Mild to moderate fetal ventriculomegaly: obstetric and postnatal outcome

Ventriculomegalia fetal ligeira a moderada: resultados obstétricos e pós-natais

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Abstract

Overview and Aims: Ventriculomegaly has an unestablished risk of psychomotor impairment, especially in mild forms. Our purpose was to evaluate the clinical characteristics and postnatal outcome of fetuses with mild to moderate ventriculomegaly.

Study design: Retrospective study.

Population: Thirty-six cases of prenatal diagnosed mild to moderate ventriculomegaly, from 2005-2011.

Methods: Review of complementary investigations performed (TORCH infection, karyotype evaluation, magnetic resonance imaging and ultrasonographic follow-up). Evaluation of pregnancy outcome and postnatal psychomotor development.

Results: Thirty-six cases of ventriculomegaly were included, 27 cases classified as mild and 9 cases as moderate, with a median atrial diameter at diagnosis of 11.2mm. Most cases presented unilateral ventriculomegaly. Association with other ultrasound abnormalities was found in 13 cases, and urinary tract anomalies were the most common finding. TORCH infection was excluded in all cases. Thirty cases were submitted to amniocentesis for karyotype examination with two cases of chromosomal abnormality detected. Thirty-four cases underwent MRI study, with diagnostic confirmation of associated cerebral malformations in all cases. Spontaneous in utero resolution of ventriculomegaly occurred in six cases. Five cases were submitted to pregnancy termination. Thirty-one babies were live born. All newborns were submitted to postnatal transfontanelar ultrasound and neurologic exam. Median postnatal follow-up was 26.0 months. Postnatal neurologic evaluation showed a complete normal outcome in most infants (27/31, 87.1%), with four cases of psychomotor delay. Only one case of isolated mild ventriculomegaly presented with abnormal neurological development.

Conclusion: In our study, mild to moderate ventriculomegaly prognosis appears to be favorable, especially with a normal karyotype and in the absence of other associated malformations.

Keywords: Ventriculomegaly; Isolated ventriculomegaly; Psychomotor delay.

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INTRODUCTION

Fetal ventriculomegaly (VM) corresponds to the dilation of cerebral ventricles and is a relatively common finding during second trimester ultrasound evaluations [1]. It has a prevalence of less than 2%, varying between 0.3 and 22 per 1000 births, and is more frequent in males, with a male-to-female sex ratio of 1.7[2,3,4].

Between 15 and 40 weeks of gestation the ventricle diameter remains stable, with reported means of 5.4 to

8.2mm[1,3]. VM is defined as an axial diameter across the atrium of the posterior horn of lateral ventricles >10mm, at any gestational age, corresponding to 2.5 to 4 standard deviations above the atrial mean[1,3]. According to the ventricle diameter, VM can be mild (10--12mm), moderate (12.1-15mm) and severe (>15mm)[3]. This classification is not consensual as in some studies mild ventriculomegaly includes all cases of atrial measurement between 10 and 15mm[3].

Fetal VM can be isolated or associated to other anomalies including structural abnormal findings, chromosomal anomalies and prenatal infections in up to 50% of cases[4,5,6]. The prognosis for fetal VM has varied from poor to very good, for both survival and postnatal neurodevelopment. The most important prognostic factors are the association to other abnormalities and the progression of ventricular dilation, which occurs in about 16% of cases[3].

Although most children will have a normal neurologic development, especially those with mild isolated VM, there is a wide variation in outcome of infants with prenatally diagnosed VM.

Our purpose was to evaluate the clinical and ultrassonografic characteristics and postnatal outcome of fetuses with mild to moderate VM (MMVM).

METHODS

We performed a retrospective observational study of all cases of MMVM diagnosed in a tertiary care referral center for prenatal diagnosis and management of fetal and neonatal pathology from 2005 to 2011. Only singleton pregnancies were included. MMVM was defined by a transverse diameter of the atrium of one or both cerebral lateral ventricles between 10.0-15.0mm. All measurements were obtained according to current recommendations [7]. All cases were submitted to complete morphologic ultrasound evaluation in our prenatal unit, and sonographic follow-up was performed every two to four weeks until delivery. Karyotype evaluation was offered in all cases. TORCH analysis was performed in all cases (maternal serologic evaluation and amniotic fluid analysis when maternal seroconvertion was detected). Fetal magnetic resonance imaging (MRI) was performed in all cases after 20 weeks gestational age to exclude associated central nervous system (CNS) abnormalities. The cases were classified according to the degree of ventricular dilation as mild (10.0-12.0mm) or moderate (12.1-15.0mm) and as isolated or non isolated depending on the presence of associated malformations, chromosomal defects and/or fetal infections. There were excluded all cases with delivery in another institution. After delivery, a detailed neonatal examination was performed to all newborns, including a neurological clinical assessment and a cerebral transfontanelar ultrasound (TF-US), repeated at one month old. All patients with postnatal confirmed VM underwent clinical follow-up in an outpatient basis by a pediatrics specialist.

RESULTS

During the analyzed period, there were identified 45 cases of fetal VM, with 36 cases of MMVM (Figure 1). Median maternal age was 29.5 ± 6.5 years, with 13 pregnant women ≥35 years (33.3%). Most cases were referred to our institution after diagnosis of fetal VM (22/36, 61.11%).

Median gestational age at diagnosis was 25.7 ± 4.9weeks, with most cases presenting after 24 weeks gestational age (23/36, 63.9%). Male/female ratio was 2.6 (26/10).

At diagnosis, VM was classified as mild in 27 cases and moderate in 9 cases, with a median atrial diameter of 11.2 ± 1.2mm (10.6 ± 0.6mm in mild cases and 13.0 ± 0.7mm in moderate). Most cases presented with unilateral ventriculomegaly (24/36, 66.7%).

There were identified associated abnormalities (structural malformations, fetal infections or chromosomal abnormalities) in 15 cases (41.7%).

Ultrasound evaluation detected 13 cases (36.1%) of associated malformations (Table I), with five cases (13.9%) presenting with other CNS structural abnormalities. Fetal hydronefrosis (5 cases) and corpus callosum agenesis (4 cases) were the most common findings. Fetal MRI, performed in 34 cases, confirmed diagnosis of VM in all cases, with total agreement regarding associated CNS structural malformations in 100% of cases. The two cases where fetal MRI was not performed were submitted to pregnancy termination before 20 weeks gestational age.

TORCH infection was excluded in all cases.

Thirty cases were submitted to amniocentesis for karyotype examination with two chromosomal abnormalities detected (2/30, 6.7%) (Table I).

Ultrasound follow-up revealed spontaneous *in utero* resolution of fetal VM in six cases (6/36, 16.7%), five cases of mild VM (5/27, 18.5%) and one case of mo-

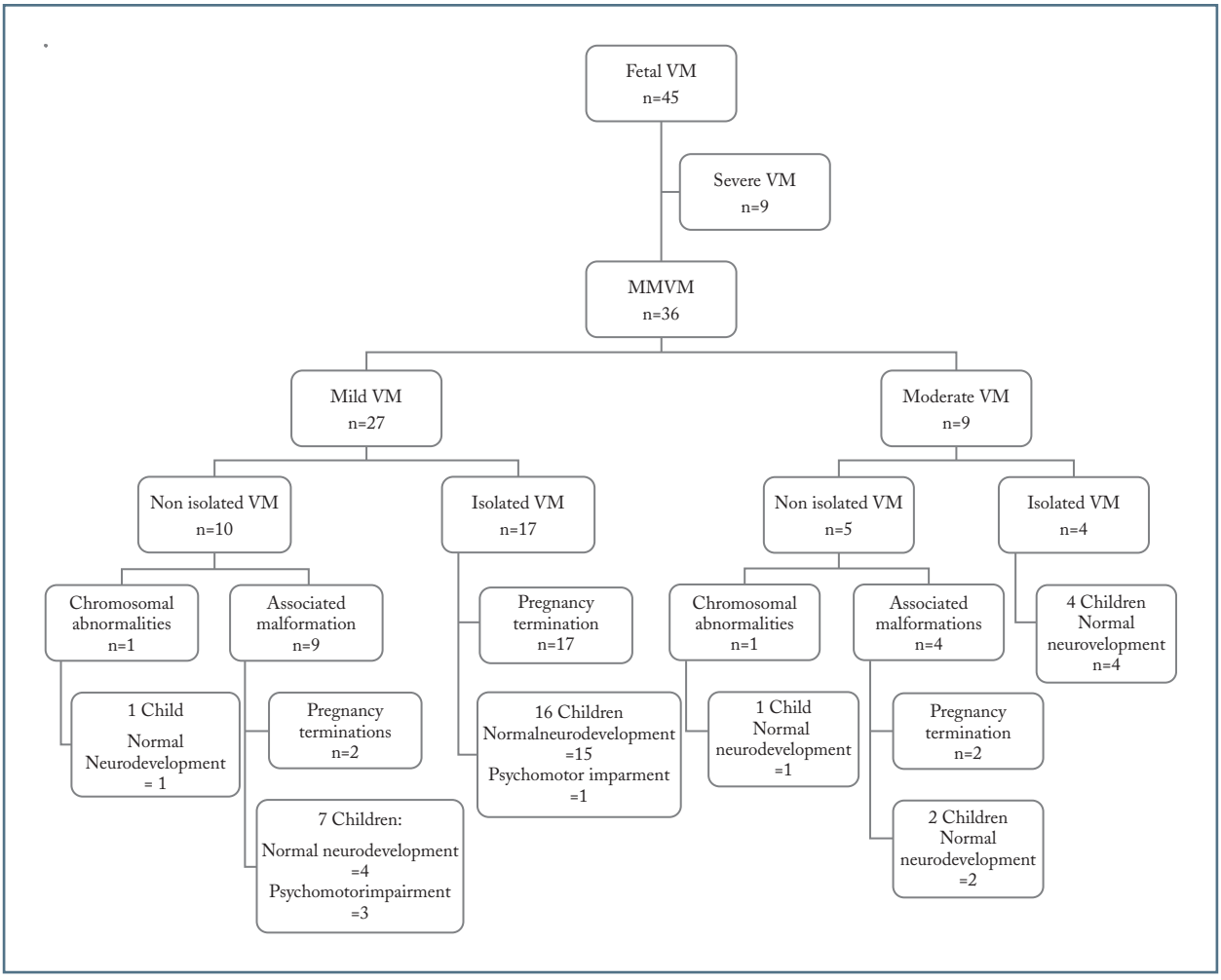

FIGURE 1. Classification of fetuses with VM and postnatal outcomes.

derate VM (1/9, 11.1%) (Table II). Stable measurements were present in 25 cases (69.4%). There were five cases (13.9%) with progressive dilation to severe VM, two cases of initially mild VM (2/27, 7.4%) and three cases of moderate VM (3/9, 33.3%).

Five cases were submitted to pregnancy termination (5/36, 13.9%). Indications were associated malformations (4 cases) and severe isolated ventriculomegaly (1 case). All associated abnormalities were confirmed at autopsy. No case of fetal demise was registered.

Thirty-one children were live born (Table II). Vaginal delivery was performed in 17 cases (54.8%). Median gestational age at birth was 37.7 ± 2.6weeks. Median birth weight was 3189.5 ± 842.5g. All newborns were at least submitted to postnatal transfontanelar ultrasound and neurologic exam at birth and at 1 month old. If there were no abnormalities present, they were discharged. Median postnatal pediatric follow-up was 26.0 ± 25.7 months. There was no registry of associated abnormalities diagnosed only in post-natal evaluation. No postnatal death was registered.

Postnatal neurologic evaluation showed an age-related normal development in most infants (27/31, 87.1%), with four cases of neurodevelopment impairment, one of them with severe psychomotor delay (Figure 1). Regarding isolated MMVM, there was registered one case of abnormal psychomotor development, with a normal development in 19 cases (19/20, 95.0%). Regarding prenatal progression to severe ventriculomegaly (5 cases), three cases were submitted to pregnancy termination, and two cases presented a normal psychomotor development.

TABLE I. ANTENATAL DIAGNOSIS OF ASSOCIATED ABNORMALITIES

Anomaly	Total	Mild	Moderate
Central nervous system abnormalities			
Agenesis of corpus callosum	4	2	2
Intraventricular hemorrhage	1	-	1
Choroid plexus cyst	1	1	-
Extracerebral abnormalities			
Hidronefrosis	5	4	1
Unique umbilical artery	2	1	1
Clubfoot	1	-	1
Intestinal hiperecogenicity	1	1	-
Bone abnormalities	1	1	-
Congenital heart disease	1	1	-
Aneuploidies			
46, XY, der(10)	1	1	-
46,XY, t(7;12)	1	-	1

Associated abnormalities were present in 15 fetuses: 13 fetuses affected with structural anomalies (1 fetus had combined cerebral and extracerebral abnormalities and 3 fetuses had more than one extracerebral malformation) and 2 fetuses affected with chromosomal anomalies

DISCUSSION

MMVM is one of the most common fetal abnormalities detected prenatally and represents a considerable challenge when counseling about postnatal outcome.

In our study group, associated anomalies (structural malformations and chromosomal abnormalities) were present in 41.7% of cases (15/36). Structural abnormalities were detected in 36.1% (13/36) of cases, and the most common alterations were fetal hydronefrosis and corpus callosum agenesis. Abnormal karyotipe was detected in 6.7% (2/30), with no case of trisomy 21. This data is consistent with other reports with chromosomal anomalies being identified in 2.8-11% of cases[1,3,4,8]. Although we registered no case of VM associated to TORCH infection, fetal infection, including CMV and Toxoplasmosis, must be excluded as other series reported infection rates of 5-47%[1,3,4,8]. In the largest prospective population-based study that included 355 cases of MMVM, associated anomalies were detected in 55% of cases, with structural abnormalities in 43%, chromosomal anomalies in 11% and congenital infection in 1% of cases[4]. Postnatal diagnosis of associated abnormalities has also been described in 10-13% of cases prenatally classified as isolate ventriculomegaly[3]. The detection of associated abnormalities is essential for proper prognosis assessment, so a complete ultrassonographic evaluation of the fetal morphology should be performed by experienced personnel and ultrasound follow-up must be kept until delivery. The two abnormal karyotype cases registered were isolated VM, which emphasizes the need of karyotipe evaluation even in the absence of other aneuploidy markers. In our study, progression of ventricular dilation occurred in about 17% of cases which is consistent with previous reports[3].

The use of fetal MRI as a supplementary method of assessing the fetal brain is not consensual. Although, in our series, fetal MRI did not add any new information to ultrasound evaluation, it was important providing diagnostic confirmation of ultrasound findings and excluding other abnormalities, especially in isolated VM cases. Some studies have failed to demonstrate that MRI is more accurate than ultrasound evaluation, especially in assessing the size of fetal ventricles[9,10]. On the other hand, MRI may have more accuracy in the evaluation of some cerebral malformations, especially failed comissuration (agenesis of corpus cal-

TABLE II. OBSTETRIC AND POSTNATAL OUTCOME

Obstetric and Postnatal outcome	Total (36)	Mild		Moderate	
		Isolated (17)	Non-isolated (10)	Isolated (4)	Non-isolated (5)
In utero spontaneous resolution VM	6 (17%)	5 (29%)	0	1 (25%)	0
In utero progression to severe VM	5 (14%)	1(6%)	1 (10%)	0	3 (60%)
Live born	31 (86%)	16 (94%)	8 (80%)	4 (100%)	3 (60%)
Normal neurodevelopment*	27 (87%)	15 (94%)	5 (63%)	4 (100%)	3 (100%)

* Percentages regarding only live-born cases

losum) and gyration[3,10-13]. In a study involving 185 third-trimester fetuses with mild VM, information relevant enough to modify obstetric management was obtained in 6% of cases[14]. A review on evaluation of isolated MMVM reported that fetal MRI may add important information in 6-10% of cases, recommending 30 to 32 weeks gestational age as the most appropriate timing to perform MRI examination[3]. In our prenatal diagnosis unit, fetal MRI is part of the study protocol of fetal VM, but is used only as a complementary method to exclude CNS associated abnormalities and not to evaluate ventricular size.

In the majority of cases, diagnosis of fetal VM was performed after 24 weeks gestational age, which results in another difficulty in parental counseling. As the Portuguese law only allows pregnancy termination because of fetal malformations until 24 weeks gestational age, this option may not be available in many cases.

The neurological outcome of children with a prenatal diagnosis of MMVM has been evaluated by many studies, but there is a wide variation in the reported results. These discrepancies may be mainly due to heterogeneity in the classification of VM and inadequate standard of development assessment. Most published studies included small samples, which is an important limitation on available prognostic information. A prospective trial that included 82 cases of MMVM, reported a risk of abnormal postnatal development of 3% and 23% in isolated mild and moderate VM, respectively[15]. A retrospective study that analyzed the mid-term postnatal outcome of 18 live born fetuses with prenatal diagnosis of isolated mild VM, reported a risk of severe cognitive retardation of 5%[16]. Another retrospective study that included 19 cases of isolated MMVM, reported an age-related normal psychomotor behavior in 92.86% of cases [6]. The largest published study evaluating neurological outcome included 167 cases of isolated MMVM and reported a risk of neurologic disease or developmental delay is 11.88% of cases[17]. A systematic review to establish the perinatal and neurodevelopment outcomes of fetuses with isolated MMVM confirmed that over 85% of fetuses with apparently isolated MMVM were developmentally normal[2]. Another recent review reported a rate of abnormal or delayed neurodevelopment in infancy of about 11% in isolated MMVM, being unclear if it is higher than in general population[3]. In our series, four cases of psychomotor delay were registered, with an overall risk of neurological impairment of 12.9%. Only one case of isolated VM had abnormal age-related development (risk of neurological impairment of 5%) which is concordant with other reports in the literature, that the absence of associated abnormalities is related with better prognosis. Although a poorer prognosis has been associated with bilateral VM compared to unilateral cases, recent reports found that the incidence of neurodevelopmental delay in cases of unilateral or bilateral ventriculomegaly was not significantly different[3,8]. In our study, bilateral ventriculomegaly was present in 12 cases; four were submitted to pregnancy termination and two cases of psychomotor delay occurred (2/8 live-born; 25%), suggesting a worst prognosis in these cases. These conclusions may be limited by the small sample size and the limited follow-up of our children. There is a lack of good quality postnatal follow-up studies with evaluation of long-term cognitive follow-up at school age. Recent reports have shown that the duration of follow-up appears to be extremely important, with an increase of development alterations when follow-up is extended for more than 20 months[2]. This issue needs further investigation to determine the true risk of neurological impairment associated with fetal VM.

CONCLUSION

Prenatal diagnosis of MMVM remains a challenging problem when counseling about neurological outcome. Diagnosis of fetal VM should prompt complete morphological evaluation, congenital infection exclusion and karyotipe evaluation. From our findings, MMVM prognosis appears to be favorable, especially in the absence of associated malformations.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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