FETAL CEREBRAL "BORDERLINE" VENTRICULOMEGALY

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ABSTRACT

Ventriculomegaly represents the dilation of the cerebral ventricles above 10 mm, being classified as it follows: mild or "borderline" (10-12 mm), moderate (13-15 mm) and severe (over 15 mm). The incidence varies very much depending on the used technique and the gestational age. The level of choice in order to obtain the most exact measurement of the ventricular diameter is at the level of choroid plexus glomus. The MRI is another method to assess the fetal brain that allows also the evaluation of the cerebral surface. Unilateral ventriculomegaly is caused by the morphologic, physical or functional obstruction of foramen Monro. "Borderline" ventriculomegaly can be associated with chromosomal anomalies, congenital infections, cerebral vascular accidents or hemorrhage, but also other extra-cerebral anomalies. The factors that influence the prognosis of children diagnosed with mild ventriculomegaly are: gender, gestational age, ventricular size, uni- or bilateral impairment, symmetrical or asymmentrical bilateral ventriculomegaly, progression of ventriculomegaly – probably the most important factor of prognosis, regression of ventriculomegaly. The parents must be informed about the fact that there are certain ultrasonographic limitations regarding the differentiation of an isolated "borderline" ventriculomegaly of a ventriculomegaly associated to other occult anomalies that can not be identified initially, in order to take an adequate decision. The control fetal ultrasound is preferable to be performed after approximately 1-2 weeks from the moment of initial diagnosis of "ventriculomegaly".

Keywords: ventriculomegaly, fetal brain, fetal ultrasound, cerebral MRI

DEFINITION AND INCIDENCE

Ventriculomegaly is a congenital pathology that consists in the dilation of cerebral ventricles above 10 mm. Depending on the degree of dilation, this pathology is divided into mild ventriculomegaly, when the size of the ventricles is between 10-15 mm, and severe ventriculomogelay when the size overpasses 15 mm (1-4). Regarding the definition of "borderline" ventriculomegaly, there are controverted studies and data, thus certain authors considered this term as a synonym for mild ventriculomegaly (5), while other concluded that this should be limited to a ventricular size of under 12 mm (6,7). Afterwards, it was introduced the term of moderate ventriculomegaly that supposes a width of the ventricle between 13-15 mm (8). Regarding the cut-off size above which ventriculomegaly should be established, Oggè et al consider that this should be lowered to 9.5 mm (9). In most of the cases, ventriculomegaly is an isolated pathology, if no other associated malformations or markers of aneuploidy are detected at the moment of initial diagnosis (3,5). By definition, this is a temporary diagnosis of exclusion (10).

Incidence

The incidence of ventriculomegaly reported to the specialty literature varies very much due to the technique differences used or to the gestational age of the fetuses included in the study. Therefore, the higher the gestational age is, the higher the prevalence of ventriculomegaly will be. Two studies performed on low-risk populations reported an incidence of 1:50, and 1:1,600, respectively (11,12).

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On the other hand, further studies indicated incidences of under 1% for mild ventriculomegaly, thus: 0.07% (13), 0.15% (14), or even 0.88% (15). Anyway, in most of the studies due to technical difficulties, ventriculomegaly was diagnosed only by the measurement of the lateral ventricle distal of transducer (10). Fetal cranial ultrasound includes mandatory the assessment of lateral ventricles (16).

Ultrasonographic measurements of the fetal cerebral lateral ventricles

Technological limitations of different devices of ultrasonography existent in certain medical centers can lead to an excess of the false-positive diagnosis. Therefore in case of multiple examinations, the physician assesses only the hemisphere distal of transduces, fact that leads to the loss of valuables information regarding the proximal hemisphere and cerebral asymmetry. The settings of the device used are very important, therefore a too strong contrast can lead to overestimating the diagnosis of ventriculomegaly. The frequency for basic evaluations of the cerebral brain are of 3.5-5 MHz, in abdominal scan, but the frequencies of 5-10 MHz used in case of the identification of certain anomalies provide a better resolution. The best level to obtain the most precise measurement of the transvers diameter of the ventricular atrium is at the level of choroid plexus glomus (17,18). There is also a difference of sizes depending on the gender, thus the lateral ventricles present slightly more increased sizes, but significantly statistic, in males comparatively with females (12,19). If there are a lot of controversies in the third trimester regarding the normal sizes of the lateral ventricles, the 2nd trimester, there is a consensus, namely a medium values of approximately 7 mm, with a standard deviation of 1 mm (11,12,19). Guibad et al proposed a standardization of the most indicated level for the measurement of the lateral ventricular, in the section with cavum septum pellucidum and the triangular "V" shape full of spinal fluid of cisterna magna (20). Afterwards, ISUOG defined the minimum necessary recommendation in order to assess the fetal anatomy in the 2nd trimester of pregnancy regarding the aspect of the lateral ventricles (21). Therefore, the multiplanary approach is the most recommended in case of the suspicion of an anomaly of the central nervous system. The transvaginal approach with high resolution provides the best details when the fetus is in cephalic position. The measurement recommended by ISUOG guide, in atrium, at the level of glomus, is reproduced in Fig. 5.

The MRI of the fetal brain is another method to assess the fetal central nervous system that provides additional information in comparison to ultrasonography in certain cases. The advantage of this examination is that allows also to assess the surface of the fetal brain and is preferable to be performed in the 3rd trimester of pregnancy between 30-32 gestational weeks (22–29).

DIAGNOSTIC CHALLENGES

The progression of the ventricular dilation. The studies suggest that the risk of progression of ventricular dilation after the initial diagnosis is of 11-15.7%, with ulterior association of other fetal anomalies that were not initially identified (10,30).

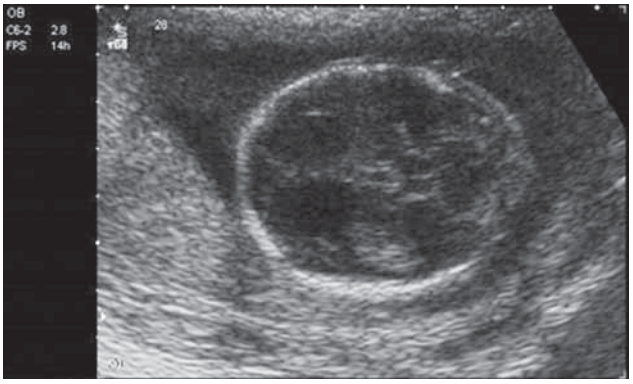

FIGURE 1. *"Borderline" ventriculomegaly at 19 gestational weeks*

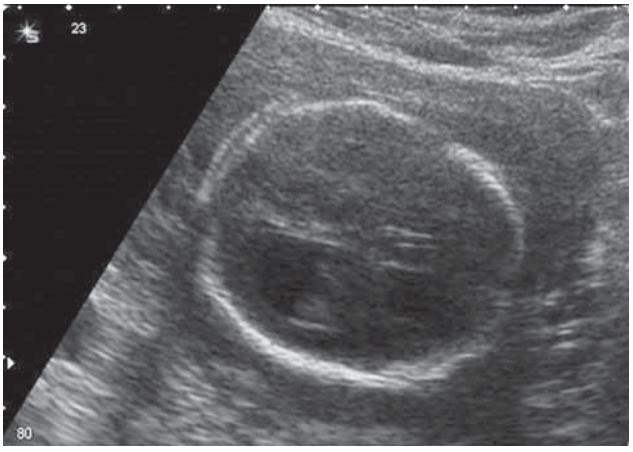

FIGURE 2. *The same fetus at 21 gestational weeks, with progression of ventriculomegaly*

Asymmetry or ventriculomegaly? The asymmetry of the lateral ventricles was reported in case of fetuses and newborns without cerebral pathology (31,32). A certain degree of asymmetry of the lateral ventricles was described in the fetal brain, detectable in utero, but with further normal evolution (33–35). In conclusion, the asymmetry of the lateral ventricles is not equal with ventriculomegaly.

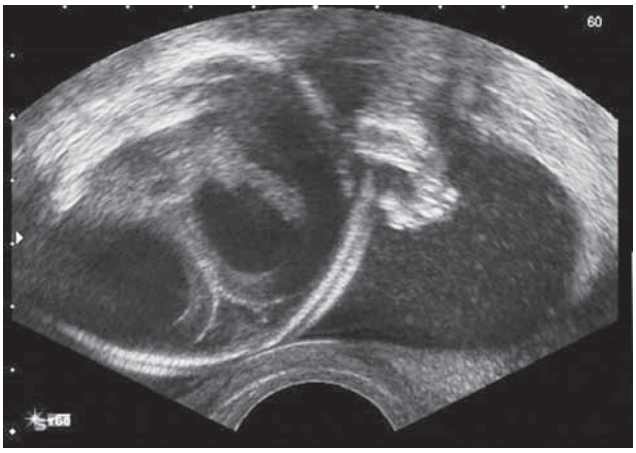

FIGURE 3. *The same fetus at 21 gestational weeks, with progressive ventriculomegaly, transvaginal approach*

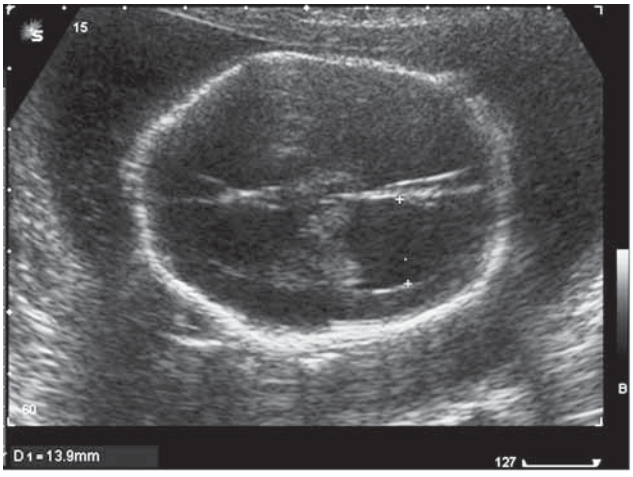

FIGURE 4. *Moderate ventriculomegaly at 21 gestational weeks*

Uni- or bilateral ventriculomegaly? In a study performed on 101 fetuses diagnosed during the intrauterine life with mild ventriculomegaly, assessing both hemispheres, Falip et al identified an incidence of unilateral ventriculomegaly of 60% (36), while Boito et al proved relatively the same frequency of uni- or bilateral ventriculomegaly in the second trimester of pregnancy (26).

ETIOLOGY

Unilateral ventriculomegaly represents the progressive dilation of a single lateral ventricle due to a perturbation of the cerebral spinal fluid flow. The most frequent cause of this circulatory perturbation is represented by the obstruction of foramen Monro. Congenital atresia is another cause. Morphological obstruction of this foramen can be caused by hemorrhage, glioma or vascular anomalies, while physical obstruction can be due to infections or trauma. It was also described the functional obstruction after ventriculostomy due to the valve action in a single way (37).

"Borderline" ventriculomegaly can be associated with chromosomal anomalies, congenital infections, cerebral vascular accidents or hemorrhage, but also extra-cerebral anomalies (10,11,14). Therefore, congenital infections such as those caused by toxoplasma, cytomegalovirus and rubella can be associated with mild ventriculomegaly. Multiple studies proved that "borderline" ventriculomegaly is present in approximately 18% of the cases diagnosed with cytomegalovirus infection (38-41). Autoimmune feto-neonatal thrombocytopenia, even though it has a low incidence, it can lead to intracranial hemorrhage, followed by porencephaly and ventriculomegaly diagnosed before or after birth (42-48). Macrocephaly can also be associated with "borderline" ventriculomegaly (49).

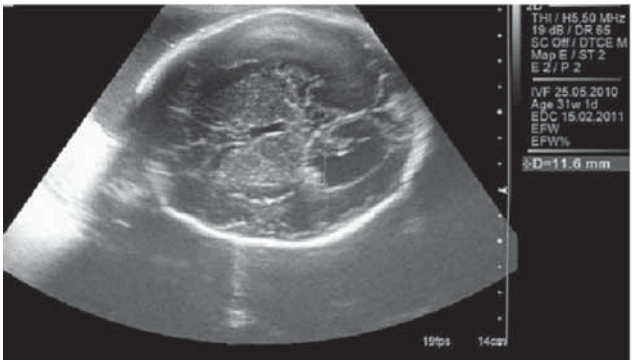

FIGURE 5. *Macrocephaly at 31 gestational weeks, with cranial circumference over 2 standard derivations. The assessment of the lateral ventricle in atrium, at the level of the glomus, of 11.6 mm*

NEONATAL EVOLUTION AND PROGNOSIS

The incidence of retardation in afterwards neurological development of fetuses and newborns diagnosed with mild ventriculomegaly varies very much, but Melchiorre et al report in his review an incidence of approximately 11% and concludes that there are not any clear data to suggest an increased incidence of neuro-psychiatric disorders, such as autism, ADHD, studying disorders or schizophrenia in children diagnosed prenatally with isolated mild ventriculomegaly (10). Also, Beeghly et al suggest that the degree of ventriculomegaly is not associated with afterwards postnatal development, but the motor function is more delayed than the cognitive or adaptive one at the age of 2 years (50). On the other hand, in another study it was identified a positive association between neurological retardation and the degree of lateral ventricles dilation (51). Nevertheless, in a longitu-

dinal study, it was proven that neurological development between 18 months and 10 years is normal in case of fetuses and newborns diagnosed with 'borderline' ventriculomegaly (8,52).

Factors that influence the prognosis. There were described certain factors supposed to have an impact on the prognosis of children diagnosed with mild ventriculomegaly, namely: gender (10,36), gestational age (53,54), ventricular size (3,5,7,8, 30,39), the impairment uni- or bilateral (8,13,30,37), symmetrical or asymmetrical bilateral ventriculomegaly (8,30,36), progression of ventriculomegaly – probably the most important factor of prognosis (10), regression of ventriculomegaly (54,55).

"Borderline" ventriculomegaly – follow-up

According to the French recommendations of "High Authority of Health regarding the management of fetal cerebral ventriculomegaly", the minimum interval before performing a control fetal ultrasound after an initial detailed assessment should of 2 weeks (56), but from our experience, we consider that the control ultrasound should be performed after a week from the moment of initial diagnosis.

Medial counseling in case of a couple with a fetus diagnosed with "borderline" ventriculomegaly

Despite the lack of some clear evidences, the afterwards neurological retardation of fetuses and newborns diagnosed with ventriculomegaly must be always taken under consideration. Therefore, the parents must be informed about the fact that there are certain ultrasonographic limitations in the differentiation of an isolated "borderline" ventriculomegaly and ventriculomegaly associated to certain occult anomalies that can not be identified initially. Performing an fetal MRI is preferable whenever there is a suspicion of other cerebral anomalies. Depending on other unfavorable prognosis factors associated, the decision of a therapeutic abortion must be considered. The gestational age at the moment of diagnosis presents a decisive role regarding the prognosis, investigations, evolution, counseling, and decision. The intrauterine diagnosis or even the suspicion of "borderline" ventriculomegaly must be confirmed and evaluated afterwards by a pediatrician, at approximately 6-7 weeks after birth. In the case where genetic syndromes associated to ventriculomegaly are diagnosed, genetic counseling is necessary in case of future pregnancies.

CONCLUSIONS

The echoghraphic assessment of the cerebral ventricles is usually performed at the time of fetal morphology in the second and third trimester of pregnancy. "Borderline" ventriculomegaly is defined by a ventricular size between 10-12 mm. If possible and if there is an indication, fetal MRI must also be considered, but also chromosomal morphologic analysis. Serologic testing for toxoplasma and cytomegalovirus, but also the detection of anti-thrombocytes antigens must be performed in case of the identification of a cerebral fetal hemorrhage. The neurological retardation in case of fetuses and newborns diagnosed with "borderline" ventriculomegaly is present in approximately 11% of the cases, but with wide variations. The most important factors that influence the prognosis of an isolated "borderline" ventriculomegaly are: the association of other anomalies identified after the moment of initial diagnosis, chromosomal anomalies, infection, autoimmune fetal thrombocytopenia, but also the progression of the ventricular dilation. Therefore, the ultrasound monitoring and/or MRI are the key elements in the assessment of fetuses diagnosed with ventriculomegaly.

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