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REVIEW ARTICLE

Fetal Isolated Ventriculomegaly: Is There any Neonatal Consequences?

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ABSTRACT

Isolated fetal ventriculomegaly is the most common cerebral anomaly encountered *in utero* during a routine pregnancy scan. Ultrasonography remains the most easy to access tool in the examination of the fetal brain, although fetal MRI is a more accurate method of evaluating fetal ventriculomegaly—associated brain anomalies are found in 17% of the cases after performing fetal MRI. Amniocentesis with chromosomal evaluation must be performed, because kariotype anomalies are more frequently encountered in fetuses with enlargement of the ventricular atrium, but the ventriculomegaly can be a cosequence of congenital infection with CMV, Toxoplasma or Rubella. Fetal isolated ventriculomegaly is a significant risk factor for developmental delay in children.

Keywords: Isolated ventriculomegaly, Neurodevelopmental delay, Fetal MRI, Associated anomalies.

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INTRODUCTION

Fetal ventriculomegaly represents an ultrasound finding, most frequently observed on a second semester routine pregnancy examination. It is one of the most frequent fetal brain anomaly, with a prevalence of 1 per 1000 live births by Bromley[1] and Goldstein[2] or even 22 per 1000 live births according to Alagappan.[3] Evaluation of the fetal lateral ventricles is recommended as part of the second semester anomaly scan. It consists in the enlargement of the cerebral lateral ventricles over 10 mm, measured at the level of the atrium—the confluence of the temporal and occipital horns of the lateral ventricles. Ventriculomegaly is often associated with a false shrinkage of the choroid plexus (inability of the choroid plexus to fill the entire cavity of the atrium) and sometimes the choroid plexus may have a 'floating aspect' in severe ventriculomegaly.

The normal dimension of the atrium was established by Cardoza et al[4] who found a mean measurement of the lateral ventricles on the second trimester scan of 7.6 ± 0.6 mm and also introduced a cut-off value of abnormality of 10 mm. The atrial diameter is constant from 14 to 38 weeks of gestation. While an atrial width of less than 10 mm can be considered normal, a value between 10 and 15 mm represents mild ventriculomegaly, and a measurement over 15 mm constitutes severe ventriculomegaly. In some studies, an atrial width of 10 to 12 mm is considered mild ventriculomegaly and a measurement of 13 to 15 mm constitutes moderate ventriculomegaly.

The ultrasound measurement of the atrium of the lateral ventricles should be done in an axial plane of the fetal head, with the calipers positioned at the level of the choroid plexus, inside the echoes generated by the ventricular walls, on an axis perpendicular to the long axis of the lateral ventricle (Fig. 1).

According to Vergani and Pilu,[5,6] ventriculomegaly can be considered isolated if there is no ultrasound evidence of any fetal malformation or markers of aneuploidy at the moment of diagnosis. Isolated fetal ventriculomegaly can be a benign finding but can also be associated with neural tube defects, agenesis of the corpus callosum, cerebral hemorrhage, chromosomal abnormalities, congenital infection (more frequently CMV and Toxoplasmosis) and neurodevelopmental impairment of the newborn.

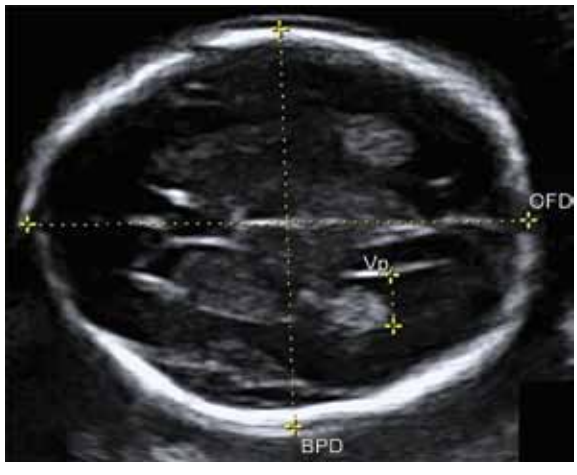

Fig. 1: Distal ventricular atrium measurement (obtained from the personal collection of Prof Dr Radu Vladareanu)

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DISCUSSION

Ultrasound Evaluation of Ventriculomegaly

Ultrasonography is the most frequently used tool for investigating fetuses with ventriculomegaly as it is routinely used in pregnancy evaluation. The diagnosis of isolated ventriculomegaly must be made only after a complete ultrasound evaluation for associated intracerebral or extracerebral anomalies had been performed.

Because fetal ventriculomegaly is most frequently discovered in a routine second trimester pregnancy scan, ultrasonography remains the most easy to access tool in the examination of the fetal brain, so it is recomended to be used in measuring the ventricular atrium every 4 weeks. It is very important to repeat the ultrasonographic examinations because the malformations can also be detected later during pregnancy. The clinical course of ventricular enlargement is also very important for the neurodevelopmental outcome of the newborn, so it is of utmost importance to be able to evaluate repeatedly the dimensions of the atrium (Fig. 2).

In various studies, associated abnormalities in fetuses with isolated ventriculomegaly, have been reported in 10 to 75% of cases.[7-10]

Fetal MRI—Improving the Evaluation of the Associated Anomalies

Fetal MRI adds important information on that obtained by ultrasound, and represents an important way to determine the presence of associated anomalies. Unforunately, it is an expensive investigation and very few medical centers can afford it. Many studies aimed to evaluate the role of fetal MRI in the discovery of associated anomalies in fetuses with isolated ventriculomegaly.

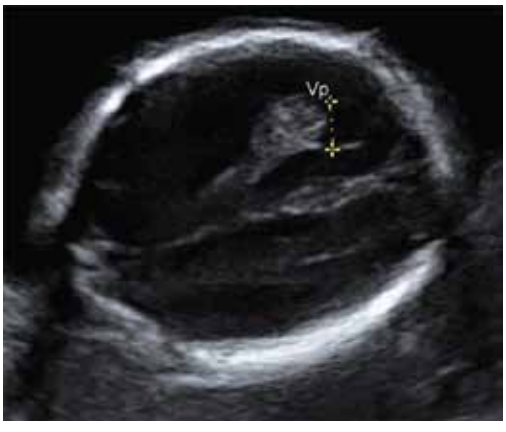

Fig. 2: Proximal measurement of the atrium (obtained from the personal collection of Prof Dr Radu Vladareanu)

Table 1: Case distribution in Ouahba et al[12] study

Normal lateral ventricles	9 (7.3%) cases
Mild bilateral asymmetrical ventriculomegaly	19 (15.4%) cases
Mild bilateral symmetrical ventriculomegaly	33 (26.8%) cases
Mild unilateral ventriculomegaly	62 (50.4%) cases
Ventriculomegaly associated with other brain anomalies—third ventricle enlargement, septum pellucidum destruction, partial agenesis of corpus callosum, agenesis of the cerebellar vermis	15 (12.2%) cases

In one of the most important studies, Griffiths et al[11] showed additional brain abnormalities by performing fetal MRI in 17% of the fetuses thought to have isolated ventriculomegaly. 147 fetuses with isolated ventriculomegaly diagnosed by ultrasound were included in the study and after performing fetal MRI in all the cases, 25 fetuses had associated anomalies. The most common fetal associated anomaly was agenesis of corpus callosum —11 cases. The ventricular atrium was also measured by MRI in all the cases, and the values were compared to the data obtained by ultrasound at the moment of diagnosis. There was complete agreement between the ultrasound and magnetic resonance atrial diameter in 90% of all the cases. In 2 cases with mild ventriculomegaly determined by ultrasound, the MRI examination found normal ventricles; in 9 cases with mild ventriculomegaly, the MRI showed moderate ventriculomegaly; in one case of moderate ventriculomegaly, the MRI diagnosed severe ventriculomegaly. The study showed that there is a relationship between the dimension of the ventriculomegaly and the risk of other brain abnormalities. Fetuses with severe ventriculomegaly had a probability ten times higher than fetuses with mild ventriculomegaly of having other abnormalities, and the chance of other brain abnormalities in fetuses with mild ventriculomegaly is 6%.

In another study, Ouahba et al[12] assessed 123 of 167 cases with isolated mild fetal ventriculomegaly (diagnosed by ultrasound) by fetal MRI between 24 and 39 weeks of gestation. The results (Table 1) show major cerebral anomalies in 15 cases, 4 of them being also revealed by ultrasound monitoring (sonographic evaluation was performed every 3-4 weeks).

Fetal MRI is a very important tool in the assessment of the fetal brain. Simon et al[13] found that 46% of 52 cases of ventriculomegaly needed a different management after performing fetal MRI. In conclusion, fetal MRI should be included in the investigation protocol of the fetuses thought to have isolated ventriculomegaly (diagnosed by ultrasonography) because it can improve the detection of additional brain anomalies and determine significant changes in clinical management.

Prenatal Karyotyping

The term isolated ventriculomegaly means that there is no other anomaly present except the enlarged ventricular atrium. The diagnosis should be made only after performing an extensive search for associated intracerebral or

extracerebral anomalies, including chromosomal abnormalities. The easiest method of determining fetal karyotype is amniocentesis. Van den Hof et al[14] found that mild ventriculomegaly is present in 0.15% of euploid fetuses and in 1.4% of fetuses with trisomy 21, so the risk of aneuploidy is higher in fetuses with ventriculomegaly. Melchiorre et al[15] found that the rate of chromosomal abnormalities in 529 fetuses with ventriculomegaly was 2.8%. In conclusion, although it is an expensive investigation, amniocentesis should be performed in all the fetuses with isolated ventriculomegaly, in order to evaluate the fetal karyotype and to exclude any chromosomal anomalies.

Congenital Infection and Fetal Ventriculomegaly

The most common congenital infections associated with ventriculomegaly are toxoplasmosis and cytomegalovirus infection. The prevalence of congenital CMV infection in newborn infants in the developed world is 0.25 to 2% (approximately 1%), but the rates varies considerably among different populations.[16] Cerebral ventriculomegaly is present in 18% of the fetuses with proven intrauterine CMV infection.[17]

The prevalence of congenital toxoplsmosis varies betwen 1:1000 to 1:10000 live births. The central nervous system is frequently affected: cerebral calcification, ventriculomegaly and cerebrospinal fluid abnormalities.

Screening for Toxoplasmosis and CMV infection during pregnancy is simple, low-cost, safe, and must be done during pregnancy.

Neurodevelopmental Outcome

An important issue is whether the rate of neurodevelopmental delay in fetuses diagnosed with isolated ventriculomegaly during pregnancy is higher than in general population. In United States, the Early Childhood Longitudinal Study Birth Cohort evaluated the development of healthy children aged 9 to 24 months and the results showed that the developmental delay was 13%.[18] Melchiorre et al[15] found that the prevalence of neurodevelopmental delay in fetuses with isolated ventriculomegaly is 10.34% (Table 2).

Table 2: Neurodevelopmental delay in children with isolated ventriculomegaly

Study	*Number of cases with neuro-developmental delay*	*Total number of cases*	*Duration of follow-up*
Ouahba et al[12]	12 (12%)	101	2-127
Breeze et al[21]	4 (19%)	21	4
Signorelli et al[22]	0 (0%)	60	18-120
den Hollander et al[23]	2 (40%)	5	10-18
Vergani et al[5]	0 (0%)	45	3-72
Bloom et al[19]	9 (31)	29	4.2-39

Two important studies evaluated children with confirmed isolated ventriculomegaly at birth using Bayley Scale of Infant Development – II and showed that isolated ventriculomegaly is a significant risk factor for developmental delay.[19,20] Bloom et al,[19] evaluated the enlarged atrium of the distal ventricle and found a developmental delay in 8 of 22 cases with prebirth isolated ventriculomegaly, *vs* one of 22 cases in the control group. Sadan et al[20] evaluated mild unilateral ventriculomegaly in 20 cases and found neurodevelopmental delay in four cases *vs* one of 20 cases in the control group. However, further research must be performed, as both studies evaluated only a small number of cases on a short period of time.

Factors that influence the Prognosis

Ouahba et al[12] found three prenatal factors associated with a poor neurodevelopmental outcome. 24.2% of children with atrial width greater or equal to 12 mm at the moment of diagnosis have a neurological disease *vs* 5.9% in the group with ventriculomegaly lesser than 12 mm. Pilu et al[6] obtained results in the same range: 13.9% of the cases with ventriculomegaly greater than 12 mm had neurodevelopmental delay *vs* 3.8% in cases with atrial width smaller than 12 mm.

Bilateral asymmetrical ventriculomegaly is associated with neurological disease in 50% of the cases, *vs* 10% in the cases with symmetrical ventriculomegaly, and 7.5% of the cases with unilateral enlargement.

In isolated mild ventriculomegaly, the postnatal neurodevelopmental outcome depends on the evolution of ventriculomegaly. Nonprogressive isolated mild ventriculomegaly has a good postnatal prognosis especially if the ventriculomegaly resolves antenatally. In his study, Ouahba et al[12] found 65 fetuses with unilateral asymetrical nonprogressive isolated mild ventriculomegaly. Of these, 6.2% had neurodevelopmental delay after birth, and 93.8% had a normal development.

A very important prognostic factor in isolated ventriculomegaly is the absence of any associated anomalies at the moment of diagnosis.[15]

Postnatal Management and Follow-up

After birth, children diagnosed *in utero* with isolated ventriculomegaly, must be evaluated by the neonatologist and the pediatrician in order to identify any anomalies that may have remained undetected prenatally.[6] Postnatal follow-up should also include an MRI during the first

year of life in order to exclude lesions of the white matter that are not detectable *in utero*. The neurodevelopmental evaluation and follow-up must be performed by some authors at least 6 years of age, using standard scales for evaluation of neorological performance—Bayley scales of infant development (mental and motor),[24] Griffiths scales of mental development (locomotor, personal social, hearing and speech, eye-hand coordination and performance, practical reasoning),[25] Schedule of Growing Skills (passive postural, active postural, locomotor, manipulative, visual, hearing and language, interactive, social and self-care).[26]

CONCLUSION

Isolated fetal ventriculomegaly is the most common cerebral anomaly encountered *in utero* during a routine pregnancy scan. A measurement of the ventricular atrium of less than 10 mm is considered to be normal, while an atrial width of 10 to 15 mm represents mild ventriculomegaly. Careful evaluation of the fetal anatomy should be performed by serial ultrasound evaluation and by fetal MRI as ventriculomegaly is more frequently associated with structural anomalies and delayed neurodevelopment. Fetal MRI must be included in the evaluation protocol as additional brain anomalies are found in 17% of the fetuses with isolated ventriculomegaly.

Amniocentesis with chromosomal evaluation should be performed because kariotype anomalies are more frequently encountered in fetuses with ventriculomegaly but also the ventriculomegaly can be a cosequence of congenital infection with CMV, Toxoplasma or Rubella.

The neurodevelopmental delay encountered in children diagnosed *in utero* with isolated mild ventriculomegaly is about 11%, but further studies must be performed.

The most important factors that affect prognosis are the dimenssions of the ventricular atrium, the bilateral asymmetrical ventriculomegaly and the progressive enlargement of the ventriculomegaly.

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