A case of thanatophoric dysplasia with Klinefelter syndrome

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Objective

To describe a case of increased nuchal translucency, Non-Invasive Prenatal Test (NIPT) suggestive of Klinefelter Syndrome (KS) and morphological scan compatible with Thanatophoric Dysplasia (TD) with postnatal confirmation.

Methods

This is a case report.

Results

A non-consanguineous young couple was referred to the Fetal Medicine Team during their first pregnancy due to ultrasound alterations suggestive of skeletal dysplasia. Ultrasound scan performed at 12 weeks+5 days evidenced increased nuchal translucency (2. 8mm), which motivated the collection of NIPT, with a result compatible with KS. Second trimester morphological scan with 23 weeks+6 days showed polyhydramnios, frontal bossa, nasal bridge depression, bell-like thorax, short long bones and curved bowed femur, suggestive of TD. Pregnancy evolved with preterm labor, a male newborn was delivered at 27 weeks and 3 days by Ballard, birth weight of 1010g and Apgar 2/3/4. At the delivery room, resuscitation procedures with orotracheal intubation were performed. Physical examination by Medical Genetics Team has shown large fontanelles, with facial dysmorphia (frontal bossa and nasal bridge depression), short and narrow thorax, protruding abdomen and short limbs (mainly proximal segments). Radiographic examination showed a marked reduction of the thoracic cage, ascites, platispondilia and bowed femurs, findings that corroborated the clinical diagnosis of TD. Due to NIPT-compatible KS, we requested a karyotype with G banding that confirmed the diagnosis of chromosomal disease (47, XXY [20]). He evolves to death on the 11th day of life due to respiratory complications.

Conclusion

TD is an autosomal dominant inherited genetic disease caused by pathogenic variants of the FGFR3 gene, usually “de novo”. TD presents an incidence of 1: 33. 000 - 1: 50. 000 live births and is considered the most frequent lethal chondrodysplasia. Death usually occurs in the perinatal period secondary to respiratory failure. and there is no predominance by sex. TD is associated with increased nuchal translucency (NT) at first-trimester screening for aneuploidies. Prenatal detection rate of sexual chromosomal aneuploidies (SCA) is below 50% for all of them, including KS. Some studies have demonstrated that NIPT can be used to identify SCA, but false positives and false negatives results have been reported. Although there are no available report on patients with simultaneous TD and KS. Other skeletal dysplasias, such as achondroplasia, have already been reported in patients with KS.