Ventriculomegaly (VM) is defined as an enlargement of the lateral ventricles of the developing fetal brain. Measurement of the size of the fetal cerebral lateral ventricles is recommended as part of the fetal scan routinely performed during the second trimester to screen for fetal anomalies. The measurement is done at the level of the atria of the lateral ventricles filled by the echogenic choroid plexuses, visible in an axial plane of the fetal brain showing also the frontal horns of the lateral ventricles and the cavum septi pellucidi. The calipers are positioned on the internal margin of the medial and lateral walls of the atria, at the level of the glomus of the choroid plexus, on an axis perpendicular to the long axis of the lateral ventricle [14].

An atrial width of <10 mm is considered normal. VM is diagnosed when the width of one or both lateral ventricles, measured according to the criteria described so far, is ≥10 mm. Measurements between 10 and 15 mm constitute mild VM, also defined as borderline (Figure 1); values above 15 mm constitute severe VM. Some authors [27] use the term “milder VM” and “moderate VM” to indicate measurements of 10–12 and 12.1–15 mm, respectively. Other authors [4] restrict the term “mild VM” to measurements between 10 and 12 mm. The most commonly used terminology, however, is “mild VM” referring to atrial measurements between 10 and 15 mm and this terminology will be used in the following discussion.

Mild VM can be bilateral or unilateral [15]. Usually in the screening ultrasound examinations, only the lateral ventricle distal to the transducer is measured as the proximal one is obscured by reverberation artifacts. Efforts should be made in order to visualize both ventricles and recognize unilateral and bilateral mild VM (Figure 2).

Mild VM may be associated with a variety of anomalies (brain malformations, genetic syndromes, chromosomopathies, and infections) or can be isolated. The prevalence of isolated mild VM is extremely variable and has been reported ranging from 0.15% to 0.7% [1, 25].

The finding of mild VM represents a cause of anxiety for the parents and a difficult task for the clinician. In order to offer appropriate counseling, an accurate diagnostic work-up is needed. The diagnostic work-up should include the following steps:

- ruling out for associated anomalies
- ruling out for congenital infections
- ruling out for feto-neonatal alloimmune thrombocytopenia
- ruling out for chromosomal abnormalities
- monitoring the development of mild VM in the progressing pregnancy.

Once the diagnostic work-up is completed an appropriate counseling can be offered to the parents.

**Ruling out for associated anomalies**

Mild VM may be associated with neural and extraneural anomalies. The percentage of association ranges from 10% to 71% with an average value of 41.4% [3, 8, 11–13, 17, 18, 23, 25, 29]. With regard to the central nervous system anomalies, an accurate and systematic evaluation of the fetal brain allows the recognition of several both severe and subtle anomalies [5].

Mild VM may also be the first sign of brain anomalies recognizable only in the third trimester or even after delivery, such as cortical malformations. The mean percentage of anomalies not recognized at the time of the first diagnosis of mild VM is 12.8% [3, 11, 13, 15, 18, 20, 27]. A more recent review of nine studies reporting data on postnatal imaging, showed a prevalence of previously undiagnosed findings of 7.4% [21]. This better result is probably the consequence of the improvements in the prenatal diagnosis of subtle brain anomalies such as agenesis of the corpus callosum.
callosum. Anyway this limitation of ultrasonography in recognizing associated anomalies should be taken in account when counseling the patient at the time of the first presentation of mild VM.

The use of magnetic resonance imaging (MRI) has been advocated as a useful tool in evaluating fetuses with mild VM [2, 19, 22, 26]; it adds important information in 6%–10% of the cases, particularly in recognizing associated cortical anomalies. For this reason the appropriate time to perform MRI is in the third trimester; it must be done by experienced operators in reference centers, following an accurate neurosonography in order to avoid useless request of such a sophisticated and expansive procedure.

Figure 2 Bilateral (A) and unilateral (B) mild VM.

Ruling out for congenital infections

Toxoplasmosis and cytomegalovirus (CMV) infections have been rarely reported in cases of mild VM. A recent review [8] reports a mean percentage of 1.5%. In fetuses with proven CMV infection, VM is the most common ultrasound finding being present in 18% of the cases [10]. Further sonographic signs may be seen both in the brain, such as small periventricular calcifications or small subependimal cysts, and in extraneural structures, such as liver calcifications, ascites, hepatosplenomegaly, echogenic bowel, placentomegaly, and growth restriction [7, 24].

MRI can provide important additional information with regard to subtle cerebral signs of infections, such as abnormal gyration, cerebellar hypoplasia, or abnormal signal in white matter [24]. Although the percentage of association of fetal infections in mild VM is very low, the tests for toxoplasmosis and CMV infections should be performed in all patients with fetuses presenting mild VM, due to the simplicity of execution on the maternal serum.

Ruling out for feto-neonatal alloimmune thrombocytopenia

Feto-neonatal alloimmune thrombocytopenia is a rare condition which can be complicated in 10%–30% of the cases with intracranial hemorrhage and VM [6]. In these cases the VM is usually associated with hyperechogenicity of the ventricular walls or with the presence of
intraventricular echogenic blood clots. Therefore, the search for anti-platelet antibodies is indicated when signs of intracranial hemorrhage are seen at ultrasound.

Ruling out for chromosomal abnormalities

Mild VM has been considered as one of the several so-called “soft markers” of abnormal fetal karyotype. However, the correlation between mild VM and chromosomal abnormalities (mainly trisomy 21) is still a cause of debate. Three reviews report different results: Melchiorre et al. [17] report an average value of 2.8%; Devaseelan et al. [8] report a percentage of 5%; and the recent review from Pagani et al. report an association of 4.7% [21]. The variation in results may depend on the prevalence of trisomies in the studied population, which in turn depends on the previously applied screening programs.

Van den Hof et al. [28] report the presence of mild VM in 0.15% of euploid fetuses and 1.4% of the fetuses with trisomy 21, providing a likelihood ratio of 9. Then the calculated risk will be high in the majority of the cases regardless of the previous low-risk results, thereby justifying the invasive procedure.

Monitoring the development of mild VM in the progressing pregnancy

When the diagnosis of apparently isolated mild VM is done, it is necessary to plan serial antenatal examinations, as there is a possibility of both worsening of the ventricular dilatation and late appearance of associated brain anomalies.

The percentage of appearance of late onset brain anomalies is 12.8% in older reviews [17] and 74% in the more recent review by Pagani et al. [21]. They are mainly represented by cortical malformations. This better result is probably the consequence of the improvements in the prenatal diagnosis of subtle brain anomalies such as agenesis of the corpus callosum.

Mild VM may increase in progressing pregnancy in 15.7% of the cases; it decreases in 34% of cases and remains stable in 55.7% of cases [17].

The timing and frequency of the follow-up in fetuses with mild VM depend on the gestational age at the time of the first diagnosis and on the protocol used by the different centers. A reasonable minimal time interval before performing a follow-up after the first diagnosis is 2 weeks, as a shorter time could not allow a variation in the size of the ventricles to become evident. Anyway at least one additional detailed examination should be performed in the third trimester, between 30 and 34 weeks of gestation, to monitor the size of the ventricles and search for cerebral anomalies not visible in the second trimester.

Neurological outcome of fetuses with isolated mild VM

The neurological outcome of fetuses with prenatal diagnosis of isolated mild VM widely varies in different studies with percentages of neurodevelopmental delay ranging from 0% to 28.6%.

Three review articles report different results: Melchiorre et al. report a prevalence of 10.9% [17]; Devaseelan et al. report 12% [8]; and the most recent review by Pagani et al. report an average value of 7.9% [21] which is slightly higher than the 2%–3% estimated for childhood disability in the general population by epidemiological studies [9, 16]. The lower value of the most recent review may be the result of the recent improvements in the prenatal recognition of associated anomalies which were more frequently missed in the past and of the exclusion of patients with associated brain abnormalities recognized on neonatal imaging.

A further explanation on the wide variation of the results reported by different authors may be the use of different protocols to assess postnatal neurological development: in most cases inadequate qualitative assessment, such as telephone interview, has been used. In other cases a short period of follow-up has been planned; the infants have been assessed at different ages and often the distinction between mild, moderate, and severe delay has not been made. An accurate evaluation of the neurodevelopmental delay in preschool children should include evaluation of locomotor activity, eye and hand co-ordination, hearing and speech capacity, and learning performance. It should be stressed that a neurodevelopmental delay in preschool children does not necessarily lead to long-term handicap. For this reason, in order to evaluate exactly the contribution of isolated mild VM to the neurodevelopmental delay in infancy a large collaborative prospective study using a unified protocol and long-term objective postnatal follow-up is needed.

A factor which can significantly influence the prognosis is the progression of VM during pregnancy. In the review by Melchiorre et al. [17] the VM progressed in
15.7%, regressed in 34%, and remained stable in 55.7% of cases. The neurodevelopmental delay in cases of isolated progressive VM was 16.7%; in this group of fetuses there was also the highest incidence of chromosomal abnormalities (22.2%) and associated anomalies (71.4%).

Counseling

Counseling the parents of fetuses with mild VM is a delicate task. The presence of associated anomalies or infections or abnormal karyotype facilitates the counseling as the cause of VM is known. However, there are some conditions associated with mild VM, such as agenesis of the corpus callosum, whose neurological postnatal outcome is extremely variable, thus generating conflicting decisions in the parents.

When mild VM is isolated the counseling regards the future neurological outcome of the neonates. The clinician can only offer to parents the percentages previously reported:
- 7.4%–12.8% of undetected associated anomalies at the first ultrasonic examination
- 15.7% of possible progression of mild VM during pregnancy carrying a worse prognosis with 16.7% of neurodevelopmental delay
- 7.9%–12% of neurodevelopmental delay in isolated nonprogressive mild VM.

Finally special postnatal evaluation and care should be coordinated by appropriate pediatric specialists.

References


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