ORIGINAL RESEARCH PAPER

Radio-Diagnosis

LETHAL SKELETAL DYSPLASIA WITH ASSOCIATED CRANIAL AND CARDIAC ANOMALIES IN A FETUS OF DIABETIC MOTHER: A CASE REPORT

KEY WORDS: Thanatophoric Dysplasia, FGFR3 Mutation, Skeletal Dysplasia, Micromelia, Reversed End Diastolic Flow.

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ABSTRACT

Thanatophoric Dysplasia (TD) is a congenital, sporadic and most lethal skeletal dysplasia caused by new mutation in FGFR3 gene.We report the case of a 33-year-old G2P1L1 female with diabetes . On antenatal scan, fetus was identified on to have features suggestive of skeletal dysplasia. Serial ultrasonography revealed markedly shortened long bones , cranial and cardiac defects and abnormal doppler parameters. At 33+0 weeks of gestation, a preterm male infant was delivered by emergency caesarean section and presented with severe respiratory distress, micromelia, and dysmorphic features. Despite aggressive neonatal resuscitation efforts, the infant succumbed shortly after birth. The constellation of findings is consistent with a lethal skeletal dysplasia, most likely thanatophoric dysplasia or a related severe osteochondrodysplasia, compounded by maternal diabetes and progressive fetal cardiovascular compromise. This 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.

INTRODUCTION

Thanatophoric dysplasia (TD) is a type of neonatal lethal skeletal dysplasias [1]. It is characterized by marked underdeveloped skeleton and short-limb dwarfism. The name TD is derived from the Greek word which means "death-bearing"[2].

TD is caused by specific autosomal dominant mutations in the gene that codifies for the Fibroblast Growth Factor Receptor 3 (FGFR3), which is located on the short arm of chromosome 4.The mutations constitutively activate the tyrosine kinase activity of the receptor [3]. This activation of FGFR3 results in decreased apoptosis and increased proliferation [4]. It was reported that hypochondroplasia, achondroplasia and thanatophoric dysplasia are the different types of mutation in FGFR3 with hypochondroplasia being the mildest and TD, the most severe form [5].

TD is Divided into Subtypes:

- TD type 1 is characterized by micromelia with bowed femurs and, uncommonly, the presence of craniosynostosis of varying severity.
- TD type 2 is characterized by micromelia with straight femurs and uniform presence of moderate-to-severe craniosynostosis .
- Since the clinical profile of TD was rarely reported, we discuss the antenatal findings of TD in the present report.

Case Report

A 33-year-old G2P1 with history of diabetes and previous lower segment caesarean section (LSCS) underwent a routine anomaly scan at 22 weeks. Transabdominal ultrasonography was performed.

The antenatal scan revealed features of skeletal dysplasia including shortening of all four limbs with percentile corresponding to <1, ventriculomegaly and ventricular cardiac defect. Parents were counselled regarding poor prognosis.The parents opted to continue the pregnancy.

On serial antenatal scans, worsening features including progressive limb shortening, ventriculomegaly and flattening of frontal bone seen.

At 31+0 weeks of gestation , routine scan revealed altered cranial morphology with cephalic index of 96% (brachycephaly), cardiac defects in form of ventricular septal defect and atrial enlargement (first sign for fatal cardiomegaly) (figure-1), narrowing of thoracic cavity (with chest to abdomen circumference of and progressive limb shortening. On doppler examination , there is reversal of end diastolic flow in umbilical artery (figure-2).

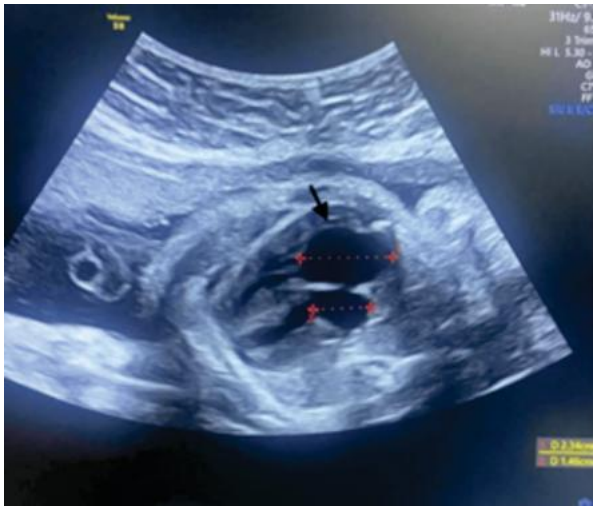

Figure 1: Four Chambered View With Dilated Heart Atrial Chambers, the Arrow Indicates the Dilated Right Atrium (First Sign of Feral Cardiomegaly).

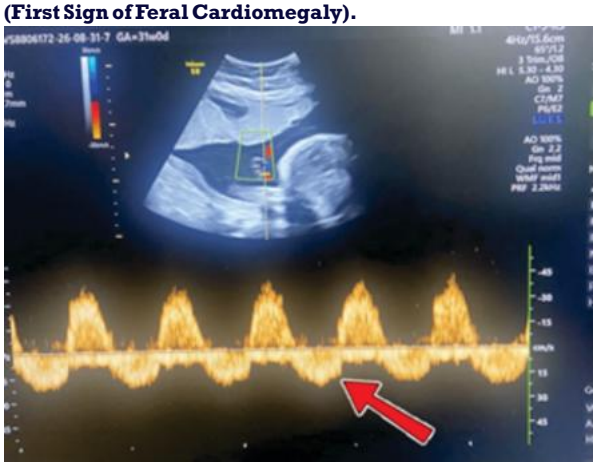

Figure 2: Reversal of Umbilical Artery End-diastolic Flow : Last Stage of Increased Umbilical Artery Resistance, Identified During Antenatal Ultrasonography by Inversion of Blood Flow During Diastole.

Emergency lower segment caesarean section was performed in view of abnormal doppler parameters. Preterm male baby

weighed 1.52 Kg was delivered which had a delayed first cry and respiratory distress. His length is 35 cm which was below 3rd percentile for his gestational age according to Fenton growth charts for preterm boys while his weight was 1520 gm which was about 43rd percentile for his gestational age according to Fenton growth charts for preterm boys. Baby showed dysmorphic features, macrocephaly (head circumference 36 cm which is above 97th percentile for his gestational age) and shortened upper and lower limbs with short fingers (figure-3).

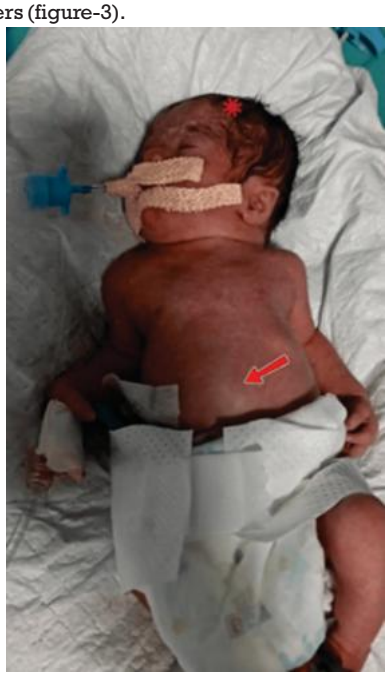

Figure 3: Clinical Photograph of the Neonate - Clinical Phenotype of a Neonate with Thanatophoric Dysplasia Exhibiting Macrocephaly(Asterisk), Short Neck, Short Limbs, and a Protuberant Abdomen (Arrow), Consistent With the Characteristic Dysmorphic Features of the Condition.

He also had a short neck, narrow chest and a protuberant abdomen with chest-to-abdominal circumference ratio = 0.76

Immediate resuscitation including intubation, chest compressions were given. Baby was placed on mechanical ventilation but showed minimal chest expansion and succumbed shortly after birth.

Full-body x-ray (Infantogram) showed macrocephaly, small long bones of limbs, relatively narrow chest and flat vertebral bodies (figure-4).

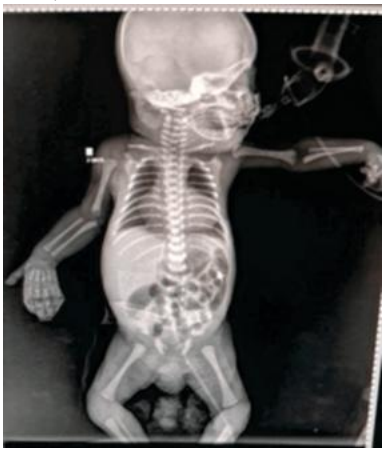

Figure 4: Baby's Radiograph-radiographic Features of Thanatophoric Dysplasia Showing Narrow Thorax, Short Long Bones, Flattened Vertebral Bodies and Macrocephaly.

DISCUSSION

Thanatophoric dysplasia or dwarfism (TD) is characterized by severe limb shortening (micromelia), bowing of limbs, narrow thorax and protuberant abdomen [6]. Other features include polyhydramnios, large head, frontal bossing, cloverleaf skull, prominent eyes, hypertelorism, small pelvis and a depressed nasal bridge. This entity has an estimated incidence of 1 in 20,000 to 50,000 births and is an autosomal dominant condition [7].

Differential diagnoses for severe antenatal limb shortening include achondroplasia and vhypo chondroplasia. A chondroplasia typically presents with less severe micromelia, normal thoracic dimensions and characteristic frontal bossing. Antenatal detection of severe micromelia and a narrow thorax should prompt evaluation for TD.

The present case showed all the classical abnormalities of TD on gross and radiological examination. This case is reported for the rare incidence and probable mode of occurrence and to review in detail the various anatomical abnormalities that are encountered in this anomaly which would aid in the early diagnosis and further work up.

CONCLUSION

Severe micromelia with thoracic hypoplasia (chest circumference < abdominal circumference), ventriculomegaly and frontal bone flattening on prenatal ultrasound strongly suggest a lethal skeletal dysplasia such as thanatophoric dysplasia. Progressive cardiac findings (small VSD evolving to atrial dilatation and reversed end-diastolic flow) signal worsening fetal compromise. In a diabetic mother these anomalies carry a dismal prognosis; early recognition enables timely counselling and avoids futile aggressive neonatal resuscitation.

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