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MESTRADO INTEGRADO EM MEDICINA

Isolated ventriculomegaly: diagnosis, etiology and pre-natal management

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2020/2021

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Dissertação de candidatura ao grau de Mestre em Medicina, submetida ao Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

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Resumo

A ventriculomegalia é definida como a dilatação dos ventrículos cerebrais num feto, quando não relacionada com o aumento da pressão cerebral. É um achado relativamente comum em imagens do segundo trimestre. Considera-se isolada quando à data do diagnóstico não existem sinais ecográficos de malformações ou alterações cromossómicas associadas. Contudo, a ventriculomegalia pode também ser o primeiro sinal associado a uma variedade de patologias que causam disfunção neurológica, cognitiva e/ou motora.

Após a sua deteção, é necessária uma avaliação pormenorizada do feto para despiste de eventuais anomalias. Tal deve incluir uma ecografia detalhada da anatomia fetal, uma amniocentese para análise cromossómica, o doseamento da alfafetoproteina e da acetilcolinesterase e o despiste de infeções como o citomegalovirus e a toxoplasmose. É também essencial manter um follow-up da grávida ao longo da gestação de forma a avaliar eventual progressão, estabilidade ou resolução do problema.

Um dos grandes desafios da ventriculomegalia baseia-se na dificuldade da gestão da doença e do aconselhamento parental por ser difícil caracterizar o risco absoluto e o grau de deficiência associado à patologia antes do nascimento da criança. Um ligeiro aumento no risco de dano cerebral pode ser causa de grande sofrimento para os pais, levando-os potencialmente a optar pela interrupção da gravidez. Ao mesmo tempo, tal decisão pode representar um dilema para os médicos, já que grande parte dos casos de ventriculomegalia isolada leve e moderada resulta no nascimento de crianças saudáveis. Assim sendo, torna-se de extrema importância saber quando valorizar a ventriculomegalia, evitando potenciais sobrediagnósticos e ansiedade parental.

Esta revisão bibliográfica tem como objetivo organizar e realçar a informação mais relevante presente na literatura atual, de modo a construir um documento esclarecedor no que diz respeito ao diagnóstico, etiologia, prognóstico e monitorização de uma gestação complicada por ventriculomegalia.

Abstract

Ventriculomegaly refers to the dilation of the fetal cerebral ventricles unrelated to increased cerebrospinal fluid pressure. It is a relatively common finding on second trimester obstetric ultrasonography. When isolated, i.e., when there are no additional abnormalities associated, the outcome is usually favourable. However, ventriculomegaly can also be the first sign of a variety of disorders that cause neurologic, cognitive and/or motor impairment.

When an enlargement of the ventricles is identified, a thorough evaluation should be performed, including a detailed ultrasonography of fetal anatomy, an amniocentesis for karyotype and chromosomal microarray analysis as well as testing for fetal infection. Follow-up ultrasound examinations are then crucial to address possible progression, regression or stagnation of the ventricular dilation.

Despite being one of the most frequent brain anomalies, counselling the parents of affected fetuses is still a challenge for the doctor as the aetiology and neurodevelopmental outcome are highly variable and difficult to determine before childbirth.

The aim of this review is to organize and highlight the most relevant knowledge present in current literature, regarding the diagnosis, etiology, prognosis and management of a pregnancy complicated by ventriculomegaly.

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Methodology

A thorough literature search was conducted in two electronic databases, namely *MEDLINE/PUBMED* and *UpToDate*, using the following terms: fetal cerebral ventriculomegaly; isolated ventriculomegaly; prenatal diagnosis; ultrasound; congenital malformations; developmental outcome; neurological outcome; central nervous system. The search was restricted to human studies, published in English.

Some books were also consulted, as well as national and international guidelines.

The literature research was carried out between the months of October 2020 and February 2021.

The articles were selected according to the content of the title and/or abstract.

Introduction

The central nervous system (CNS) is a complex system among fetuses and adults and one of the most common sites of congenital anomalies, second only to cardiac malformations. Such anomalies are of great clinical importance, because they are associated with high rates of fetal morbidity and mortality.

The fetal cerebrum changes dramatically throughout pregnancy. In the early stages the fluid filled ventricles occupy most of the available space, while from week 16 onwards the brain tissue predominates. Ventriculomegaly is a relatively common finding during a routine second trimester ultrasonography at 18 to 22. weeks of gestation but can also be diagnosed in the late second trimester or the third trimester [1]. It is defined as an atrial dilation of the fetal lateral ventricles greater than or equal to 10 mm. Prevalence of ventriculomegaly varies according to different studies from 0.08%-1%, while isolated ventriculomegaly is estimated to affect circa 0,04-0,4% of all newborns. [2] [3] Males are more affected than females in a 1.7 male-to-female sex ratio. [1]

Once diagnosed, the finding should be followed by a systemic analysis of the fetal brain. While a mild increase in the size of the atria can be a normal variant associated with a benign outcome, it can also be a sign of multiple disorders including syndromic, malformative and clastic pathologies, which can lead to neurologic, motor and/or cognitive impairment [4]. Therefore, a full screening with neurosonography, a detailed ultrasonography depicting all organs and systems, a workup for possible fetal infection and an amniocentesis for karyotype and microarray are of great importance. When no abnormalities are found the ventriculomegaly is classified as isolated. In case of a mild isolated ventriculomegaly (10-12mm) the chance of survival without neurodevelopment deficits is >90% [5]. Same doesn't apply to moderate (13-15mm) and severe (>15mm) ventriculomegaly. Generally, the larger the atrium, the greater the probability of an abnormal outcome [6].

The list of differential diagnosis is vast and goes from a benign normal variant to severe pathologies with great impairment. Ventriculomegaly can be caused by two different processes: either by the increased pressure of the cerebrospinal fluid (CSF) due to obstruction flow or increased production of CSF or because of an abnormal development of the brain tissue. [7]

However, there are two considerations that cannot be disregarded. First, there is significant interobserver variability in the ventricles' measurement, specially at borderline diameters.

Second, not all architectural changes are detectable on prenatal ultrasonography and MRI [1]. Therefore, managing the condition and counselling parents proves to be a hard task for the doctors, since the etiology, absolute risk and deficit level are difficult to determine during gestation [8].

Addressing Ventriculomegaly

The ventricular system consists of four connected cavities, namely the right and left lateral ventricles, the third and the fourth ventricle. Within each lateral ventricle there is a choroid plexus responsible for the production of cerebral spinal fluid (CSF). The CSF drains from the lateral ventricles into the third ventricle via paired foramen of Monro and reaches the fourth ventricle through the cerebral aqueduct of Sylvius. From there it passes into the subarachnoidal space through the foramen of Lushka laterally or the foramen of Magendie medially, filling the subarachnoid space of the cisterns and overlying the cerebral cortex or filling up the spinal subarachnoid space respectively. The CSF is then reabsorbed into the superior sagittal sinus through the arachnoid granulations. This allows the CSF to flow from the subarachnoid space, a high-pressured compartment, into the low-pressure venous system [9] [10].

The fetal cerebral ventricles start developing before the 8th week. The lateral ones stem from the telencephalon, the third ventricle from the mesencephalon and the fourth from the metencephalon. From week 7 of gestation the lateral ventricles are depicted as small round vesicles on the ultrasonography while the choroid plexus only becomes visible on the 9th week of gestation [10].

An ultrasonographic examination to observe the anatomy of the fetus is recommended between week 18 and 22 of gestation by the American College of Obstetricians and Gynecologists. At this age, major organs, such as the heart and the brain, can be adequately visualized with sufficient clarity to detect significant malformations. Thus, after week 18 the obstetrician is expected to assess the anatomical components listed in Table I.

Table I Components to be checked after week 18 on ultrasonography. Adapted from the American Institute of Ultrasound in Medicine, 2013.

Head, face and neck	Chest	Abdomen
Lateral cerebral ventricles	Four-chamber view of the heart	Stomach (presence, size, situs)
Choroid plexus	Left and right ventricular outflow tract	Kidneys
Midline falx	Spine	Urinary bladder
Cavum spetum pellucidi	Cervical, thoracic, lumbar, sacral	Umbilical cord insertion into fetal abdomen
Cerebellum	Extremities	Umbilical cord vessel number
Cisterna magna	Legs and arms	
Upper lip	Fetal sex	
Consideration of nuchal fold measurement at 15-20 weeks	In multifetal gestation and when medically indicated	

It is also recommended to estimate the cranial biometric, which depends on two parameters: the head circumference, corresponding to the outer perimeter of the skull, and the biparietal diameter taken from the outer edge of the proximal skull to the inner edge of the distal skull. [11] (Figure 1).

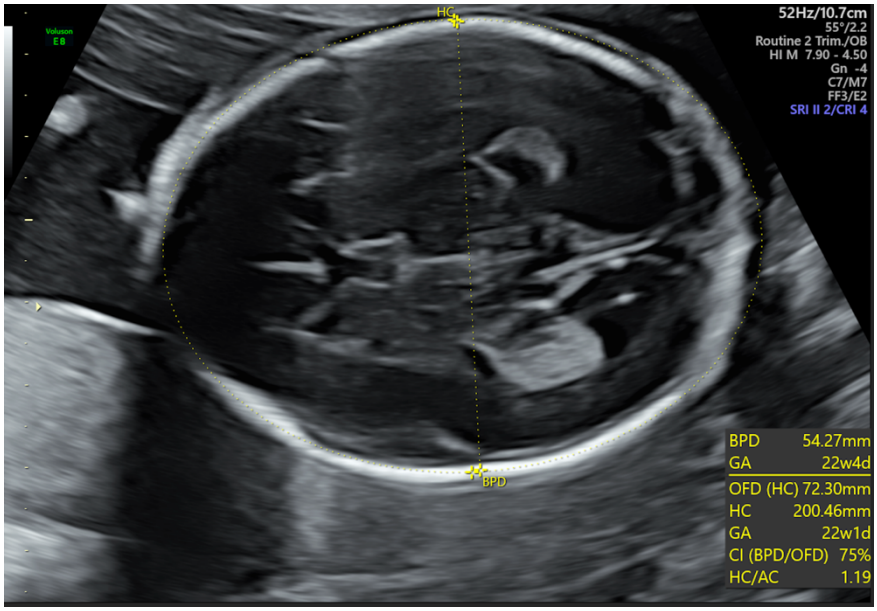

Figure 1 Ultrasonography of a fetal skull. BPD Biparietal diameter; HC Head Circumference. Library picture of Centro Materno-Infantil do Norte, 2021.

There are three standard views used to examine the elements of fetal head: the transventricular, the transcerebellar and the transthalamic view [12] (Figure 2).

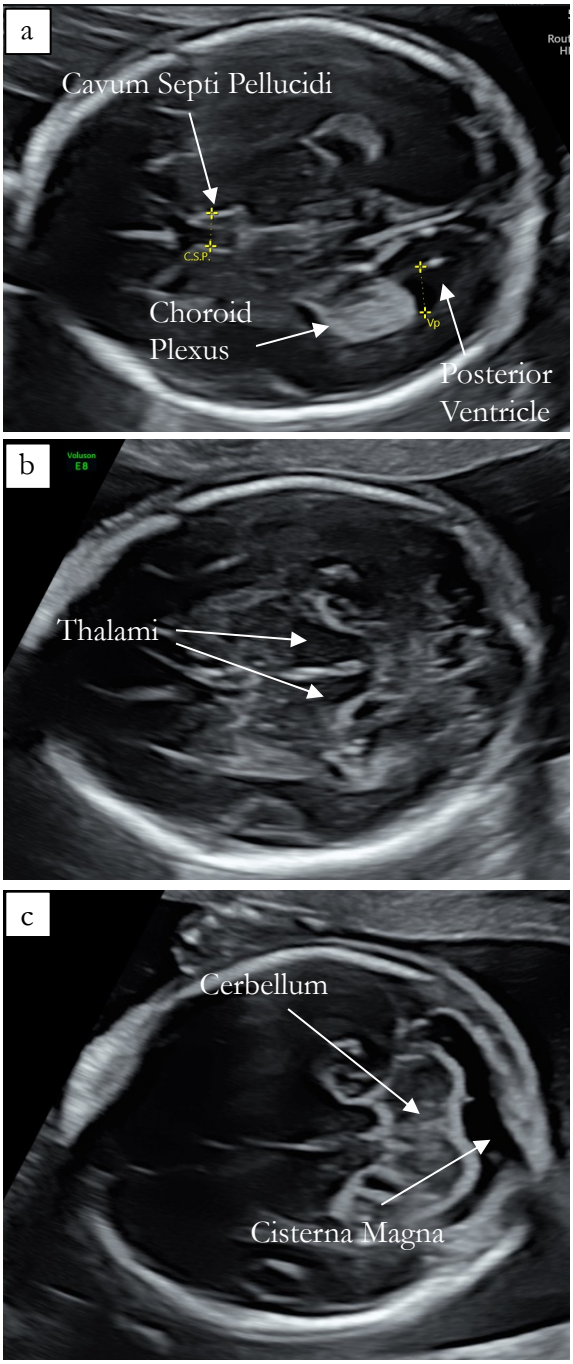

Figure 2 Axial views of the fetal head. (a) Transventricular plane; (b) transthalamic plane; (c) transcerebellar plane. Library picture of Centro Materno-infantil do Norte.

As the name implies, the transventricular view depicts the anterior and posterior horn of the lateral ventricles. The anterior horns are two c-shaped structures filled with fluid. They are separated medially by the cavum septi pellucidi (CSP), a cavity delimited by two thin

membranes. Later in gestation or on the early neonatal period these membranes will obliterate and form the septum pellucidum. The CSP should be always visible between week 18 and 37 of gestation or when the biparietal diameter measures 44-88mm. [13] From week 16 the posterior horn is formed by an atrium which contains the choroid plexus, depicted by an echogenic structure.

As mentioned, ventriculomegaly is diagnosed based on the size of the atria of the lateral ventricles. This is mainly due to three facts:

i. The posterior horn of the lateral ventricles is the first area to dilate and the atrium dilates more than other ventricle regions, such as the frontal horns. This happens because, unlike the anterior areas of the ventricle, the atrium is not constricted by the striatum. [10] [14]
ii. The walls of the ventricular atrium are perpendicular to the ultrasound beam in the transventricular view. Thus, they can be virtually identified in any fetus.
iii. The choroid plexus, an echogenic structure on ultrasonography, is easily identified and serves as a marker for the lateral ventricular wall. When the lateral ventricle is dilated, the choroid plexus appears to fall toward the dependent ventricular wall and is referred as “dangling choroid” [15] . In healthy fetuses the plexus should generally take up to at least half of the ventricle’s area. However, it will take up less than one-half of the CSF space when the ventricle is dilated [16].

The size of the lateral ventricles remains stable between week 15 and 40 of gestation. The mean diameter ranges between 6.2 ± 1.2 to 7.6 ± 0.6 mm [17]. A fetus with an atrial diameter greater than 10 mm is considered to have ventriculomegaly at any stage of pregnancy [18]. The atrium is measured on a transventricular view at the level of the anterior horn and CSP. The cerebral hemispheres should look symmetric on screen. The calipers are then placed on the inner margin of the medial and lateral walls of the atrium at the level of the parieto-occipital groove. Ventriculomegaly is characterized as mild if the atrium measures 10-12 mm, moderate if 13-15 mm and severe if ≥ 16mm. [6]

The Society for Maternal-Fetal summarized the criteria for appropriate measurement of the lateral ventricles (Table II).

Table II Criteria for appropriate measurement of the lateral ventricles. The Society for Maternal-Fetal Medicine, 2018.

Measurement of the lateral ventricles
i. Head is in axial plane
ii. Image is magnified appropriately, so that fetal head fills majority of image
iii. Focal zone is at appropriate level
iv. Cerebral ventricles are symmetric in appearance
v. Midline falx is imaged
vi. Atrium and occipital horn of lateral ventricle
vii. Atrium of lateral ventricle is measured at level of parietooccipital groove
viii. Calipers are placed on medial and lateral walls of atrium perpendicular to long axis of ventricle

However, there is a great variability between observers specially at borderline measures near 10 mm or when other CNS abnormalities are detected, which increases the number of false positive results. Levine et al. concluded in their study that among fetuses referred for ventriculomegaly, there is a 40% discrepancy in opinions on ultrasonography exams and 47% on magnetic resonance studies. Furthermore, when the result between both images did not match, the readers favoring ventriculomegaly recorded larger ventricular diameter by a margin over 2mm in the mean diameter [19]. The consequences of these variations are clinically important, since ventriculomegaly can be regarded as a nonspecific indicator of abnormal brain development, requiring invasive procedures when diagnosed. The diagnosis can also cause significant anxiety for the parents, even when associated anomalies are ruled out or when the karyotype is normal. In fact, the very presence of a subtle deviation from the norm of the fetal cerebral structure raises the idea of brain damage in the minds of most parents. [8] [20]

In addition to the size of the ventricles, the laterality should also be assessed. Fetal ventriculomegaly can be either symmetrical, affecting both lateral ventricles (bilateral) or unilateral. Around 50-60% of cases of ventriculomegaly are unilateral, the rest being bilateral [21] [22]. Nonetheless, the etiology and outcome of unilateral and bilateral ventriculomegaly is similar, making management and counseling of the two mainly the same [23]. It is important to stress that some asymmetry between both lateral ventricles should be considered normal [24]. Asymmetries below 2mm are not associated with an unfavorable outcome when both ventricles are <10 mm. [25]

Unilateral ventriculomegaly should raise the concern of an underlying clastic vascular pathology caused by an ischaemo-hemorrhagic event [26]. Apart from the asymmetry, this pattern usually includes the presence of a hyperechogenic ventricular wall, echogenic

deposits or real clots within the ventricular cavity. In extended ischaemo-hemorrhagic insults the borders of the ventricles are also affected, becoming irregular due to the destruction of the periventricular parenchyma. However, asymmetric ventriculomegaly is not pathognomonic of a clastic lesion. It can also show up in malformative pathologies, such as hemimegalencephaly, which is characterized by unilateral ventriculomegaly and dysmorphic dilated ventricles [27] [28].

Etiology

Ventriculomegaly can be caused by different pathologies, varying from idiopathic to structural or chromosomal abnormalities. Therefore, any diagnosed fetus should be carefully examined for its cause and other associated malformations. Causes of ventriculomegaly can be broadly divided into loss of cerebral tissue (cerebral atrophy), obstruction of the cerebrospinal fluid (CSF) pathway or increase of its production [10].

A loss of fetal brain tissue associated with cerebral atrophy can result in an expansion of the ventricles that will fill the available space in the brain. This can be caused by a variety of diseases, such as metabolic disorders, infections or cerebral infarctions. The dilated ventricles will often look asymmetrical.

The abnormal turnover of CSF can be caused due to an obstruction to its flow or an increase of its production. The type of obstruction can be divided into two groups:

i. If the obstruction is inhibiting the communication between the ventricular system and the subarachnoid space, it is classified as 'noncommunicating' (e.g., stenosis of the aqueduct of Sylvius, Dandy-Walker malformation)
ii. A communicating obstruction allows the connection between the ventricles and the subarachnoid space, i.e., the obstruction is in the arachnoid space (e.g., Chiari malformation, encephalocele, fibrosis due to hemorrhage)

Noncommunicating obstructions can occur at different parts of the ventricular system. The most frequent one is the stenosis of the aqueduct of Sylvius, due to its narrowing, forking or due to the presence of a septum [10]. Aqueductal stenosis can be either genetic or can result from fibrosis secondary to fetal infection (e.g., toxoplasmosis or cytomegalovirus) or bleeding. In some cases, bleedings will also destroy the arachnoid villi, leading to a decreased reabsorption of the CSF, which, in turn, will increase the size of the ventricles.

A mass or a cerebral tumor can also lead to compression of the aqueduct, causing ventriculomegaly. Although rare, some types of tumors, such as the choroid plexus papilloma may lead to an overproduction of CSF with consequent ventriculomegaly. [29] Large isolated choroid plexus cysts may also temporarily dilate the fetal cerebral ventricles. However, they are typically benign and the associated mild ventriculomegaly has usually a good outcome.

About 5% of mild to moderate ventriculomegaly cases are correlated to congenital fetal infections, most commonly toxoplasmosis, cytomegalovirus and Zika virus [30]. Rare cases were also linked to other viruses, such as mumps enterovirus 71, parvovirus B19, parainfluenza virus type 3 and lymphocytic choriomeningitis virus [31]. Congenital infections are responsible for causing cerebral atrophy, aqueductal stenosis due to fibrosis or communicating hydrocephalus due destruction of the arachnoid villi. Some cases of congenital infections lead to common signs on ultrasonography such as fetal growth restriction, periventricular/hepatic and other intraabdominal calcifications, hepatosplenomegaly, echogenic fetal bowel, ascites, meconium peritonitis, polyhydramnios or microcephaly. However, not all infected fetuses show these signs, and some features will only be evident later in gestation. [32]

Finally, ventriculomegaly can also be caused by genetic disorders or malformations. The risk of aneuploidies is higher in non-isolated ventriculomegalies regardless of the degree of dilation [33]. The most frequent genetic disorder is trisomy 21 [34]. Other less frequent diseases include the X-linked idiopathic hydrocephalus, agenesis of the corpus callosum or Dandy-Walker malformation. These conditions are usually associated with more severe cases of ventriculomegaly as well as other extra anomalies that can be seen either on ultrasonography or magnetic resonance imaging.

Post-diagnostic Evaluation

Post-diagnostic evaluation of ventriculomegaly should focus on the following three steps: additional imaging exams to determine if other abnormalities are present, mother's serology to exclude possible infection, diagnostic amniocentesis to exclude potential chromosomal abnormalities and counseling parents on the prognosis and potential further interventions.

In obstetric follow-up, ultrasonography has been the main imaging tool to assess fetal growth and development. The improvements of technology and the increased experience in ultrasound practice have allowed ultrasound imaging to be used for both routine purposes and detailed fetal investigation [35]. As mentioned before, the first suspicion of ventriculomegaly is usually found on the anomaly ultrasound scan during the second trimester. Mothers will then be referred for a more detailed scanning performed by a specialist. Ultrasonographic scanning has been reported to have a sensitivity of 73 to 92% for major abnormalities [36].

The operator is expected to give special attention to the cerebral anatomy, including the lateral, third and fourth ventricles, the corpus callosum, thalami, cerebellum and the cerebellar vermis [32]. It is also important to look for signs of fetal infection, such as calcification, ascites and hepatosplenomegaly. Finally, the ultrasonographic scan should also include an assessment of fetal biometry, in order to look for evidence of eventual growth restriction and an echocardiogram of the fetal heart.

However, the examination of the ventricular system by ultrasonography can be affected by different factors, such as fetal location, position of the brain, skull ossification and technical skills of the operator. All of these can increase the chances of misdiagnosis or missed diagnosis.

Hence, fetal magnetic resonance imaging (MRI) can be used to confirm ultrasound results or to detect additional malformations [37] [38]. According to different studies, the probability of identifying additional malformations on MRI goes from 10% to 76% but appears to be <50% in most studies [39] [40]. It usually depends on the degree of ventricular dilation, the quality of the original ultrasound and whether the previous ultrasonographic scan was performed by an experienced specialist or not [41]. The most frequent abnormality depicted on MRI missed on ultrasonography is the agenesis of the corpus callosum [40] [42]. However,

Salomon et al concluded in their study that the most frequent disagreement between MRI and US is the classification of the degree of ventriculomegaly itself [23].

Fetal MRI has several advantages, including a high soft-tissue contrast, a high-spatial resolution and a wide imaging field [43]. It is not affected by the acoustic shadowing of the fetal skull, amniotic fluid volume, fetal position or maternal obesity, leading to a more precise view of the brain components. Another particular advantage of fetal MRI is that it allows the analysis of gyration, especially in the third trimester of gestation [44]. Thus, fetal MRI has been proved to be particularly useful in cases of fetuses with known infection, hemorrhage or ischemia, since it allows the assessment of the extent of destructive injury. It may also be beneficial when other central nervous system malformations are present. However, the MRI is considered to be unnecessary in cases of detected karyotype anomalies, as these will typically already entail a negative neurological outcome [32].

Nevertheless, if imaging exams depict no other anatomical signs of etiology, further investigation is indicated. Isolated ventriculomegaly has been associated with chromosomal abnormalities, mostly trisomy 21 [34]. Thus, assessment of the fetal karyotype is an essential step of the diagnosis. For over half a century the gold standard method has been the evaluation of the fetal karyotype through chorionic villus sampling until the 13th week of gestation or amniocentesis [45]. It can detect aneuploidies, translocations, large deletions or duplications with a resolution less than 5 to 10 megabases in size. A diagnostic amniocentesis is offered to women ≥ 15 weeks of gestation.

However, it is now known that copy number variants (CNVs) are also associated with poor neurological outcome in fetuses with isolated ventriculomegaly [8]. CNVs are 1 kilobase or greater deletions and duplications which cannot be diagnosed using regular karyotype.

Hence, the amniotic fluid is tested for: chromosomal microarray to detect CNVs; alpha-fetoprotein and acetylcholinesterase to exclude an occult open neural tube defect; Polymerase chain reaction (PCR) for the most common infections; and in selected cases DNA testing for a specific mutation in the L1 spectrum [1].

It's worth mentioning that in many cases of ventriculomegaly caused by infections, the fetus may present other sonographic findings as described before. However, in some cases, the dilation of the ventricles might be the first and only sign. It's important to review the woman's history and look for symptoms suggestive of infection or exposure to potential sources of contamination (e.g., outdoor cats, consumption of undercooked meat). Hence,

TORCH infection screening should be offered to all pregnant women with a diagnosis of isolated ventriculomegaly. It includes testing for Toxoplasmosis, Other (syphilis, parvovirus, hepatitis B, varicella-zoster, Epstein-Barr), Rubella, Cytomegalovirus and Herpes. Maternal serology test should be used as a first step, followed by polymerase chain reaction (PCR) on amniotic fluid in non-negative outcomes (i.e., positive or uncertain result).

In some cases, family history is also evaluated in order to identify a possible existence of L1 cell adhesion molecule (L1CAM) mutations in the family. L1CAM is a neuronal cell adhesion molecule that plays an important role in nervous system development, interfering in cell migration and differentiation. L1CAM mutations are associated to X-linked syndromes, in which other anomalies are usually present, such as hydrocephalus, agenesis of the corpus callosum, Hirschsprung disease or any other intestinal-obstructive diseases, and limb anomalies. Thus, if a severe ventriculomegaly is detected on a male fetus or if the family history is suggestive of any of these disorders, DNA testing for a mutation in the L1 spectrum is recommended [46] [47].

Lastly, it is advisable to perform follow-up ultrasounds after the initial detection of ventriculomegaly to assess stability, resolution or progression [32]. In about 16% of cases ventriculomegaly will progress, which, in turn, will worsen its diagnosis and prognosis [8]; contrarily, stabilization or regression of the size of the atrial diameter are usually positive predictors [34]. It is difficult to determine an ideal timing and frequency of follow-up ultrasound examinations, since it will mostly depend on the etiology of the ventriculomegaly as well as on the initial gestational age at diagnosis. Melchiorre K. et al suggest in their report that at least one additional detailed ultrasound scan should be carried out between 28 and 34 weeks, in order to search for other abnormalities that could not be clearly identified on the second trimester scan [8]. On the other hand, *Centro Materno-Infantil do Norte* recommends an ultrasonography every two to four weeks since the diagnosis of a mild to moderate ventriculomegaly. Additionally, an MRI should be considered on weeks 22 and 32. A stricter protocol is outlined for severe ventriculomegaly, recommending an ultrasound scan every two weeks and an MRI on week 22 and 32.

Counseling

Most of the times the cause of ventriculomegaly cannot be determined in utero and there is a wide discrepancy in outcome of infants with prenatal diagnose of ventriculomegaly. Thus, counseling is always regarded as a big challenge for the doctors.

If the etiology of ventriculomegaly has been depicted on a comprehensive sonographic evaluation or detected on a diagnostic amniocentesis (e.g., agenesis of the corpus callosum, trisomy 21), parents can be given more specific information than in cases where the increase of the atrial diameter is the only marker.

In most studies children with isolated mild and even moderate ventriculomegaly have a normal outcome [48] [49] [50]. It is important that the future parents understand that fully confirming if the ventriculomegaly is isolated is not possible before birth [32]. In a meta-analysis carried out by Pagani G. et al. the rate of neurodevelopmental delay in isolated mild ventriculomegaly fetuses was 7.9%. In 7.4% of them, postnatal imaging depicted undiagnosed findings, some of which with impact on prognosis [48].

The most important prognostic factors in isolated mild ventriculomegaly are the co-existence of other anomalies and the progression of ventricular dilation [8]. According to different studies, the survival rate of newborns with isolated mild ventriculomegaly is approximately 93-98% [33] [34]. The likelihood of a normal outcome is >90% [2] [33]. Thus, it is recommended that after completing a detailed evaluation, women whose fetuses have a ventriculomegaly between 10 and 12mm, be advised of the favourable outcome and that no issues are expected for the child [32] [51].

On the other hand, fetuses with isolated moderate ventriculomegaly are more likely to have adverse outcomes compared to fetuses with mild ventriculomegaly. The survival rate ranges from 80 to 97% and 75 to 93% of the newborns have a normal neurodevelopmental outcome [33] [34]. The Society for Maternal-Fetal Medicine advises that, after a thorough examination, women be counseled that the outcome is likely to be favourable, but that there is an increased risk of neurodevelopmental delays.

When additional abnormalities are found in fetuses with mild and moderate ventriculomegaly, the prognosis depends mostly on the specific pathology itself rather than the degree of ventricular dilation [49]. As mentioned, newborns whose ventriculomegaly has progressed during pregnancy, are more likely to have an adverse outcome.

With regards to severe ventriculomegaly, neurologic, motor and cognitive impairment are more likely. In a meta-analysis carried out by Carta S. et al the survival rate was approximately 88%, but only 42% of these newborns had a normal neurodevelopment. However, it is important to remember that data on the outcome of children with prenatally diagnosed severe ventriculomegaly, regardless of being isolated or not, is scarce. The condition is rare and the rate of termination of pregnancies is high.

Even when all further tests are negative, the doctor should ensure that the parents are aware of the fetus condition and the potential negative outcome in order for them to be able to make an informed and timely decision on the continuation of their pregnancy. In those parents who choose to terminate their pregnancy, evaluation to confirm or assess the etiology is advisable, since identifying a cause can be helpful in determining the recurrence risk in future pregnancies.

Prenatal Management

Despite significant advances in imaging and prenatal diagnostic testing, prenatal care of fetal ventriculomegaly is still very limited.

The timing of delivery is based on standard obstetric indications. If early delivery is being planned in order to improve postnatal outcome, then neonatal and pediatric neurologists and neurosurgeons should be consulted [1]. Most fetuses with ventriculomegaly do not have an increased risk of macrocephaly, therefore, cesarian delivery is usually not required [52]. The parameters to be taken into account when deciding to opt for a cesarean delivery are head circumference, size of the maternal pelvis and gestational age at delivery. For head circumferences above 40cm cesarian section should be considered.

If worsening of hydrocephalus is documented in the last trimester of pregnancy, planned preterm delivery by cesarean section should be considered [53]. However, it is important to mention that the incidence of rapidly progressing ventriculomegaly is low and issues linked with lung maturation in premature babies is more important than the hydrocephaly itself [54].

Furthermore, detailed evaluation and genetic counseling should be given to parents of an affected child to determine potential genetical implications. For example, couples who are at risk for X-linked hydrocephalus spectrum should undergo a DNA diagnosis due to is recurrence risk (50% in males) [1]. If the newborn had a previous diagnosis of isolated mild ventriculomegaly and no other additional abnormalities are identified at birth, then a thorough post-natal genetic work-up may not be indicated in most cases [1]. Parents of an affected child are advised to perform a detailed ultrasound scan at 18 to 20 weeks of gestation in a future pregnancy in order to search for recurrence [55]. However, since in some cases ventriculomegaly may develop just in late gestation, a normal mid-trimester ultrasound does not rule out a potential diagnosis.

Conclusion

Ventriculomegaly is defined as an enlargement of the fetal cerebral ventricles and is a relatively common finding on prenatal ultrasounds. It may be isolated, meaning that the dilation is the only abnormality detected on ultrasonography, or it may occur in the setting of additional anomalies. The latter is usually linked to adverse outcomes.

When increase of the lateral ventricles is identified, an exhaustive evaluation is recommended. It includes a comprehensive fetal ultrasonography, preferably performed by an experienced doctor, an amniocentesis for karyotype, chromosomal microarray analysis, alpha-fetoprotein and acetylcholinesterase and testing for fetal infections, ideally performed by polymerase chain reaction on amniotic fluid. Several studies demonstrated improvements in diagnosis when an ultrasonography and an additional fetal MRI are performed. The latter should be considered, especially in cases of isolated ventriculomegaly in which etiology is unknown and additional information would change counseling and management decisions.

A follow-up ultrasound examination should be performed at 28 to 34 weeks of gestation to assess for progression or regression of the ventricular dilation. Obstetrical management, timing and mode of delivery should be based on standard obstetric indications.

Parental counseling is still a delicate task for the doctor, as the cause, absolute risk and handicap degree cannot be stated with confidence. Even in cases of apparently normal findings, parents must be informed about the possibility that some anomalies can only be diagnosed before or right after birth. Hence, postnatal evaluation and care should be handled by an appropriate pediatric specialist.

As the effectiveness of patient counseling is directly linked to the preciseness of the diagnosis, current research is focusing on improving image analysis in order to rely on prenatal data as a predictor of child conditions at birth.

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