

Isolated anomalies of the fetal hand – two case reports and a review of the literature

CLAUDIU MĂRGINEAN¹⁾, CLAUDIU MOLNAR-VARLAM¹⁾, LORENA ELENA MELIȚ²⁾, MARIA OANA MĂRGINEAN²⁾, VLĂDUȚ ȘTEFAN BOGDAN SĂȘĂRAN²⁾, DANIEL MUREȘAN³⁾

¹⁾Department of Obstetrics and Gynecology I, University of Medicine and Pharmacy of Tîrgu Mureș, Romania

²⁾Department of Pediatrics I, University of Medicine and Pharmacy of Tîrgu Mureș, Romania

³⁾Department of Obstetrics and Gynecology I, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Abstract

Fetal ultrasonography remains the main diagnostic tool for the assessment of different malformation. Fetal limb anomalies can be either isolated, either associated with other malformations in context of different syndromes. We present two cases of isolated fetal limb anomalies involving the distal part of the upper limb, namely the fetal hand consisting in phalangeal aplasia detected through routine ultrasound fetal examination. We could not identify the etiology in any of the cases, but in one of them, we discovered a bilateral thumb anomaly of the mother's hand. Both fetuses were aborted spontaneously without any relation to the detected anomaly. The upper limb anomaly was confirmed by the clinical, radiological and anatomopathological examinations of the aborted fetuses. The early detection of fetal limb anomalies provides the opportunity of choosing the best therapeutic management. Genetic counseling must also be taken under consideration for further pregnancies.

Keywords: fetal superior hand anomalies, fetal ultrasonography, fingers, phalanges.

Introduction

Prenatal detection and diagnosis of different fetal anomalies are important tools in obstetrics than can lead to an adequate therapeutic decision. Upper limb anomalies are also included in the great amount of fetal anomalies, and once they are detected by fetal ultrasonography, the physician can provide adequate parental counseling, and also they can raise the suspicion of associated malformations and increase the possibility of an early diagnosis. Fetal ultrasonography remains the main tool for the assessment of the fetal morphology and the one that can lead to the early detection different fetal malformations. The specificity of prenatal detection of fetal anomalies through ultrasonography has improved very much in the last decades due to a sum of factors, such as: technological advances, improved resolution, standardization of prenatal ultrasound protocols, and training of physicians [1–6]. It seems that even though the sensitivity of ultrasound detection for different major fetal anomalies is over 70%, the prenatal detection of anomalies involving the fetal skeleton and muscles remain under 50%, between 18–40% [5, 7]. The assessment of the upper superior limb can impose different difficulties for the physician, and the small bone structures of the fetal hand can be even more difficult to assess leading to a sensitivity for potential anomalies detection between 20–30% [6–8]. The prevalence of fetal limb anomalies is reported to be approximately six in 10 000 live births, and the impairment of the upper limb seems to present a higher incidence in comparison to the inferior limb [9]. Also, this type of fetal abnormalities is more frequently unilateral, presenting a higher incidence on the right side in comparison to the left [10]. The development of fetal limbs occurs between the 4–8 gestational

weeks and the primary ossification centers by the 12th week of gestation [11, 12]. The formation of fetal limbs is regulated by different genes, such as: homeobox (HOX) gene family involved in the position of limbs along the craniocaudal axis of the embryo, while limb outgrowth depends on fibroblast growth factor (FGF) genes together with the bone morphogenetic proteins (BMPs). The position in the anteroposterior axis is regulated by the sonic hedgehog (SHH) genes [12, 13].

Limb anomalies can be isolated or they can be associated with other malformations, being just a part of a syndrome or genetic disease. The association of other malformations will enhance the accuracy of detection for fetal limb anomalies [12]. The etiology of fetal limb abnormalities is very complex, involving factors such as: gene disorders, chromosomal abnormalities, intrauterine factors, vascular events, maternal diseases or maternal exposure to different risk factors [12]. Unfortunately, despite the physician's effort to identify the causing factor, the etiology remains unknown in many cases. Anyway, the identification of the etiology it is a key point in the management of further pregnancies. Therefore, an accurate anamnesis leads to a more accurate diagnosis, and enhances substantially the possibility of establishing the etiology. The false negative rates of the upper extremity anomalies can be rendered also by the fact that according to the current fetal imaging guidelines, the upper and lower limbs should be examined during the standard second trimester ultrasonography [14]. Despite this recommendations, it seems that the ideal moment in order to better assess the fetal hands and improve the sensitivity of diagnosis of fetal hand anomalies is at the late first and early second trimester due to the fact that the fingers tend to be extended and abducted, while ultrasound assessments

at a later gestational age are hindered by fetal position and flexed digits [8]. On the other hand, the obstetrician must also take under consideration the possibility of false positive diagnosis in order to prevent a parental misguiding into taking a decision regarding the future of the pregnancy.

Aim

Our paper aims to present two case reports of fetal hand anomalies diagnosed in a Tertiary Department of Obstetrics and Gynecology from Tîrgu Mureș, Romania, in March 2011 and November 2016, respectively. The diagnosis was made by fetal ultrasonography without identifying other associated fetal malformations and without presenting any impact on the evolution of the pregnancy. Moreover, we want to underline that even though the etiology was not identified at the moment of birth, in one of the cases an anomaly of the mother's thumbs was revealed by the clinical exam.

Case presentations

Case No. 1

We report the case of a 21-year-old pregnant woman, admitted in our Clinic in March 2011, at her first pregnancy, who presented in the emergency room for abdominal pain, especially in the hypogastric area, and also lumbar pain with repetitive character during the last five hours. We mention that the patient was not monitored by any obstetrics physician until the present moment. Her family and personal history did not reveal any relevant pathologies (denies chronic or autoimmune disorders in the family, or other congenital malformations). The mother did not present a sign of any viral or bacterial infection during pregnancy, neither had she ingested any drug, toxic (alcohol) during pregnancy and she did not work in a polluted, stressful environment or inappropriate conditions,

being unemployed. The clinical exam revealed a distended abdomen due to the pregnant uterus, with the height of the uterine fundus reaching the umbilical scar, normal basal uterine tonus and painful uterine contractions. The mother's laboratory tests performed at the admission, such as complete blood count (CBC), liver transaminases, glycemia, hemoleukogramme, urine exam were all in the normal range. Performing the vaginal local exam, we noticed minimal modifications of the uterine cervix, without visible loss of amniotic fluid or blood. The next diagnostic step was represented by the abdominal ultrasound, which showed dilation phenomena of the cervical canal and the funneling of the internal cervical orifice. The fetal measurements indicated a gestational age of 23 weeks, and we also observed the lack or hypoplasia of the 2–5 right fetal fingers. The fetal biometry was adequate for the gestational age, and the rest of the fetal structures appeared normal at ultrasound. Even though, we searched for other type of malformations such as renal, cardiac or digestive ones, we did not identify any type at ultrasonography. Due to the increased risk of abortion, we decided to administer tocolytic agents intravenously. The uroculture, bacteriological exam of the vagina, serum iron, serology for congenital infections, thyroid-stimulating hormone (TSH) were all in normal ranges.

Despite our therapeutic efforts, the abortion was imminent after approximately 48 hours. The male fetus weighed 680 g and was without any life signs. Examining the fetus, we confirmed the suspicion raised by the ultrasound exam, the fetus presenting only the first phalange of the 2–5 fingers of the right hand (Figure 1). The aborted fetus was also submitted to an anatomopathological exam, which also confirmed the malformation of the right fetal hand, with the lack of the medium and distal phalanges (Figure 2), and did not identify any other type of malformation.

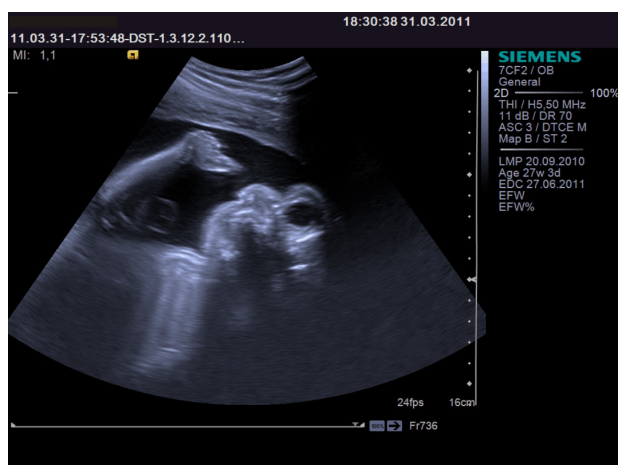


Figure 1 – Ultrasound image of the right fetal hand: it is noticed the presence of a single finger – the pollicis finger, the other four fingers presenting a single phalanx, difficult to be distinguished.

Case No. 2

The second case reveals a 26-year-old pregnant woman, admitted in our Clinic in November 2016, at her first pregnancy, who presented in the emergency room with vaginally hemorrhage. The family and personal history



Figure 2 – First case – macroscopic aspect of right hand of the aborted fetus: the presence of a normal pollicis finger, the other four fingers presenting only the first phalanx.

were not significant for the actual pathology (denies chronic or autoimmune disorders in the family, or other congenital malformations). The mother did not present any viral or bacterial infection during pregnancy, neither had she ingested any drug, toxic (alcohol) during pregnancy and she did not work in a polluted, stressful environment

or inappropriate conditions, the mother having a superior level of education. Regarding the present pregnancy, we must mention that the patient was monitored by an obstetrician specialist from another regional hospital, who raised the suspicion of an anomaly of the right fetal superior limb by performing the regular fetal ultrasound. The mother's laboratory tests performed at the beginning of the pregnancy and later on the 20th week of gestation, such as CBC count, liver transaminases, serum iron, glycemia, TSH, serology for congenital infections were all in normal ranges. Performing a thorough clinical exam of the pregnant patient, we noticed that the thumbs were abnormal, presenting hypoplasia of the last phalanx and a flattened shape (Figure 3).

We also performed an obstetrical exam, which revealed a gestational age of 22 weeks with abortion imminence. The local exam indicated the dilation of the uterine col. Once we performed a fetal ultrasound, we noticed an anomaly of the right fetal superior limb, consisting in hypoplasia of the fingers 2–5 of the right fetal hand. The fetal biometry was adequate for the gestational age, and the rest of the fetal structures appeared normal at ultrasound (without skeletal, renal, cardiac or digestive malformations), except the abnormal described limb.

Due to the signs of abortion imminence revealed by the clinical exam, we tried to cease the contractions by

administering tocolytic agents by vein. Unfortunately, these agents presented no influence on the repeated painful contractions, and the patient presented a spontaneous abortion after 24 hours. The aborted fetus was a male and weighed 530 g, but did not present any life signs. At the fetal examination, we confirmed the anomaly suggested by the ultrasound signs, namely the lack of the middle and distal phalanges of 2–5 right fetal fingers (Figure 4). The macroscopic aspect of the aborted fetus (Figure 5), and the radiological one (Figure 6), confirmed the antenatal diagnosis. The anatomopathological exam identified the distal limb anomaly, without any other type of malformation.

The particularity of the two case reports

The prenatal detection of isolated anomalies of the distal upper extremity through fetal ultrasonography are very difficult and challenging for an obstetrician. Both of the two cases presented above presented phalangeal aplasia diagnosed *in utero*, and confirmed after delivery by the clinical, radiological and anatomopathological examinations of the aborted fetuses. Even though, no etiology could be identified in any of the two cases, for the second case, we identified an anomaly of bilateral maternal thumbs, suggesting a possible genetic involvements.



Figure 3 – Aspect of the maternal thumbs of the second case: hypoplasia of the last phalanx and a flattened shape.



Figure 4 – Second case – 3D aspect of the fetal hand (ultrasonography): a normal pollicis finger, the other four fingers presenting only the first phalanx.



Figure 5 – Macroscopic aspect of the fetal hand (second case) after abortion: right hand with a normal pollicis finger and the other four fingers very short (only the first phalanx).



Figure 6 – Second case – radiological aspect of the right fetal hand after abortion: right pollicis finger with two phalanges, and the other four fingers of the right hand only with the first phalanx.

Discussion

Isolated limb anomalies represent a fetal malformation, relatively difficult to diagnose by ultrasonography *in utero*. The general prevalence of limb abnormalities is of approximately six in 10 000 live births, affecting more commonly the upper limbs, unilaterally, being more frequent on the right side in comparison to the left side [9, 10]. The anomalies encountered in the two cases presented above were also unilaterally, on the right side, namely affecting the right hand. If the limb anomalies are associated with other fetal malformations, their chance of being detected will be higher in comparison to the isolated ones [12]. Both our cases presented isolated limb anomalies, without any other malformations detected by the fetal ultrasonography or the anatomopathological exam of the aborted fetus. In certain cases, three-dimensional (3D) ultrasound can also be used in order to improve the chance of diagnosis. According to several studies, by using 3D ultrasonography, the chance of prenatal detection of hand anomalies can be up to 50% higher [6, 8, 15]. We also used 3D imaging in order to establish a more accurate diagnosis. Regarding this topic Kennelly & Moran stated that 3D ultrasound can be used either to confirm the anomalies detected by the standard ultrasonography, but it can allow the diagnosis of additional anomalies [15]. Hata *et al.* compared the two-dimensional (2D) imaging with the 3D one in a study performed on 97 healthy fetuses and concluded that 3D ultrasonography showed greater details when assessing the fingers and toes than 2D ultrasonography [16]. Similarly, in a study performed on 72 fetuses, the authors found that 3D ultrasound was most useful in order to visualize with a higher accuracy the bony structure of the fingers and toes, as a result of the ability to rotate the volume box in order to achieve the best view of the digits [17]. Another essential utility of the 3D ultrasonography is the possibility to achieve real time images that provide a better understanding of the fetal anomaly for the parents or other physicians leading therefore to a correct decision regarding the evolution of the pregnancy based on comprehensive information provided by a multidisciplinary team.

The prenatal detection of musculoskeletal anomalies, especially of the distal parts of the upper limb represented always a challenge for an obstetrician/sonologist. Therefore, a study performed in 1992 found an ultrasound sensitivity for detecting isolated anomalies of approximately 15%, and 48% for multiple anomalies when performing the second trimester prenatal ultrasound [2]. A more recent study, performed in 2005 on 4366 fetuses concluded that the prenatal detection rate for both, upper and lower limb reduction defects was of 34% [5]. Nevertheless, the diagnosis will be more accurate in the presence of other anomalies, thus Stoll *et al.* found that the chance of prenatal detection of limb reduction defects with associated malformations is approximately twice (49%) higher in comparison to isolated limb reduction defects (25%) [18]. The same author underlined also the fact that the detection of proximal limb reduction defects is much better than of the hand or finger [19]. On the other hand, it is also important to mention the possibility of false positive diagnosis. Therefore, Gray *et al.* encountered that of a total of 31% upper extremity anomalies detected prenatally,

only 18% were correctly diagnosed [6]. The accurate diagnosis depends on factors such as patient body habitus, quality of ultrasound machine and operator skills that can lead to the improvement of diagnostic outcome diminishing substantially the false negative or false positive rates [20].

Multiple factors have been incriminated in the etiology of fetal limb anomalies, but unfortunately in case of isolated anomalies, this remains unknown. Nevertheless, certain risk factors have been identified to have an impact on the developmental disorders, such as environmental or occupational exposures [21], medications [22], smoking [23], the use of illicit drugs [24] and alcohol [25], maternal diseases, like pregestational diabetes mellitus [26] and thyroid dysfunction [27] and congenital infections [28, 29]. In the two cases presented by us, none of the factors mentioned above were identified. In fact, we did not encounter any potential risk factor in none of the two cases that could have led to a fetal malformation.

Knowing the etiology, the physician can provide adequate parental counseling regarding the prognosis of their fetus anomaly, and in certain cases, if possible, to provide measures to prevent the recurrence for further pregnancies [12, 30]. In order to enhance the chance of discovering the potential etiology and to provide the parents as many information as possible regarding the prognosis or a possible recurrence, the multidisciplinary approach is essential, involving an obstetrician, radiologist, clinical geneticist, neonatologist/pediatrician, and a pediatric orthopedic surgeon [12]. In order to perform an accurate diagnosis, the physician should be aware of the pregnancy history, of the mother's pathological history (maternal diseases such as diabetes mellitus, hypercoagulability, systemic erythematous lupus, other autoimmune diseases, arterial hypertension), maternal exposure to different teratogens such as drugs, alcohol, cigarette smoke, and also of family history regarding other family members with congenital limb abnormalities or other type of anomalies, mental retardation, recurrent miscarriage, inherited conditions or consanguinity [12].

The prenatal detection of fetal limb anomalies provides essential benefits for both, the parents and the physicians. Regarding the parental benefits, it is very important for them to receive all the information about their child's anomaly and to understand the potential risks and possible therapeutic options in order to decide what is best for them and their offspring. The decision to terminate the pregnancy in case of untreatable conditions presents a high emotional impact on the parents, therefore the prenatal detection must be as accurate as possible. On the other hand, in case of treatable anomalies, a multidisciplinary approach is needed in order to improve the postnatal outcome by providing the best postnatal care [31]. Another important benefit is the genetic counseling due to the fact that certain conditions present a genetic inheritance and in some cases the recurrence rate in further pregnancies is very high. Therefore, the parents must be aware of this fact and they must also be informed regarding the possible prevention methods, and they must also use screening in case of further pregnancies. Once an obstetrician detects a fetal malformation, he is given the possibility to gather a multidisciplinary team and to inform his colleagues about the case in order to provide the parents with the best therapeutic options. In certain cases, the detection of

a fetal anomaly provides to chance to refer the pregnant woman to a tertiary care center for a better neonatal and maternal outcome.

✉ Conclusions

Fetal limb anomalies can be isolated or associated to other fetal malformations and included in different genetic syndromes. Isolated fetal limb anomalies are very difficult to be detected prenatally and their etiology is very difficult to establish. The anomalies of the distal parts of the upper limb are even more difficult to be diagnosed in comparison to the proximal ones. The detection rate is higher in case of fetal limb anomalies associated with other malformations. The early detection of fetal limb anomalies provides the opportunity of choosing the best therapeutic management.

Conflict of interests

The authors declare that they have no conflict of interests.

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Corresponding author

Maria Oana Mărginean, Student, Department of Pediatrics I, University of Medicine and Pharmacy of Tîrgu Mureş, 38 Gheorghe Marinescu Street, 540139 Tîrgu Mureş, Romania; Phone +40720–332 503, e-mail: oanam93@yahoo.com