , achondrogenesis , campomelic dwarfism , rhizomelic chondrodysplasia punctata, severe hypophosphatasia. The presence of a characteristic cloverleaf skull with telephone receiver appearance of humerus and femur with platyspondyly, small conical thorax and a very high mortality differentiates TD from the other causes of severe short stature with micromelia.[6]

CONLUSION:

Thanatophoric dysplasia (TD) is a congenital and sporadic skeletal dysplasia, recognized as the most lethal at birth. Diagnosis is strongly suggested by ultrasonography (USG). Despite the severity, pregnancies with TD can continue into the late third trimester without miscarriage. Confirmation of TD is achieved through prenatal molecular analysis, clinical features at birth, or autopsy.

Most fetuses with TD die in utero; those who survive are typically ventilator-dependent and have significant mental deficiencies. Almost all TD cases result from new mutations in the FGFR3 gene, occurring without a family history, which complicates prenatal screening and diagnosis. Therefore, second-trimester USG is crucial for detecting congenital anomalies, highlighting the importance of anomaly scans during pregnancy.

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