Prenatal diagnosis of thanatophoric dwarfism in second trimester. A case report

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Summary

Thanatophoric dwarfism is a lethal, rare osteochondrodysplasia and results from mutations on the fibroblast growth factor receptor 3 (FBGFR3) gene, on the short arm of chromosome 4. In this paper, we present a case of thanatophoric dwarfism diagnosed in the 18th pregnancy week.

Key words: Thanatophoric dwarfism; Prenatal diagnosis; Ultrasonography.

Introduction

The use of ultrasonography has enabled an important improvement in the prenatal diagnosis of fetal anomalies. The major congenital anomalies can be diagnosed easily by ultrasonography but the diagnosis of rare congenital anomalies requires specific attention and experience of the physician.

Thanatophoric dwarfism is a lethal osteochondrodysplasia and results from dominant new mutations. It occurs with an incidence of approximately one in 20,000-37,000 live births [1, 2]. Mutations on the fibroblast growth factor receptor 3 (FBGFR3) gene, on the short arm of chromosome 4 have been described in cases with thanatophoric dwarfism [3, 4]. Thanatophoric dwarfism can be detected by ultrasonography, but other skeleton system anomalies such as osteogenesis imperfecta, achondrogenesis, achondroplasia and hypocondroplasia must also be taken into consideration for the differential diagnosis [5, 6]. Thanatophoric dwarfism has two subtypes (type 1 and type 2). In the most common subtype, thantophoric dwarfism type 1, femurs are curved, whereas in thanatophoric dwarfism type 2, straight femurs are associated with a cloverleaf skull. The typical ultrasonographic findings of thanatophoric dwarfism are curved or straight short femurs, symmetric tetramicromelia, narrow chest, protuberant abdomen, and relatively large head.

In this paper, we present a case of thanatophoric dwarfism diagnosed in the 18th pregnancy week and terminated in the 21st pregnancy week.

Case Report

A 27-year-old nullipara, nulligravida, in the 18th pregnancy week was referred to our department because of polyhydramnios. Family history of the woman and the partner was uneventful. Ultrasonographic examination showed polyhydramnios, a narrow thorax with short ribs, a protuberant abdomen, short and curved femora (under the 5th percentile), short fingers, and decreased intrauterine movements. The biparietal diameter was 42 mm (the 50th percentile). Facial abnormality and hypertelorism were not detected by ultrasonography.

A maternal serum screening test revealed a low risk for chromosomal anomalies (1/14,000 for Down's syndrome) and neural tube defects (1/22,000). The patient rejected pregnancy termination at the first visit.

The second ultrasonographic examination in the 21st pregnancy week showed a femur length of 18 mm (under the 5th percentile) and a biparietal diameter of 56 mm (50th percentile). Other abnormal ultrasonographic findings such as polyhydramnios, a narrow thorax with short ribs, a protuberant abdomen, short and curved femora short fingers, and decreased intrauterine movements were also present. According to these findings, lethal osteochondrodysplasia was diagnosed and the pregnancy was terminated.

Birth weight of the male fetus was 700 gr. and birth length was 22 cm. The fetus had a short neck, a narrow chest, and a protuberant abdomen (Fig. 1). Symmetric micromelia of all four extremities, short fingers, evident pes equino varus were also present (Fig. 1).

According to the radiological examination, the calvarium was large in proportion to the face.

All of the vertebrae were plattyspondyl and looked like H or reverse U. The costae were short and curved on distal and proximal ends. The clavicula was in the shape of a door-handle. The scapulae and the iliac bones were hypoplastic. All tubular bones were short and the humerus, femur and fibula had an evident curve. According to these findings, the diagnosis of thanatophoric dwarfism was confirmed.

Discussion

Thanatophoric dwarfism is a lethal skeletal system anomaly because of respiratory insufficiency which arises secondary to chest constriction or to foramen magnun stenosis and resultant failure of respiratory control. In some cases, thanatophoric dwarfism is associated with a cloverleaf skull. In advanced pregnancy the relatively large head may cause distocia during labor. Therefore, early diagnosis of thanatophoric dwarfism prevents birth complications in pregnant women.

During ultrasonographic prenatal examination the screening of extremities for lethal skeletal system anomalies should be applied carefully. Discriminant analysis has shown that the femur length is the best biometric

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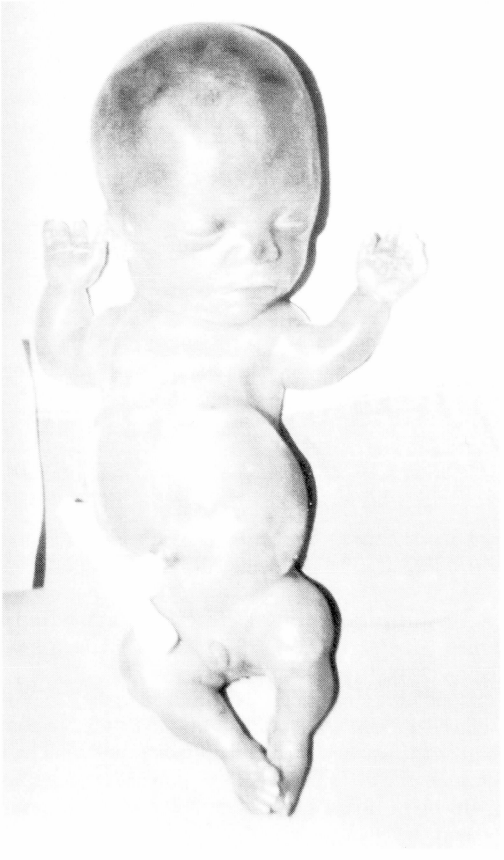

Figure 1. — Postpartum photo of thanatophoric dwarfism case.

parameter to distinguish among the five most common skeletal system anomalies such as thanatophoric dwarfism, osteogenesis imperfecta, achondrogenesis, achondroplasia, and hypocondroplasia [6]. In a multicenter study, Goncalves and Jeanty reported that 78% of the femur measurements between 40-60% of the mean for gestational age have either thanatophoric dysplasia or osteogenesis imperfecta type II [6]. The femur length of the presented case in the 18th as well as in the 21st pregnancy week was under the 5th percentile. We observed no head and face anomalies of the presented case by ultrasonography. Although thanatophoric dwarfism is lethal, some thanatophoric dwarfism cases with long-term survival (5 years and 9 years) have been reported [7] but these cases are alive with tracheostomy and respiratory support and with gastrostomy.

So far as we know, the earliest prenatal diagnosis of thanatophoric dwarfism was at the 18th pregnancy week [8]. We diagnosed thanatophoric dwarfism at the 18th pregnancy week, but pregnancy termination was rejected at the first visit.

The patient was referred to our department by a gynecologist because of polyhydramnios. Polyhydramnios is associated with 30% of fetal development anomalies [5] and was remarkable in the presented case. This shows the importance of an accurate examination of the fetus by ultrasonography, if an abnormal finding is present.

References

[1] Tavormina P. L., Shiang R., Thompson L. M., Zhu Y. Z., Wilking D. J., Lachman R. S., Wilcox W. R. *et al.*: "Thanatophoric dysplasia (types I and II) caused by distinct mutations in fibroblast growth factor receptor 3". *Nat. Genet.*, 1995, *9*, 321.

[2] Martinez-Frias M. L., Ramos-Arroyo M. A., Salvador J.: "Thanatophoric dysplasia: An autosomal dominant condition?". *Am. J. Med. Genet.*, 1988, *31*, 815.

[3] Bonaventure J., Rosseau F., Legeai-Mallet L., Le M. M., Munnich A., Maroteaux P.: "Common mutations in the fibroblast growth factor receptor 3 (FGFR 3) gene account for achondroplasia, hypochondroplasia, and thanatophoric dwarfism". *Am. J. Med. Genet.*, 1996, *63*, 148.

[4] Rosseau F., El G. V., Delezoide A. L., Legeai-Mallet L., Le M. M., Munnich A., Bonaventure J.: "Missense FGFR 3 mutations create cysteine residues in thanatophoric dwarfism type I (TD1)". *Hum. Mol. Genet.*, 1996, *5*, 509.

[5] Gerihauser H., Schuster C., Immervoll H., Sochor G.: "Prenatal diagnosis of thanatophoric dwarfism (Prenatale Diagnose eines thanatophoren Zwergwuchses). *Ultraschall Med.*, 1992, *13*, 41.

[6] Goncalves L., Jeanty P.: "Fetal biometry of skeletal dysplasias: a multicentric study [corrected and republished article originally printed in J. Ultrasound Med. 1994 Oct.; 13 (10), 767-75]. *J. Ultrasound Med.*, 1994, *13*, 977.

[7] Baker K. M., Olson D. S., Harding C. O., Pauli R. M.: "Long-term survival in typical thanatophoric dysplasia type I". *Am. J. Med. Genet.*, 1997, *70*, 427.

[8] Nerlich A. G., Freisinger P., Bonaventure J.: "Radiological and histological variants of thanatophoric dysplasia are associated with common mutations in FGFR-3". *Am. J. Med. Genet.*, 1996, *63*, 155.

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