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Thanatophoric Dysplasia: A Case Report and Literature Review

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Abstract **Case Report**

Thanatophoric dysplasia is a lethal skeletal dysplasia characterized by marked underdevelopment of the skeleton and short-limbed dwarfism [1]. The child will present with a short neck, narrow chest, and prominent abdomen. Other anatomical features include a relatively enlarged head with frontal prominence, prominent eyes, hypertelorism, and a depressed nasal bridge. Diagnosis is typically established by ultrasound in the second trimester of pregnancy. In this study, we report a case of this rare entity, emphasizing its anatomical characteristics, anomalies, and clinical profile, along with a relevant literature review.

Keywords: Thanatophoric dysplasia, ultrasound, mutation, lethal.

INTRODUCTION

Thanatophoric dysplasia is a type of lethal neonatal skeletal dysplasia characterized by markedly underdeveloped skeleton and short-limbed dwarfism. It is caused by a mutation in the fibroblast growth factor receptor 3 (FGFR3) gene. Hypochondroplasia, achondroplasia, and thanatophoric dysplasia are reported as different types of mutations in FGFR3, with hypochondroplasia being the mildest form and thanatophoric dysplasia the most severe [2]. Given that the clinical profile of this anomaly is rarely reported, in our case, we will discuss the anatomical characteristics, anomalies, and clinical profile of thanatophoric dysplasia.

OBSERVATION

A 35-year-old patient, G4P3 (3 living children delivered vaginally), with no notable medical history, poorly followed pregnancy, referred to our facility for suspected fetal malformation at 30 weeks and 4 days of gestation based on the last menstrual period. On examination, the patient was stable hemodynamically and respiratorily, normocardic, normotensive, and afebrile.

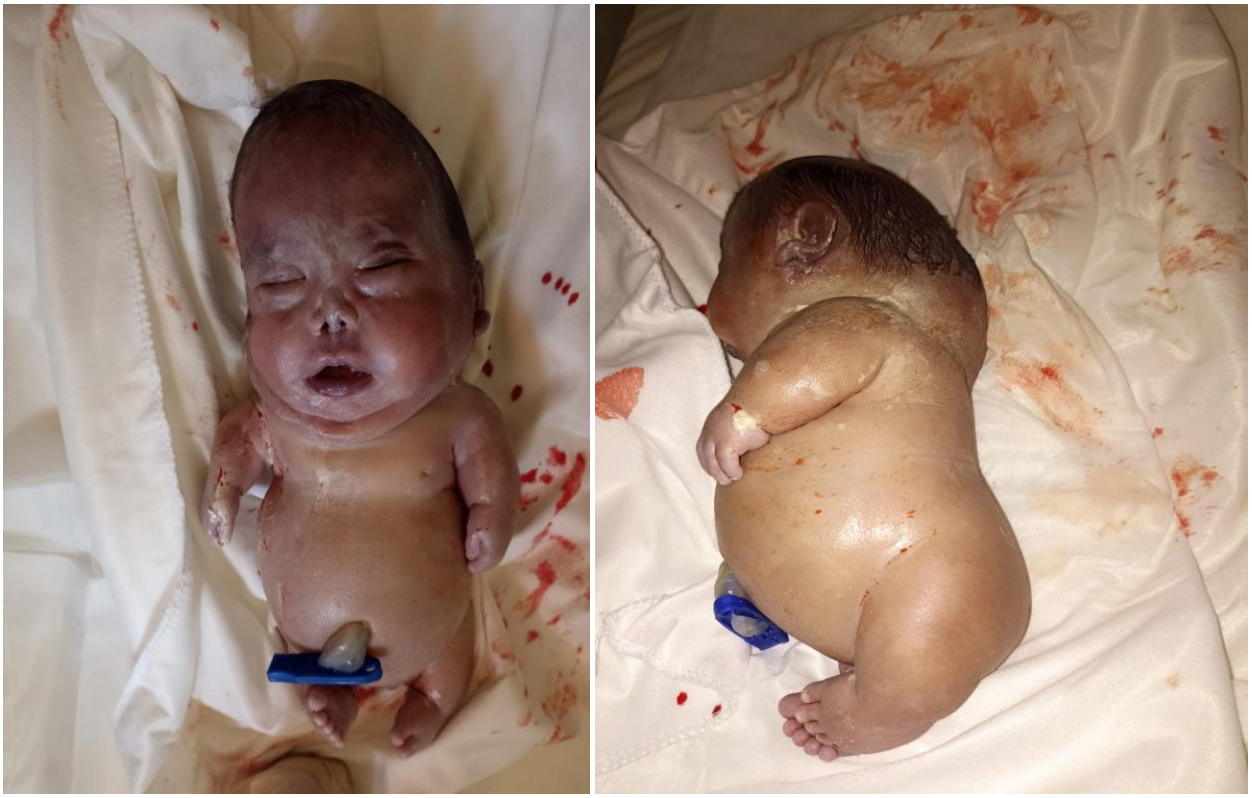
Obstetrical Examination:

Normal uterine height for gestational age, irregular fetal heart rate, and on vaginal examination, a multiparous cervix with intact membranes.

Obstetrical Ultrasound:

Single evolving pregnancy, positive cardiac activity with irregular rhythm, cephalic presentation with slight hydrocephalus and brachycephaly. The ultrasound also noted anterior narrowing of the skull, short ribs, narrow chest, increased nuchal translucency, frontal prominence, short fetal limbs, and a prominent abdomen. Other observed features included the absence of the corpus callosum, flattened vertebral bodies, and a narrow spinal canal. The ultrasound concluded thanatophoric dysplasia with cloverleaf skull deformation.

The patient returned after a week in labor, and a repeated ultrasound showed negative cardiac activity. Subsequently, the patient progressed into labor, delivering a stillborn with multiple malformations: short limbs (upper limbs not reaching the umbilicus), macrocephaly, hypertelorism, flat nasal bridge, prominent occiput, low-set ears, long forehead with midfacial hypoplasia, cloverleaf-shaped skull, short neck, trident hand with brachydactyly, bell-shaped chest, and prominent abdomen. The weight was 2 kg, the head circumference was 35 cm, and the thoracic circumference was 26 cm. The segmental length of the upper and lower limbs was the same, each measuring 4 cm.



Dysmorphic Features of Thanatophoric Dysplasia include macrocephaly, hypertelorism, flat nasal bridge, low-set ears, long forehead with midfacial hypoplasia, cloverleaf-shaped skull, short neck, short limbs, trident hand, bell-shaped thorax, and prominent abdomen

DISCUSSION

Thanatophoric dysplasia, also known as lethal short-limbed dwarfism, is a condition characterized by severe limb shortening (micromelia), bowed limbs, narrow chest, and a prominent abdomen [3]. Other features include polyhydramnios, an enlarged head, frontal bossing, a cloverleaf-shaped skull, prominent eyes, hypertelorism, a small pelvis, and a depressed nasal bridge. Abnormal development of the temporal lobe is a common associated feature that can be visualized as early as the second trimester on ultrasound [1].

There are two types of thanatophoric dwarfism. Type I is characterized by a markedly underdeveloped skeleton and short, bowed long bones, with underdeveloped pelvic bones and spines [5]. The cloverleaf-shaped skull may or may not be present. In contrast, Type II is characterized by long bones that are less short than in Type I and not bowed. Foetuses with Type II often have a cloverleaf skull with trilobed aspects, and premature closure of the coronal and lambdoid sutures is frequently observed [1].

As the name suggests, "thanatophoric," meaning "bringing death," the condition is often lethal in utero or shortly after birth. Respiratory insufficiency is a frequent cause of death, attributed to a narrow thoracic cavity, hypoplastic lungs, compression of the brainstem, or a combination of these factors [4]. Surviving individuals typically require intensive medical support and generally live only into early childhood, facing physical and developmental challenges [4].

Diagnosis is crucial for appropriate genetic counseling and evaluation. The condition is usually suspected through prenatal ultrasound, with confirmation through molecular analysis on amniocytes. While modern obstetric care has reduced the incidence of full-term thanatophoric dysplasia, counseling remains essential for affected families. Proper genetic counseling can help address concerns regarding future pregnancies, emphasizing that the recurrence risk is low for a single affected fetus, and extended family members do not have an increased risk. Prenatal ultrasound examinations in subsequent pregnancies may be offered for early identification of TD features, and if necessary, amniocentesis and molecular analysis can provide a definitive diagnosis.

CONCLUSION

Thanatophoric dysplasia with typical clinico-radiological features is a severe skeletal dysplasia that is lethal in the neonatal period due to significant dysplasia of the thoracic cavity, leading to pulmonary hypoplasia and compression of the brainstem. By raising awareness of such rare and often fatal conditions, the accuracy of prenatal diagnosis can be improved, contributing to genetic counseling and the successful management of pregnancies.

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