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CASE REPORT

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Thanatophoric Dysplasia in One of a Set of Dichorionic Twin: A Case Report

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Abstract
Thanatophoric dysplasia is a fatal type of skeletal dysplasia resulting from mutations in the fibroblast growth factor receptor 3 (FGFR3) gene. Several reports of singleton pregnancies affected by this condition in Nigeria and other countries are available in the literature. A case of early second-trimester diagnosis in a set of dichorionic twins had been reported in Korea. To the best of our knowledge, this represents the first documented case in Nigeria of a twin diagnosed with thanatophoric dysplasia following a delayed prenatal ultrasound. This case involved a set of dichorionic twins delivered via caesarean section, in which one twin presented with skeletal abnormalities (shortened limbs) and cardiorespiratory instability. Radiological investigations confirmed the diagnosis of thanatophoric dysplasia. Supportive care, including the use of continuous positive airway pressure, was instituted. This case report highlights the rare occurrence of thanatophoric dysplasia in twins, creating awareness about this rare condition.

Keywords: Dysmorphism, Fibroblast Growth Factor Receptor (FGFR) 3, Prenatal diagnosis, Skeletal dysplasia.

Introduction

Thanatophoric dysplasia (TD) is the most common form of skeletal dysplasia and is lethal during the neonatal period. The incidence is 1.68–8.3 per 100,000 births with no gender predilection.[1,2] The condition is associated with an autosomal dominant point mutation that involves the fibroblast growth factor receptor (FGFR) 3 gene, mapped to the short arm of chromosome 4 (4p16.3).[1,2] Newborns with TD are frequently stillborn or die shortly after their birth, usually within 48 hours of life due to severe respiratory insufficiency arising from reduced thoracic capacity, hypoplastic lungs and respiratory failure due to brain stem compression.[2,3] We report in line with the SCARE criteria[4] a case of dichorionic twin gestation with TD in one baby, which was prenatally diagnosed through ultrasonography in the third trimester.

Case Report

We report a case of TD in the first twin of a set (T1). He was delivered to a 32-year-old Gravida 2, Para 1 (1 alive) mother with no previous history of foetal anomaly. The mother was referred to Sacred Heart Hospital, Lantoro, Abeokuta, Nigeria, from a primary health centre on account of ultrasound findings of abnormality in the first twin at 38 weeks and 6 days gestational age (GA). Ultrasonography revealed diamniotic dichorionic live intrauterine fetuses. T1's measurements included a biparietal diameter (BPD) of 112.5 mm, humeral length of 30.3 mm, femur length of 17.3 mm, and estimated fetal weight (EFW) of 1518g, while the second twin had normal measurements and an EFW of 3342g. The babies were delivered by caesarean section at 39 weeks due to severe pre-eclampsia. The Apgar scores for T1 were 3 at 1 minute and 4 at 5 minutes, with a birth weight of 2.795 kg and body length of 37 cm. Other significant physical abnormalities include macrocephaly (occipitofrontal circumference of 39.6 cm), limb shortening (upper and lower limbs measured 9 and 12 cm, respectively, with an upper-to-lower segment ratio of 0.75:1), a narrow thorax (chest circumference of 27 cm), and bowed limbs. Despite supportive care with maintenance intravenous fluid and respiratory support with continuous positive airway pressure, T1 succumbed to respiratory failure at 38 hours of life. Radiography demonstrated thin flattened vertebrae, short ribs, small sacrosciatic notch, extremely short, long tubular bones, and markedly short and curved femurs (telephone receiver–like appearance) [Figure 1]. A post-mortem examination to ascertain the extent of other systemic involvement was not performed on T1, as the parents declined consent due to their cultural beliefs.

Figure 1: Radiograph of T1 showing features of Thanatophoric dysplasia

Figure 2: Anthropometric disparity between T1 and the second twin

The second twin was healthy, with a birth weight of 3.1 kg and a body length of 50 cm (Figure 2). This case underscores the emotional and counselling complexities of a dichorionic twin pregnancy where one foetus has a congenital anomaly, and the other is healthy, presenting a difficult contrast during a period usually filled with anticipation.

Discussion

Skeletal dysplasia is a genetically and clinically heterogeneous group of disorders of skeletal growth and development.[2] Thanatophoric dysplasia, a member of this heterogeneous family, occurs as a result of a mutation in the Fibroblast Growth Factor Receptor 3 (FGFR3). This mutation leads to increased activation of receptors that alter endochondral ossification along all long bones. This condition is the most frequent lethal skeletal dysplasia caused by FGFR3 gene mutations.[2] There are two types of TD: Type 1 and Type 2. In Type 1 TD, there are curved femurs and flattening of the vertebral body. In contrast, in Type 2 TD, the femur is straight with taller vertebrae, with craniosynostosis and a typical skull deformity (Cloverleaf skull).[5]

The mother of the index case had a first pregnancy, which produced a healthy baby with no obvious anomalies, and she also had no history of exposure to teratogens. Additionally, there was no family history of a similar condition, highlighting its sporadic nature. These factors may explain the delayed diagnosis in the index case, as there were no clinical indications to prompt a targeted anomaly scan, which is not a standard practice in routine antenatal care in every state in Nigeria. She had her first USS at about 12 weeks of gestation and only had a repeat USS at an EGA of 38 weeks, where it was found that one of the twins had short limbs. As in the index case, TD is most reliably detected in the third trimester, when skeletal abnormalities become more evident due to the increased activity of endochondral ossification. Long bones that appear normal at 20 weeks often begin to fall off the growth curve later in gestation.[5,6] The USS findings of the twins being diamniotic and dichorionic may suggest a possibility of being dizygotic; hence, only one foetus was affected by the disorder. The same was also reported by Choi *et al.* in a member of a twin gestation prenatally diagnosed at 15 weeks in Korea.[7] The affected fetus was delivered alive via emergency cesarean section on account of severe pre-eclampsia in the mother; the Apgar scores in the affected baby were 3 at 1 minute and 4 at 5 minutes, while the unaffected twin had scores of 9 at 1 minute, and 10 at 5 minutes. The low Apgar scores may not always be directly related to the asphyxiating nature of the disorder, as higher scores have also been reported in 16 of 20 neonates with TD.[8] The index case exhibited severe respiratory distress, likely due to hypoplastic lungs and resulting respiratory insufficiency, a hallmark feature of TD and the usual cause of death.[9,10]

The index case had severe respiratory insufficiency with persistent hypoxaemia before succumbing to the condition at 38 hours of life. This is consistent with the commonly reported cases of live births. [2,3] It has been reported that neonates with TD may not always die in the early neonatal period but can survive this period with appropriate respiratory management.[2]

The babygram of T1 revealed a curved femur, consistent with Type 1 TD, which is the form associated with most recorded cases of long-term survival and a greater incidence. Although severe disability occurs, it is predicted that the long-term survival of individuals with TD will increase as medical management becomes more efficient.[8]

Limitations of the report

Genetic testing could not be performed on the parents or either of the twins, as we do not have access to such diagnostic facilities.

Parent's Perspective

The parents' responses were as follows: "We are taken aback by this condition in one of our set of twins, but we are happy to have a child to take home after the nine months of pregnancy" and "There are no such problems in our family". However, the grandparents were not available for further details.

Conclusion

Thanatophoric dysplasia is a lethal form of skeletal dysplasia that occurs sporadically, although its inheritance pattern is autosomal dominant. This case report highlights the sporadic and lethal nature of the dysplastic condition. It also highlights the need for routine anomaly scans during pregnancy.

Ethics: The Ethics Committee of the Sacred Heart Hospital, Lantoro. Abeokuta gave ethical approval for this research (approval number SHH/EC/01/07/23). A written informed consent was also obtained from the patient's father for the use of the baby's data and the accompanying images in the research.

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Authors' Contributions: All the authors conceived the study and wrote the draft of the manuscript. OTE, AYT, OIE and ISB did the literature review. DIOF, AOH and ISB revised the draft for sound intellectual content. All the authors approved the final version of the manuscript.

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