Taiwanese Journal of Obstetrics & Gynecology 53 (2014) 170–177

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

A retrospective study on the course and outcome of fetal ventriculomegaly

Tsung-Hong Chiu, Ghazali Haliza, Ying-Hsuan Lin, Tai-Ho Hung, Jenn-Jeih Hsu, T'sang-T'ang Hsieh, Liang-Ming Lo*

Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Taipei, Taiwan

ARTICLE INFO

Article history:
Accepted 11 September 2012

Keywords:
atrium measurement of lateral ventricles
fetal ventriculomegaly
gray zone findings

ABSTRACT

Objective: To evaluate the outcomes associated with fetal ventriculomegaly.
Materials and methods: Reports of women who underwent ultrasound scanning between 18 and 36 weeks of gestation during the period from January 1, 2000, to December 31, 2010, were reviewed. According to the defined severity of ventriculomegaly of affected fetuses, the women were divided into the following groups: (1) mild ventriculomegaly (Group A); (2) moderate ventriculomegaly (Group B); and (3) severe ventriculomegaly (Group C). The women were classified into the "gray zone" group if the fetal lateral ventricle measured between 7 mm and <10 mm. All cases were followed up with additional ultrasound scans. Postnatal information was obtained from the computer database or the medical charts.
Results: A total of 41 cases were recruited for this analysis. Four (9.8%) cases had an abnormal karyotype. Twelve women (29.3%) opted for termination of pregnancy. Of the 29 women who delivered, 56.1% ($N = 23$) were from Group A, 14.6% ($N = 6$) were from Group B, and none was from Group C. All children in Group A had normal neurological development. Three children in Group B had normal neurological development, whereas the other three had neurologic deficits. A total of 432 cases were classified into the "gray zone" group. Of these cases, 2.8% ($N = 12$) progressed to ventriculomegaly.
Conclusion: Cases of isolated and mild ventriculomegaly without additional structural anomalies or chromosomal aberrations had good prognoses. However, the parents of fetuses with moderate or severe ventriculomegaly should be counseled regarding related risks. If the ventricular size of the fetus falls within the "gray zone", at least one additional exam in the third trimester should be performed, for early detection of ventriculomegaly and other related abnormalities. It is important to make the parents of these fetuses aware of these risks, from a medico-legal point of view.

Introduction

Hydrocephalus and ventriculomegaly refer to an excess of fluid causing dilatation of the lateral ventricles. Hydrocephalus causes an increase in intraventricular pressure and a subsequent increase in fetal head size. Ventriculomegaly refers to dilatation of the fetal lateral ventricles in the presence of normal fetal intraventricular pressure [1]. The incidence of ventriculomegaly is less than 2% [2]; and the incidence of mild idiopathic ventriculomegaly between 16 and 22 weeks of gestation was reported to be 0.15% [3]. A previous study, which researched fetal development between 18 and 24 weeks of gestation, showed the prevalence of confirmed mild to moderate ventriculomegaly to be 7.8/10,000 live births [4].

Measuring the atrial region of the lateral ventricle in the fetus is a sensitive method for determining ventricular size. It is also the earliest ultrasonographic indicator capable of detecting trivial changes in ventricular dilatation in the fetal brain. If the atrial measurements fall within definite ranges of ventriculomegaly, it is crucial to search for potential underlying causes using other imaging modalities. Managing this condition and counseling expectant mothers with fetuses that show symptoms of ventriculomegaly during early second trimester are difficult, because the causes, absolute risk, and degree of resulting handicap cannot be confidently determined [5].

* Corresponding author. Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Number 199, Dunhua North Road, Songshan District, Taipei City 105, Taiwan.
E-mail address: lmlo@cgmh.org.tw (L.-M. Lo).

http://dx.doi.org/10.1016/j.tjog.2014.04.008

Ventriculomegaly is defined as lateral ventricles with a width measuring ≥ 10 mm [6,7]. Most previous studies have researched the outcome of fetuses with lateral ventricles measuring at least 10 mm; however, some authors have considered fetal lateral ventricles between 10 and 12 mm as a simple variation of the norm [8]. In addition to conventional cases of ventriculomegaly, this study considered fetal lateral ventricular atrium measuring between 7 and <10 mm (near abnormal), to elucidate how these cases evolved. Atrium measurements within these ranges were labeled as the "gray zone".

The purpose of this study was to evaluate the local population, to help council expectant mothers and their families on how to manage the condition of ventriculomegaly.

Methods

Ultrasound reports of women who underwent Level II ultrasound scanning at Maternal Fetal Medicine Units of Chang-Gung Memorial Hospital (Taipei, Taiwan) from January 1, 2000, to December 31, 2010, were retrospectively reviewed. Ultrasound scanning for all selected cases was performed by the same attending staff (T.-H.C.).

In this study, patients were between 18 and 36 weeks of gestation. Measurements were taken along the shortest perpendicular distance between parallel echogenic inner and outer ventricular walls, at the caudal termination of the choroid plexus [5], through the axial plane of the brain. Fetal lateral ventricle measurements falling between 7 and <10 mm were classified in the "gray zone" group. According to the conventional definition, these measurements fall within the normal range; however, this study sought to determine how many "gray zone" cases would evolve into ventriculomegaly in the late second trimester. Follow up was done on all cases in this group, and patients were given additional care depending on the severity of the condition.

Cases with ventriculomegaly were then divided into groups according to sonographic measurements of the enlarged fetal lateral ventricles. The groups were defined as follows:

- Group A: 10.0 to <12.0 mm (mild ventriculomegaly)
- Group B: 12.0 to <15.0 mm (moderate ventriculomegaly)
- Group C: Over 15.0 mm (severe ventriculomegaly)

A complete ultrasound examination was also performed to exclude other structural abnormalities associated with ventriculomegaly.

An additional ultrasound scan was performed 2–4 weeks later, or several weeks before delivery, depending on the severity of the initial measurement. Chromosomal evaluation by amniocentesis was offered to a number of patients, as indicated. Multiple pregnancies were excluded from this study. The outcome of the pregnancies, such as gestation at delivery, termination of pregnancy (TOP), fetal demise, associated anomalies, or postnatal neurodevelopment was also noted. To determine the health status of the baby, additional information was obtained from the postnatal record and the computer data system. Health status of the neonates was monitored for a follow-up period of 4 months to 6 years.

Results

Following exclusion of multiple pregnancies, 66 cases of ventriculomegaly were diagnosed between January 2000 and December 2010 (Fig. 1). According to severity, the incidence distribution was 66.6% ($N = 44$) cases of mild ventriculomegaly, 22.7% ($N = 15$) cases of moderate severity, and 10.6% ($N = 7$) cases of severe ventriculomegaly. Among these, 25 cases had incomplete follow up; therefore, 41 cases were recruited for further analysis. The percentages of women of advanced maternal age (≥35 years) were 30.3%.

The study group comprised 41 cases of ventriculomegaly (Fig. 1). Of these, 73.2% ($N = 30$) were mild, 17.0% ($N = 7$) were moderate, and 9.8% ($N = 4$) were severe. Karyotyping data were available for 17 patients (41.5%). Of these results, four (9.8%) were abnormal (3 cases of trisomy 18 and 1 case of trisomy 13). All four fetuses possessing chromosomal aberrations were grouped within the mild ventriculomegaly category. Other associated structural anomalies observed in the fetuses were bilateral choroid plexus cysts, cleft lip and palate, horseshoe kidney, and ventricular septal defect. All of these mothers opted to terminate the pregnancy.

A total of 12 women (29.3%) opted for TOP. Four of these women carried fetuses with severe fetal ventriculomegaly. Of these, the karyotype for three of the fetuses was unknown, and the other fetus possessed a normal 46,XX karyotype. However, this fetus showed abnormal Doppler findings in the middle cerebral artery. Only one woman from the moderate ventriculomegaly group (atrium measurement of 14.8 mm) opted for TOP. This patient did not know the karyotype of the fetus and was unaware of any associated structural anomalies. Seven cases of mild ventriculomegaly were terminated, including the four aforementioned cases of trisomy, one case of severe fetal hydrops, and two other cases without any associated anomalies.

Of the 41 ventriculomegaly cases (Fig. 1) reviewed in this study, 70.7% ($N = 29$) of the women delivered in the study center. Of these, 56.1% ($N = 23$) were from Group A (mild), 14.6% ($N = 6$) were from Group B (moderate), and none was from Group C.

In the mild ventriculomegaly group, none of the fetuses (23 cases) had specified laterality of ventriculomegaly, and nearly all delivered at term with a good Apgar Score of 8–9 at 1 minute postdelivery. However, one baby, delivered at 35 weeks of gestation, had a birth weight of 2580 g and an Apgar score of 7 at 1 minute postdelivery. The mean Apgar score in this group was 8.8 and the mean birth weight was 3300 g. In nine cases (39.1%), atrium measurements had regressed to normal before delivery. Atrium measurements in the remaining 14 cases (60.9%) were within mild ventriculomegaly parameters. Furthermore, eight cases of mild ventriculomegaly had developed from the "gray zone" group and four of these cases had subependymal cysts (SECs), as revealed by postnatal brain echo. The duration of follow up varied from 4 months to 6 years. All children in this group had normal neurological development. One child complained of occasional giddiness; however, a brain echo performed at the age of 4 years found no significant abnormal findings.

Regarding the six cases of moderate ventriculomegaly (Fig. 1 and Table 1) reviewed in this study, the infants were delivered at term with a mean body weight of 3010 g (2568–3462 g). Among these, three cases showed normal neurological development; however, a brain echo found an SEC in one case. The two other cases had normal brain echo reports at 4 and 8 months of age. One of these children had attention deficit and hyperkinetic disorder (ADHD). Although the brain echo performed on this child at Day 2 postdelivery indicated hypoplasia of the corpus callosum, the last brain echo imaging follow up, performed at 11 months of age, found nothing abnormal in the corpus callosum and lateral ventricles. However, another electroencephalography, conducted at 2 years of age, revealed rare focal epileptiform activities over the bilateral frontal and left middle temporal area. This child is still undergoing follow-up observation. Another child had epilepsy. A magnetic resonance imaging (MRI) performed on this child at Day 3 postdelivery confirmed agenesis of the corpus callosum (ACC), and follow-up imaging yielded the same results 1 year later. The final case (sixth case) had a normal postnatal brain MRI; however,

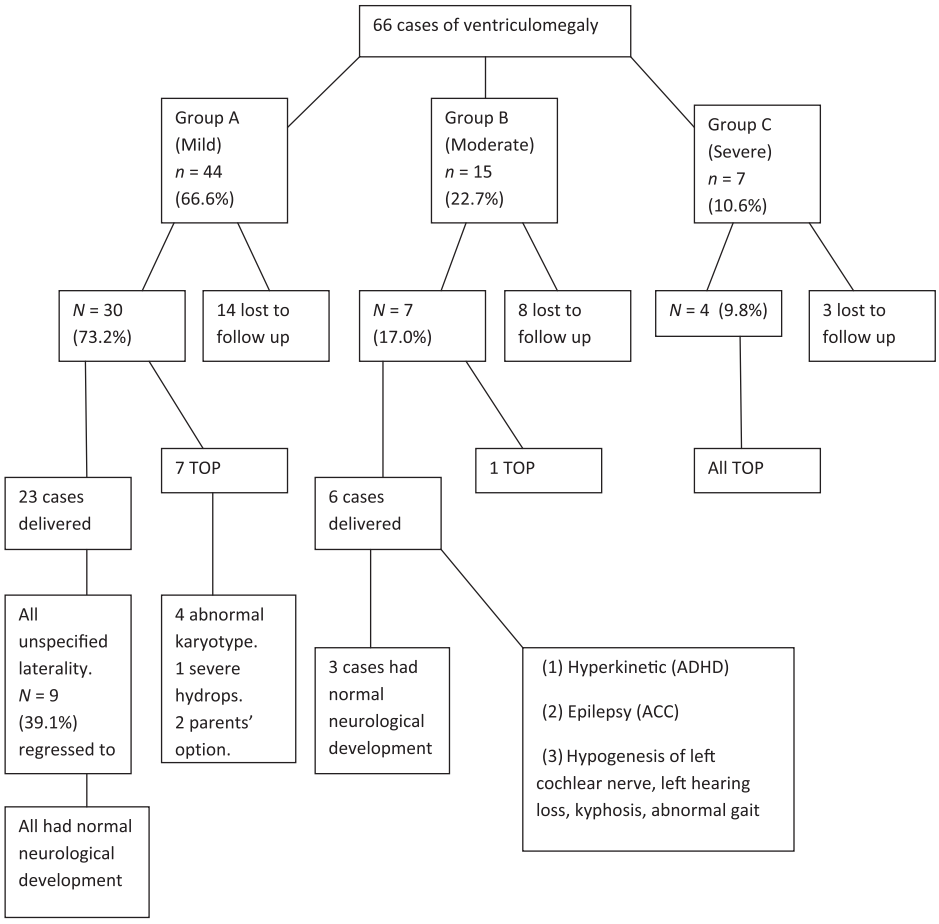

Fig. 1. Cases of ventriculomegaly and outcome. ACC = agenesis of corpus callosum; ADHD = attention deficit and hyperkinetic disorders; TOP = termination of pregnancy.

coincidental findings indicated that the child suffered from kyphosis, abnormal gait, and hearing loss resulting from hypogenesis of the left cochlear nerve.

Regarding the six cases of moderate ventriculomegaly (Table 1) reviewed in this study, 33% ($N = 2$) were initially part of the "gray zone" group and later progressed to moderate ventriculomegaly. Another 50% ($N = 3$) evolved from mild ventriculomegaly in the second trimester. The final case (17%) was initially diagnosed with moderate ventriculomegaly during a second trimester level II ultrasound scan.

Level II ultrasound scanning conducted in the second trimester found 432 cases within the "gray zone". Of these cases, 2.8% ($N = 12$) progressed to ventriculomegaly. Two patients did not undergo any follow up; therefore, 10 cases were evaluated (Fig. 2 and Table 2). The cases grouped in the "gray zone" were between 22 and 26 weeks of gestational age. A small number of these cases progressed to ventriculomegaly at a mean gestational age of 32 weeks (27–36 weeks). Eight cases progressed into Group A (mild) and two cases progressed into Group B (moderate). None of these cases were associated with structural abnormalities. Two cases of mild ventriculomegaly had karyotyping reports available, which showed normal chromosome profiles. All of these cases were delivered at term, and follow-up assessments conducted between 4 months and 6 years indicated normal neurological development. Interestingly, in 50% ($N = 5$) of the cases, brain echo or MRI conducted 1 day to 1 month postdelivery found SECs. All the cysts disappeared within a follow-up period of up to 3 years. Moreover, the postnatal computed tomography scan of one child found lenticulostriate vasculopathy. However, asymmetrical mild ventriculomegaly persisted in the other child until 8 months of postnatal follow up.

Discussion

Ventriculomegaly is defined as lateral ventricles with an atrial diameter of 10 mm or more [6,7]. Measurement of the atrium in the second trimester is an important means of determining ventricular size, and an indicator of normal brain development. In a study of axial sonograms, Cardoza et al reported that the atrium of the lateral ventricles remained relatively stable between 15 and 40 weeks of gestation. The study by Cardoza et al further showed that the ventricular atria had a mean diameter of 7.6 ± 0.6 mm [6]. In our study, the mean atrial measurement was 0.67 ± 0.12 cm ($N = 1125$). When cases of ventriculomegaly were excluded, the mean atrial size was 0.66 ± 0.09 cm ($N = 1099$). Our unpublished pooled data since 1987 revealed a mean atrial size of 0.65 ± 0.11 cm ($N = 9989$). When cases of ventriculomegaly were excluded from this data set, the mean atrial size was 0.64 ± 0.08 cm ($N = 9917$).

After ventriculomegaly is diagnosed, laterality should be defined to examine possible underlying causes in the central nervous system. If a coronal sectional plane can be obtained, the status of the corpus callosum should be assessed, because the rate of associated malformations is high, particularly in instances of moderate and severe ventriculomegaly. Larcos et al found that cases of moderate ventriculomegaly (12.1–14.9 mm) had a significantly higher association with structural anomalies (75%) than mild

Table 1
Evaluation on moderate ventriculomegaly.

Case	Laterality of ventriculomegaly	Gestational age at diagnosis (wk)	From "gray zone" or mild group	Associated abnormal ultrasound findings	Outcome	Karyotype	Age at last follow up	MRI/brain echo	Neurological development
1	Laterality unspecified	28	From mild group (11 mm at 24 wk to 12.3 mm at 28 wk)	—	3230 g at 38 wk	46 XY	4 y and 8 mo	Day 2 Brain echo: suspected hypoplasia of corpus callosum. Brain echo at 11 mo: corpus callosum visible. No ventriculomegaly	Hyperkinetic, attention deficit. EEG at 2 y and 11 mo of age showed rare focal epileptiform activities over bilateral frontal and left middle temporal area.
2	Laterality unspecified	24	Mild to moderate (10.1 mm at 20 wk to 13.3 mm at 24 wk)	—	2760 g at 37 wk	46 XY	3 y	Day 3 MRI showed agenesis of corpus callosum. MRI at 1 y still showed agenesis of corpus callosum.	Epilepsy and still on follow up.
3	Laterality unspecified	29 wk	Mild to moderate (10.1 mm at 24 wk to 12.3 mm at 29 wk)	—	2568 g at 37 wk	—	4 y and 10 mo	MRI of brain at Day 4: normal	Kyphosis, flat foot, abnormal gait. Left hearing loss, hypogenesis of left cochlear nerve
4	Laterality unspecified	28 wk	From "gray zone" to moderate (9.3 mm at 24 wk to 12.6 mm at 28 wk). Atrial size return to normal before delivery.	—	3462 g at 38 wk	—	4 mo	Day 2 Brain echo: subependymal cyst. Brain echo at 2 mo still showed left subependymal cyst	Normal until 4 mo of age
5	Laterality unspecified	23 wk	Atrium 12.2 mm at 23 wk (moderate ventriculomegaly at first ultrasound at study center	—	3335 g at 40 wk	46 XX	1 y	Brain echo at Day 2: echolucency over bilateral caudothalamic groove. Brain echo at 4 mo: normal	Normal
6	Laterality unspecified	30 wk	From "gray zone" to mild then moderate (atrium 8.4 mm at 22 wk, 10.7 mm at 26 wk then 13.5 mm at 30 wk)	—	2710 g at 38 wk	—	8 mo	Brain echo at Day 2: mild lateral ventriculomegaly. Brain echo at 8 mo: normal	Normal

EEG = electroencephalography; MRI = magnetic resonance imaging.

(10–12 mm) cases (41%) [9]. The literature contains considerable variation (10–76%) in the frequency of anomalies associated with borderline ventriculomegaly. In our study, the frequency of structural abnormalities occurring with mild ventriculomegaly was 16%. These consisted mainly of abnormal karyotyping (4 of 5 cases). The rate of confirmed or postnatal anomalies associated with cases of moderate ventriculomegaly was 33%. These comprised ACC, hearing loss resulting from hypogenesis of the left cochlear nerve, kyphosis, and abnormal gait. We were unable to evaluate cases of severe ventriculomegaly, as all these patients opted for TOP.

We next conducted a review of data obtained from amniocentesis investigations. The frequency of chromosomal aberrations reported in the literature ranges from 4 to 14% [4,9,10]. Karyotyping was available for 17 patients: four cases (9.8%) displayed abnormal results and all of these were within the mild ventriculomegaly group. Ideally, amniocentesis should be performed on all patients with ventriculomegaly. However, not all patients reviewed in this study consented to an amniocentesis investigation.

Ventriculomegaly is considered "isolated" when the fetus does not present any other structural anomalies and possesses normal karyotyping. In cases of isolated, mild ventriculomegaly, the absence of any associated anomalies was correlated with a good prognosis. In our research, all fetuses with mild ventriculomegaly who were delivered in the study center displayed unspecified laterality, without any associated structural anomalies. All of these infants showed normal neurodevelopment at the time of the last follow-up assessment. The mean follow-up period was 28 months.

Signorelli et al concluded that isolated ventriculomegaly of 10–12 mm atrial width is associated with normal neurodevelopment for up to 10 years after birth. He further proposed that in the absence of anomalies, an atrial width of 10–12 mm might be considered a variant of the norm [8]. However, even though it may be possible that some fetuses with mild unilateral isolated ventriculomegaly represent a normal anatomical variation of the fetal brain, 9.1% ($N = 3$) of mild ventriculomegaly cases in this study progressed to moderate severity (Table 1). Moreover, these children were all positive for neurological deficit. These conditions comprised cases of ADHD, epilepsy, and one child with multiple abnormalities (i.e., kyphosis, abnormal gait, and hypogenesis of left cochlear nerve with left hearing loss). The children with ADHD and epilepsy had normal karyotypes. In addition, the percentage of cases from the "gray zone" group (Fig. 2 and Table 2) that progressed to mild or moderate ventriculomegaly were 2.3% and 0.5%, respectively. In this study, the progressive evolution of ventriculomegaly appears to have been related to the severity of the outcome, with a less favorable prognosis when patients in the "gray zone" group progressed to moderate ventriculomegaly. To summarize, the total progression from the "gray zone" group to ventriculomegaly was 2.8%. Thus, we suggest that fetuses with atrial measurements falling within the "gray zone" should undergo an additional atrium measurement at least once in the third trimester. Although the percentage of cases progressing from the "gray zone" to ventriculomegaly is low, if problems are detected before delivery, the risk can be discussed with the couple and investigations can be performed prenatally.

Fifty percent of "gray zone" cases ($N = 5$; Fig. 2 and Table 3) showed positive imaging for SECs. In this data set, all children had normal neurodevelopment. Moreover, the SECs eventually disappeared. SEC may be due to a variety of pathologic disorders; however, they may also occur as an isolated change without any obvious cause. In a study by Larcos et al, neurodevelopment was normal in 13 of the 14 babies and only one term baby had mild dysmorphic features and mild global developmental delay. In the majority of cases, isolated SEC does not seriously influence neurodevelopment and most cysts were resolved after a certain period [9]. Furthermore, Larcos et al interpreted the SEC as the result of

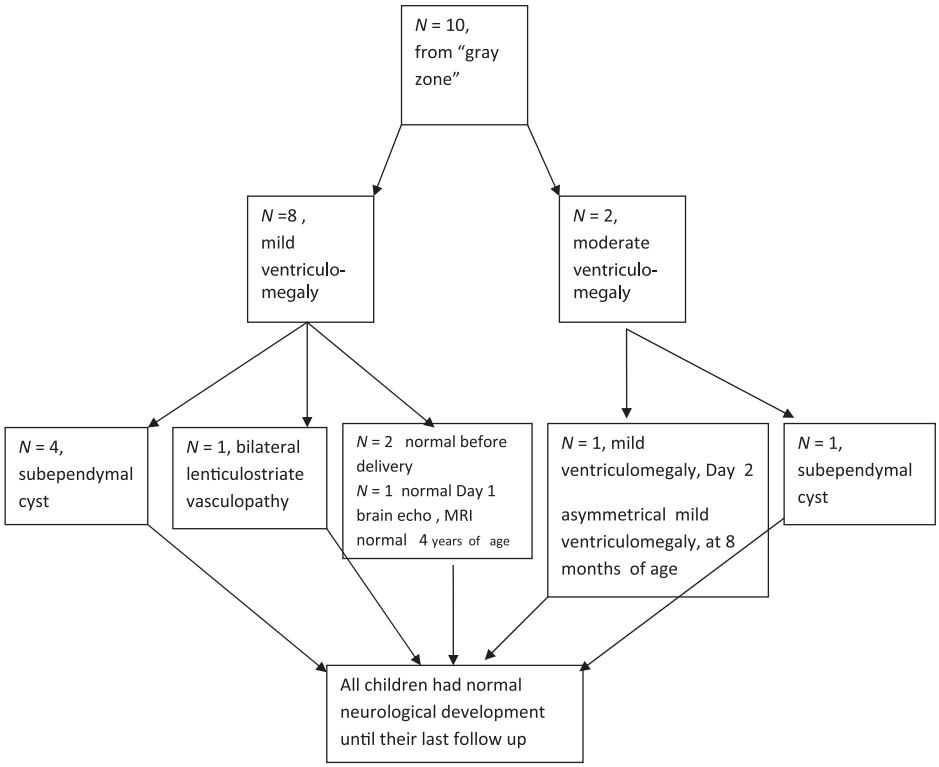

Fig. 2. Postnatal brain finding on ventriculomegaly evolved from "gray zone" group. MRI = magnetic resonance imaging. Cases with "subependymal cyst": 50% ($N = 5$). Normal before delivery: 20% ($N = 2$). Normal MRI: 10% ($N = 1$). Others: 20% ($N = 2$).

Table 2
Outcome of 10 cases of ventriculomegaly derived from the "gray zone" group.

Case no.	Severity of ventriculomegaly	Gestational age at diagnosis (wk) 1. Gray zone 2. Ventriculomegaly	Advanced maternal age	Associated abnormal ultrasound findings	Outcome	Karyotype	Age at last follow up	Brain echo/CT MRI	Neurological development
1	Mild	1. 25–9.5 mm 2. 29–11.0 mm	—	—	3162 g at 39 wk	—	19 mo	Ultrasound was normal before delivery.	Normal
2	Mild	1. 26–9.0 mm 2. 36–11.2 mm	—	—	3036 g at 38 wk	—	3 y	Ultrasound was normal before delivery.	Normal
3	Mild	1. 23–7.2 mm 2. 27–10.7 mm	—	—	2580 g at 38 wk	—	6 y	1. At Day 1 of life: normal brain echo. 2. MRI at 4 y: normal	Normal development but complaint of occasional dizziness.
4	Moderate	1. 24–9.3 mm 2. 28–12.6 mm	—	—	3462 g at 38 wk	—	4 mo	1. Brain echo at Day 2 of life showed subependymal cyst. 2: Brain echo at 2 mo still showed Left subependymal cyst.	Normal until 4 mo of age
5	Mild	1. 25–8.7 mm 2. 34–10.1 mm	—	—	3042 g at 38 wk	—	6 y	1. Brain echo at 3 mo: bilateral subependymal cysts, minimal subdural collection. 2. MRI at 6 mo: left subependymal cyst. 3. MRI at 1 y and 8 mo: normal.	Normal
6	Mild	1. 25–8.3 mm 2. 36–11.9 mm	Yes	—	3150 g at 40 wk	46XX	4 y	1. Brain echo at 1 mo: subependymal cyst, minimal subdural collection without ventriculomegaly. 2. Brain echo at 10 mo: normal.	Normal
7	Mild	1. 23–9.6 mm 2. 27–11.2 mm	Yes	—	3840 g at 40 wk	—	2 y and 9 mo	1. Brain echo Day 2 of life: subependymal cyst. 2: Brain echo at 7 mo: subependymal cyst.	Normal
8	Mild	1. 26–8.5 mm 2. 28–11.9 mm	Yes	—	3680 g at 38 wk	46XY	3 y and 11 mo	1. Brain echo at D1 of life: mild ventriculomegaly, left subependymal cyst. 2. EEG at 3 y: normal. 3. Brain echo at 3 y: normal.	Normal
9	Mild	1. 23–8.6 mm 2. 28–10.3 mm	—	—	3755 g at 39 wk	—	1 y	Brain CT at 1 mo: Bilateral lenticulostriate vasculopathy	Normal
10	Moderate	1. 22–8.4 mm 2. 27–10.7 mm 3. 30–13.5 mm	—	—	2710 g at 38 wk	—	8 mo	1. Brain echo Day 2 of life: mild ventriculomegaly. 2. Brain echo at 8 mo: asymmetrical mild ventriculomegaly.	Normal

CT = computed tomography; EEG = electroencephalography; MRI = magnetic resonance imaging.

Table 3
Cases with positive imaging findings.

Case	Severity	Neurodevelopment	MRI	CT scan	Brain echo	Findings
1	Moderate	ADHD	—	—	✓	Day 2: Suspected hypoplasia of corpus callosum.
					✓	At 11 mo: corpus callosum visible. No ventriculomegaly.
2	Mild	Normal	—	—	✓	Day 3: Bilateral subependymal cysts, mild ventriculomegaly.
					✓	At 1 y and 10 mo: No more subependymal cysts.
3	Mild	Normal	—	—	✓	At 9 mo: Bilateral subependymal cysts.
4	Moderate	Normal	—	—	✓	Day 2: Subependymal cyst.
					✓	At 2 mo still showed left subependymal cyst.
5	Moderate	Epilepsy		—	✓	Day 1: Agenesis corpus callosum.
			✓			Day 3 MRI: Agenesis corpus callosum.
					✓	At 1 y still showed agenesis corpus callosum.
6	Mild	Normal		—	✓	At 3 mo: Bilateral subependymal cysts, minimal subdural collection.
			✓			At 6 mo: Left subependymal cyst.
			✓			At 1 y and 8 mo: Normal.
7	Mild	Normal	—	—	✓	At 1 mo: Subependymal cyst, minimal subdural collection without ventriculomegaly.
					✓	At 10 mo: Normal.
8	Mild	Normal	—	—	✓	Day 2 of life: Normal.
					✓	At 7 mo: Left subependymal cyst.
9	Mild	Normal	—	—	✓	At Day 1 of life: Minimal ventriculomegaly, left subependymal cyst.
					✓	At 3 y: Normal.
10	Mild	Normal	—	—	✓	Day 21: Subependymal cyst.
11	Mild	Normal	—	—	✓	At 1 mo: Choroid plexus cyst.
12	Mild	Normal	—	—	✓	At 1 mo: Bilateral lenticulostriate vasculopathy.
					✓	At 5 mo: Minimal extraaxial collection.
13	Mild	Normal	—	—	✓	At 1 mo: Bilateral lenticulostriate vasculopathy.
14	Moderate	Normal	—	—	✓	At Day 2: Echolucency over bilateral caudate thalamic groove.
					✓	At 4 mo: Normal.
15	Moderate	Normal	—	—	✓	Day 2 of life: Mild lateral ventriculomegaly.
					✓	At 8 mo: Asymmetrical mild lateral ventriculomegaly.

CT = computed tomography; ADHD = attention deficit and hyperkinetic disorder; MRI = magnetic resonance imaging.

undifferentiated cell germinolysis in the germinal matrix of the subependymal lining of the lateral ventricles during the prenatal period [10]. Another hypothesis is that intrauterine hypoxia may cause concealed subependymal hemorrhaging several weeks before delivery, which can result in the formation of cysts [11]. When SEC is diagnosed, it is necessary to search for pathologic conditions capable of indicating a predisposition to ischemic hemorrhagic lesions of the brain (e.g., preeclampsia, intrauterine growth restriction, fetal alloimmune thrombocytopenia, trauma, drug abuse, or congenital infections). The prognosis of the fetus will depend on the underlying pathology and the extent of cystic lesions. In the absence of an identifiable cause, the prognosis is usually good [12].

In this study, all cases of mild ventriculomegaly resulted in a normal neurodevelopmental outcome. Furthermore, neurodevelopment was normal in 50% of patients with moderate ventriculomegaly. However, our sample size was small compared with other studies. Signorelli et al published results obtained from 60 cases of mild isolated ventriculomegaly (<12 mm), and reported a normal neurodevelopmental outcome in 100% of patients [8]. In addition, in a literature review of 141 cases, Pilu et al reported an abnormal neurodevelopment rate of 3.8% when the atrial width exceeded 12 mm, compared with 14% when it was 12–15 mm [7]. Finally, another study of 234 cases of isolated mild ventriculomegaly revealed associated anomalies during ultrasound follow up in 8.6% of patients [13].

Follow-up ultrasound should be performed to elucidate the progression or regression of ventriculomegaly, as well as to reassess structural anomalies. Furthermore, fetal MRI should be performed in cases of isolated mild ventriculomegaly with suspicious etiology to provide more precise information on the cerebral parenchyma and the posterior fossa. An MRI can determine the atrial width in any position of the fetal head and identify defects that are not easily detected by ultrasound (e.g., ACC).

Counseling is very important because even a slight increase in the risk of cerebral damage can cause severe distress to the parents, potentially influencing them to terminate the pregnancy. However, this may constitute a dilemma for doctors, because most isolated cases of mild ventriculomegaly result in the birth of healthy babies. Even after thorough investigations and careful counseling, parental decisions must be respected. Proper documentation is also extremely important, as a comprehensive record may help resolve future medico-legal challenges.

Conclusion

Despite the small sample size of this study, our results suggest that for fetuses with lateral ventricles within the "gray zone" should be reassessed later in the pregnancy due to the potential of such fetuses to develop ventriculomegaly. We therefore suggest that cases in which the lateral ventricles measure 7–10 mm in the second trimester (called the "gray zone" in this study) should be reassessed later in the pregnancy. We further suggest performing an additional ultrasound to examine the lateral ventricles at least once during the third trimester, because progression to ventriculomegaly would yield a less favorable outcome postdelivery. A more comprehensive investigation of fetal health could also assist in parental planning and management of medical conditions. Moreover, diagnosis, clinical significance, and defining the expected outcome of ventriculomegaly cases would facilitate appropriate parental counseling, obstetric management, and potentially help to resolve medico-legal challenges. In the future, we plan to perform a similar study with a larger sample size.

Conflicts of interest

All contributing authors declare no conflicts of interest.

References

[1] Monteagudo A, Timor-Tritch IE. Fetal neurosonography of congenital brain anomalies. In: Timor-Tritch IE, Monteagudo A, Cohen H, editors. Ultrasonography of prenatal and neonatal brain. New York City, NY, USA: McGraw-Hill Medical Publishing; 1996. pp. 147–219.

[2] Alagappan R, Browning PD, Laorr A, McGahan JP. Distal lateral ventricular atrium: reevaluation of normal range. Radiology 1994;193:405–8.

[3] Achiron R, Schimmel M, Achiron A, Mashiach S. Fetal mild idiopathic lateral ventriculomegaly: is there a correlation with fetal trisomy? Ultrasound Obstet Gynecol 1993;3:89–92.

[4] Sethna F, Tennant PW, Rankin J, C Robson S. Prevalence, natural history, and clinical outcome of mild to moderate ventriculomegaly. Obstet Gynecol 2011;117:867–76.

[5] Wyldes M, Watkinson M. Isolated mild fetal ventriculomegaly. Arch Dis Child Fetal Neonatal Ed 2004;89:F9–13.

[6] Cardoza JD, Goldstein RB, Filly RA. Exclusion of fetal ventriculomegaly with a single measurement: the width of the lateral ventricular atrium. Radiology 1988;169:711–4.

[7] Pilu G, Reece EA, Goldstein I, Hobbins JC, Bovicelli L. Sonographic evaluation of the normal developmental anatomy of the fetal cerebral ventricles: II. The atria. Obstet Gynecol 1989;73:250–6.

[8] Signorelli M, Tiberti A, Valseriati D, Molin E, Cerri V, Groli C, et al. Width of the fetal lateral ventricular atrium between 10 and 12 mm: a simple variation of the norm? Ultrasound Obstet Gynecol 2004;23:14–8.

[9] Larcos G, Gruenewald SM, Lui K. Neonatal subependymal cysts detected by sonography: prevalence, sonographic findings, and clinical significance. AJR Am J Roentgenol 1994;162:953–6.

[10] Shaw CM, Alvord EC. Subependymal germinolysis. Arch Neurol 1974;31:374–81.

[11] Shen EY, Huang FY. Subependymal cysts in normal neonates. Arch Dis Child 1985;60:1072–4.

[12] D'Addario V, Selvaggio S, Pinto V, Resta M, Di Cagno L, Fama A. Fetal subependymal cysts with normal neonatal outcome. A case report. Fetal Diagn Ther 2003;18:170–3.

[13] Pilu G, Falco B, Gabrielli S, Perolo A, Sandri F, Bovicelli L. The clinical significance of fetal isolated cerebral borderline ventriculomegaly: report of 31 cases and review of the literature. Ultrasound Obstet Gynecol 1999;14:320–6.