Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/15846
DOI URL: http://dx.doi.org/10.21474/IJAR01/15846

RESEARCH ARTICLE

CONTRIBUTION OF ULTRASOUND IN THE DIAGNOSIS OF THANATOPHORE DYSPLASIA:ABOUT A CASE IN BAMAKO

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Manuscript Info

Manuscript History
Received: 10 October 2022
Final Accepted: 14 November 2022
Published: December 2022

Key words:-
Thanatophore, Ultrasound, Diagnostic Dysplasia and Bamako

Abstract

Thanatophore dysplasia is a rare lethal bone dysplasia. It is caused bya genetic mutation. There are two subtypes which are very similar in their distinct radiological characteristics and genetic mutations. Early diagnosis is imperative and based on antenatal ultrasound data.We report a case of type I thanatophore dysplasia diagnosed at 32 weeks of amenorrhea and 14 days by a routine antenatal ultrasound in an 18-year-old woman, with no known family malformation history, at the commune II reference health center. of the district of Bamako. The objective of this work is to clarify the contribution of ultrasound in the diagnosis of thanatophore dysplasia.

Introduction:-

Thanatophore dysplasia or thanatophore dwarfism is a congenital malformation, the most common form of lethal neonatal skeletal dysplasia **[1].** It is one of the lethal chondrodysplasias linked to major anomalies in the structure of bone or cartilage, which include the most severe forms of constitutional bone diseases. It is characterized by marked underdevelopment of the skeleton with short limbs. It is a very rare malformation with an incidence of 1.68-8.3% of births **[1].**Thanatophore dysplasia is caused by a mutation of the FGFR3 gene (Fibroblast growth factor receptor 3), located on the short arm of chromosome 4 **[2].** There are two subtypes which are very similar in their radiological characteristics and distinct genetic mutations based on the presence or absence of a "cloverleaf" skull [3] or the presence of curved/straight femurs. Early diagnosis is imperative and based on antenatal ultrasound data **[2].** Postnatal diagnosis of thanatophore dysplasia was based on radiographic abnormalities of the newborn's skeleton. The objective of our work is to clarify the contribution of ultrasound in the diagnosis of thanatophore dysplasia.

Observation:-

It was a woman, 18 years old G1P0 received at the reference center of the commune II of the district of Bamako, for the realization of an obstetric ultrasound. The patient was referred by the gyneco-obstetrics department for prenatal check-up. There was no known family history of congenital malformation or notion of consanguinity. The

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radiological examination was carried out by a Mindray color doppler ultrasound device fitted with two convex and linear probes commissioned in 2010. The ultrasound performed at 32 SA and 4 days revealed a female fetus with a head of normal volume (BIP= 88.8 mm, i.e. 32 SA and 4 days), a poorly developed thorax containing a normal-looking heart with a regular heart rate at 171 beats per minute **(figure 1).**

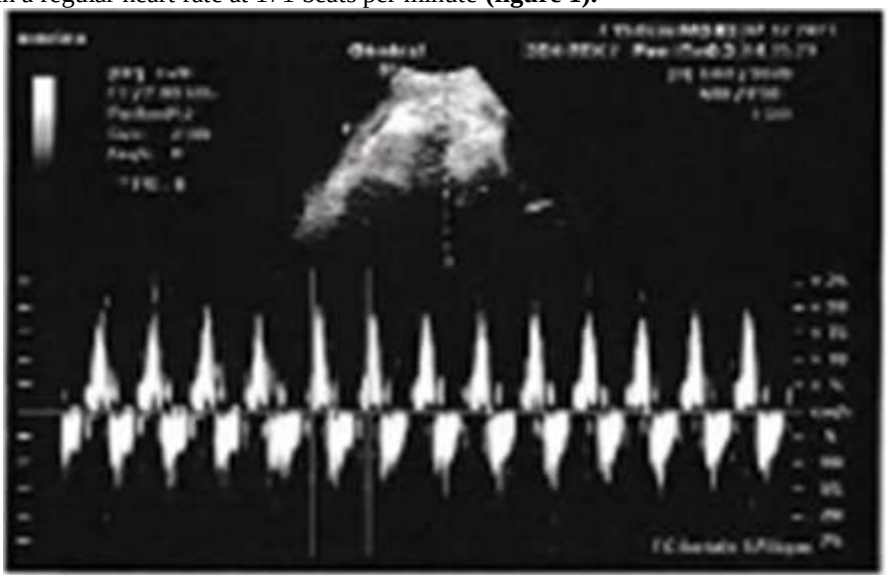

Figure 1:- Regular heart rate (171 beats/min) of the fetus at 32 weeks + 4 days.

A regular thoraco-lumbar spine, an abdomen of normal volume (AC=280 mm, i.e., 32 SA and 1 day) and above all a shortening of the bones of the four limbs with femurs which are curved (LF = 16.8 mm, i.e. 15 SA) and with a BIP/LF ratio =5.28. There was no other associated morphological abnormality. Oligohydramnios was observed (Indexof LA: 25mm) **(figure 2).**

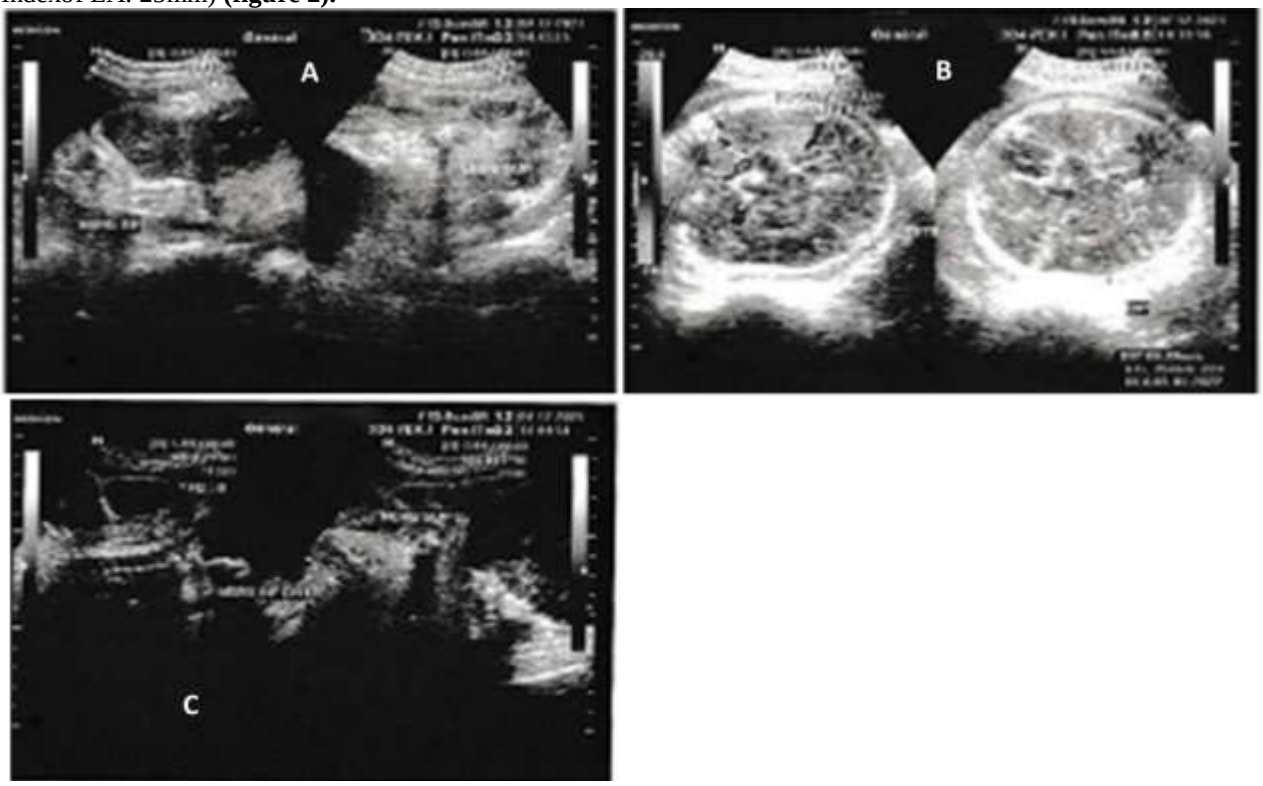

Figure 2:- (A, B and C): Ultrasound sections at 32 weeks and 4 days showing a fetus with shortening of the limbs and oligoamnios (A), skull (B) and spine (C) without abnormality**.**

The diagnosis of thanatophore dysplasia type I was made on these findings and the couple was clearly informed about the fetal pathology. An appointment had been set to perform a scan with the agreement of the patient and her companion for the next day, but unfortunately, she gave birth the day before in a maternity ward in commune I of the district of Bamako of a female fetus with a weight fetus weighing 1127 grams who died immediately after delivery. A photo of the fetus was taken after delivery to confirm the diagnosis of thanatophore dysplasia type I **(figure 3)**

Figure 3:- Photo of a female newborn delivered vaginally, showing shortening of the limbs with thickening of the soft tissues.

Genetic control tests were requested from the couple by gynecologists.

Discussion:-

Skeletal dysplasias are a heterogeneous group of bone growth abnormalities resulting in abnormal shape and size of the skeleton. It is the most common lethal osteochondrodysplasia **[1, 4].** The word "thanatophore", from the Greek, means "bringer of death". This disease has a very high neonatal lethality rate. That is to say, death occurs soon after birth, usually by breathing disorders. In our observation, the fetus died a few minutes after delivery. Cases reaching a more advanced age or even adulthood do exist, but remain marginal **[4].** Thanatophore dysplasia was first described in 1967 by Maroteaux et al**. [5].** It is caused by the activation of the FGFR3 gene located on the short arm of chromosome 4 leading to a negative regulation of bone growth **[2, 4].** The activation of FGFR3 in a majority is due to mutations. The mode of inheritance of this malformation is autosomal dominant but practically all cases of thanatophore dysplasia occur in people without a family history of **[6].**

In our case, there was no history of genetic abnormality in the family which is confirmed by some studies in the literature **[5].** There are two subtypes which are very similar in their clinical characteristics but nevertheless have distinct radiological characteristics and genetic mutations **[4, 7].** Type I accounts for 80% of cases and type II accounts for 20% of cases. The two subtypes can be differentiated radiologically by the morphology of the skull and femur **[8, 9].** Type I, the most frequent, is characterized by macrocrania, a short and curved femur giving the shape of a “telephone handset” **[8,9].** In our observation, it was indeed type I. Fetuses affected by thanatophore dysplasia type II have a cloverleaf skull, the premature closure of the coronal and lambdoid sutures is often the cause of this deformation of the skull. The antenatal diagnosis of thanatophore dysplasia is based on the following ultrasound arguments: a relatively narrow chest cavity, short, thick and curved tubular bones, particularly those of the lower

limbs, thickening of the soft parts of the extremities, a relatively large head with a frontal bump. In our case the ultrasound showed a shortening of the bones of the four limbs with femurs that are curved. The BPD/FL ratio can probably be a useful marker to detect an aberrant abnormality like thanatophore dysplasia even in early pregnancy **[10].**If a BPD/FL ratio is higher, fetal skeletal development should be carefully monitored. The elements which guided the diagnosis in our case are: a narrowness of the thoracic cavity, a shortened aspect of the bones of the limbs with a curved aspect of the femurs and a BIP/LF ratio of 5.28. It can be difficult to establish an accurate diagnosis before the 2nd trimester (22 weeks). Prenatal diagnosis can be confirmed by molecular analysis of the FGFR3 gene mutation extracted from fetal cells obtained by amniocentesis usually performed at 15-18 weeks of amenorrhea or by chorionic villus sampling around 10-12 weeks of amenorrhea **[11**]. The main differential diagnosis of thanatophore dysplasia is achondroplasia, but there may also be osteogenesisimperfecta (we note the presence of a fracture) and achondrogenesis (hypo bone mineralization) **[11].** The life expectancy of newborns affected by thanatophoric dysplasia is estimated at approximately 1 hour after birth by NOE and Al **[4],** who mentioned a few rare cases of survival up to five or eight years. In our study, the newborn with thanatophore dysplasia survived 45 minutes after birth. Sarah and Al had found survival at 1 hour after birth **[3].**

Conclusion:-

Thanatophore dysplasia is an autosomal dominant genetic congenital malformation corresponding to the most frequent lethal neonatal skeletal dysplasia. The morphological obstetrical ultrasound revealed the presence of a short femur with a curved aspect of the femur in "telephone handset" the narrowness of the thoracic cavity and the other shortenings of the limbs which are basic elements of the diagnosis and allow to differentiate it from other causes of micromelic dwarfism. Its early antenatal diagnosis by ultrasound is imperative because it will help obstetricians and parents in making a decision regarding the option of medical termination of pregnancy**.**

Conflict of interest:

The authors all participated in the writing of the manuscript directly or indirectly and declare that they had no conflict of interest

Informed consent:

The couple to give their informed consent for the publication of the case.

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