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Full length article

Is fetal magnetic resonance imaging indicated in patients with isolated ventriculomegaly?

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ABSTRACT

Objective: Ventriculomegaly is one of the most common anomalies encountered at obstetric ultrasound and it necessitates follow up. Fetal magnetic resonance imaging (MRI) can be used to confirm the ultrasound diagnose or to detect additional anomalies. Aim of this study is to assess follow up and management of fetal ventriculomegaly shown by ultrasound, and to evaluate additional diagnostic contribution of MRI.

Study Design: This study was conducted retrospectively including 89 patients who had fetal MRI subsequent to ultrasound diagnose of ventriculomegaly in between 2011-2017. Medical records of patients were investigated and accompanying anomalies, congenital infection, chromosomal examination, degree and progression of ventriculomegaly, neonatal imaging and diagnose, and neurodevelopmental findings on follow up were evaluated. Patients were classified in two groups as isolated and nonisolated ventriculomegaly, and subgroups mild, moderate, severe were formed according to their findings. SPSS 23.0 programme was used for statistical analysis.

Results: Ultrasound and following MRI was performed in a range of 18-35th gestational weeks, diagnoses were isolated ventriculomegaly for 56 patients and nonisolated ventriculomegaly for 33 patients. Progression and neurodevelopmental delay was higher in severe nonisolated ventriculomegaly group. There was not significant contribution of MRI in the follow up of isolated ventriculomegaly ($p < 0.001$), and diagnostic imaging findings declined in neonatal period with proceeding normal neurodevelopment in 92.7% of patients followed with diagnosis of isolated ventriculomegaly.

Conclusion: When isolated ventriculomegaly is detected, ultrasound performed by an experienced team is mostly sufficient. MRI can be used in suspicious cases or when ventriculomegaly progresses.

Introduction

In obstetric follow up, ultrasound is the main imaging tool to monitor fetal growth and development. Technologic development and increased experience in ultrasound practice in recent years has allowed ultrasound imaging for both routin purposes and detailed fetal investigation to provide better information in management of the patient [1]. However, beyond major anomalies that can be exactly shown by detailed obstetric ultrasound including fetal neurosonogram, suspicious findings that necessitate to be clarified in the proceeding visits can also be encountered. One suchlike finding involves lateral ventricle measurement which is an important part of central nervous system evaluation. According to ISUOG (International Society of Ultrasound in Obstetrics and Gynecology) guidelines, measurement of atrial width at the level of glomus of the choroid plexus, perpendicular to the long axis of ventricle, using the inner edges of the lateral walls is recommended for ventricular measurement, and $\geq$ 10 mm is described as ventriculomegaly [2]. Ventriculomegaly, prevalance of which is reported to be 0.3–2%, may be unilateral or bilateral [3]. Furthermore, mild, moderate or severe forms which are defined due to measured width of lateral ventricle may be seen, although the exact definition concerning cut-off values varies at different studies [4,5]. Ventriculomegaly may regress or progress during follow up, it may also accompany other cranial or extracranial anomalies. Whether serious fetal anomalia is doubted, fetal magnetic resonance imaging (MRI), which is especially helpful for assessment of central nervous system anomalies, can be used to confirm the ultrasound diagnose or to detect additional anomalies [6]. Aim of this study is to assess follow up and management of fetal ventriculomegaly shown by detailed obstetric ultrasound, and to evaluate additional diagnostic contribution of MRI on this process.

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Materials and methods

This retrospective study was conducted at a university hospital and included 89 pregnant patients followed between October 2011 and October 2017. Patients followed at our perinatology unit are routinely performed detailed obstetric ultrasound at 18–22th gestational weeks. All patients whose detailed obstetric ultrasound revealed ventriculomegaly alone or in combination with other findings underwent MRI examination within a week, and all patients who had fetal MRI subsequent to ultrasound for this purpose were included in the study. Patients who were followed at other hospitals and who were admitted for consultation of progressive or new onset ventriculomegaly at later weeks were also included in the study. Medical records of the patiens were examined, their age, body mass index, obstetric history, presence of uterin scar and amniotic fluid index as contributory of image quality, gestational weeks of patients at the time of ultrasound and MRI, ultrasound diagnose, MRI diagnose, accompanying anomalies, laboratory results of infection such as Toxoplasma, Rubella, and CMV (TORCH), and karyotype examination results if present were inspected. Besides, unilaterality/bilaterality, degree and progression of ventriculomegaly, neonatal diagnose, results of neonatal diagnostic imaging, and neurodevelopmental findings on follow up were evaluated.

MRI was performed to evaluate central nervous system. Measurements of ventricle width were obtained both by ultrasound and MRI. All ultrasound examinations were performed by Voluson E8 (5–8 MHz 3D transducer, General Electric Healthcare, Little Chalfont, UK) via transabdominal route. Sagittal and coronal planes including transventricular, transthalamic and transcerebellar planes are all examined according to ISUOG recommendations and sufficient images are obtained during fetal neurosonograms for all patients [2,7]. Endovaginal route was not used routinely as transabdominal images were satisfactory.

Brain MRI scans were performed on 1.5-tesla MRI scanner (Magnetorm Avanto, Siemens Medical Solutions, Erlangen, Germany). Most fetal MRI was primarily performed using ultrafast T2-W sequences known as single-shot rapid acquisition with refocused echoes. Images were acquired in the axial, sagittal, and coronal planes. Single-shot echo planar diffusion-weighted images were acquired, and gradient echo-planar T2-weighted images were performed primarily to detect hemorrhage.

Beyond imaging methods, all patients were offered amniocentesis or cordocentesis due to their gestational week, in order to evaluate aneuploidy. Assessment of TORCH infection was based on serological markers, amniocentesis was not performed for this purpose.

After completing laboratory and additional imaging process, the patients were consulted to neurosurgery department or other related departments due to existing anomalies, and followed by multidisciplinary team in antenatal and neonatal periods.

All babies were examined by a neuropediatrician at birth and neurological follow up was continued at pediatric neurology department. Cranial/transfontanel ultrasound and/or MRI or computerized tomography (CT) were performed for neonatal diagnostic imaging in the presence of persistant findings antenatally. Cases resulted in intrauterine/neonatal exitus were also assessed. Missing data was completed via phone calls. Neurological follow up of babies continued until time of this report, therefore the follow up period varied between 1–6 years.

Patients were classified in two groups as isolated and nonisolated ventriculomegaly according to their findings, based on the previous studies in literature [4,8,9]. Thus, lacking any accompanying cranial and/or extracranial anomalia on imaging, infection or chromosomal abnormality were evaluated as isolated ventriculomegaly, while having at least one of these features including any structural abnormalities in the entire fetus were considered as nonisolated ventriculomegaly. However, as this study aimed to evaluate the additional diagnostic contribution of MRI to ultrasound examination, the distribution of patients as isolated and nonisolated was based on the ultrasound images. Furthermore, according to measured width of lateral ventricle, subgroups mild (10–<12 mm), moderate (≥12–<15 mm) and severe (≥15 mm) were formed, again based on the previous studies [4,5,10].

SPSS 23.0 program was used for statistical analysis. Categorical measurements were assessed as number and percent, continious measurements were summarized as mean and standard deviation (median, minimum and maximum when needed). Chi square or Fisher test statistics were used to compare categorical variables. To compare continious variables between groups, ranges were assessed, one way variance analysis Anova for variables in parametric range were used. $p < 0.05$ was considered significant for all tests.

Results

Ultrasound and following MRI of patients were found to be dated in a range of 18–35th gestational weeks. One third of the patients were in 18–22nd gestational weeks, while others were in third trimester.

Follow up diagnoses were isolated ventriculomegaly for 56 patients and nonisolated ventriculomegaly for 33 patients. Subgroups are shown in the flow chart (Fig. 1). The groups did not show significant difference with respect to age, body mass index, gestational week of ultrasound and MRI examination, side of ventriculomegaly, presence of uterine scar and amount of amniotic fluid (Table 1). None of our patients had TORCH infection. Although karyotype examination was offered to all patients, most of them did not accept the test because of complication risks, as they decided not to terminate their pregnancy even in the case of fetal aneuploidy. However, genetic examination was performed for a few babies in the neonatal period. Patients who did not have karyotype analysis were followed in isolated ventriculomegaly group, provided that infection or any other anomalia was not detected.

Patients in the nonisolated ventriculomegaly group showed significantly more progression radiologically (Table 2). Pregnancy of eight patients were terminated due to accompanying anomalies, and four neonates underwent surgery in nonisolated ventriculomegaly group. Neurodevelopmental delay was also much more seen in severe nonisolated ventriculomegaly group (Table 3).

In the group of patients who were considered to have isolated ventriculomegaly at ultrasound, MRI revealed additional findings of variational connatal cyst in one patient and retrovermian cyst in another patient. Besides, ultrasound and MRI measurements differed slightly at 12 of 55 patients (excluding one severe isolated case), however, when correlation between ultrasound and MRI was inspected, inter rater correlation was found to be 0.47 (CI:0.29–0.65), $p = 0.001$, therefore, the difference did not reveal prognostic significance.

While 19 of 56 newborns in isolated ventriculomegaly group were inspected by an imaging technique, others were not inspected, owing to the regression or stable state of intrauterine follow up findings except one intrauterin exitus at 26th week. Cranial/transfontanel ultrasound for 12 babies, MRI for 5 babies, and CT for 2 babies were performed. Diagnostic imaging findings in neonatal period declined significantly in isolated ventriculomegaly group when compared to nonisolated ventriculomegaly group ($p = 0.001$).

MRI demonstrated additional findings at 22 of 33 patients (66.6%) in nonisolated ventriculomegaly group, while in isolated ventriculomegaly group, only 2 (3.6%) patients were shown to have

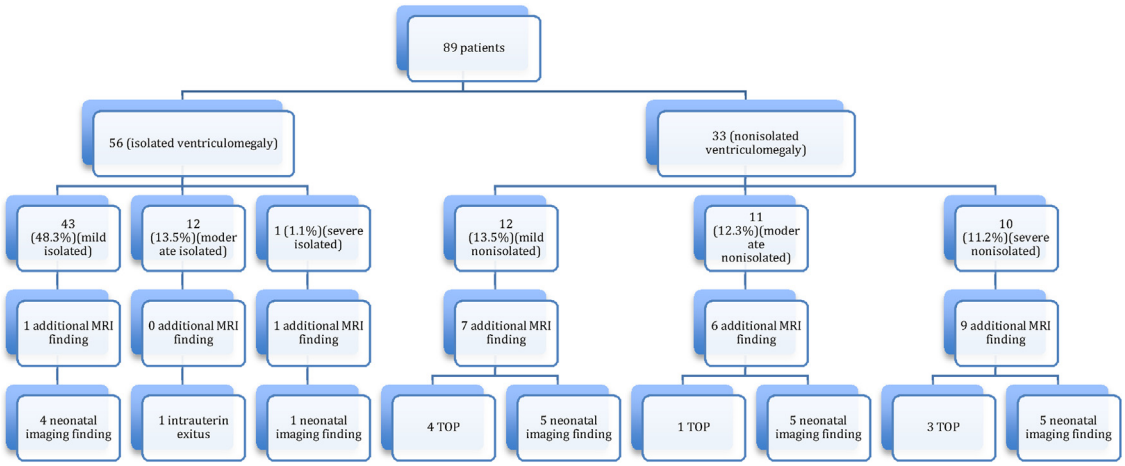

Fig. 1. Flow chart of the distribution of the patients in each group. (TOP: termination of pregnancy).

Table 1
Maternel and fetal characteristics (IVM: isolated ventriculomegaly, NIVM: nonisolated ventriculomegaly, BMI: body mass index, US: ultrasound, MRI: magnetic resonance imaging).

	IVM (n:56)	NIVM (n:33)	p
Maternal age	29.02 ± 5.19	29.36 ± 5.61	0.769
BMI	24.97 ± 5.54	24.12 ± 3.85	0.605
Gestational week of US	26.73 ± 3.50	25.61 ± 5.27	0.234
Gestational week of MRI	27.00 ± 3.46	25.91 ± 5.07	0.234
bilaterality	27 (48.21%)	23 (69.69%)	0.044
Presence of uterine scar (%)	14 (25%)	10 (30.30%)	0.315
Oligohydramniosis (%)	1 (1.78%)	2 (6.06%)	0.279

Table 2
Radiological progression of IVM and NIVM (IVM: isolated ventriculomegaly, NIVM: nonisolated ventriculomegaly).

Progression	IVM (n:56)	NIVM (n: 33)	p
persisted	28 (50.0%)	10 (30.3%)	0.001
regressed	20(35.7%)	3 (9.1%)	
progressed	1 (1.8%)	6 (18.2%)	
drop out of follow up	7 (12.5%)	14 (42.4%)	

additional cranial anomalia at MRI (Table 4). However, the relation between progression of ventriculomegaly and additional information provided by MRI was not found to be significant (p = 0.589 in isolated group, p = 0.386 in nonisolated group).

Proceeding neurodevelopment was normal in 92.7% of babies followed as isolated ventriculomegaly, while only 66.7% of babies followed as nonisolated ventriculomegaly had normal neurodevelopment ($p < 0.05$).

In isolated ventriculomegaly group, only one patient showed progression in ventriculomegaly, and neurodevelopment of the newborns were normal except four patients. Neonatal MRI of a baby revealed poor myelinization at white matter, and subsequently neurodevelopmental delay occured. Atypical otism was diagnosed at another baby whose imaging findings were normal. Two babies had abnormality in neonatal MRI (one of them was reported as periventricular perivascular enlargement and the other was reported as periventricular leucomalasia) and abnormal clinical results of psychometric evaluation. Out of these, an intrauterin exitus occured in moderate isolated ventriculomegaly group in 26th week, though there was no other abnormality at ultrasound/MRI examination. Imaging findings of other patients followed with isolated ventriculomegaly regressed in neonatal period and following neurodevelopmental findings were normal.

In nonisolated ventriculomegaly group pregnancy of eight patients were terminated due to accompanying serious anomalies. These anomalies were glial tumor, vermian agenesia, corpus callosum agenesia (CCA), CCA-hydrocephalus, CCA-cerebellar hypoplasia-interhemispheric cyst, facial tumor-renal agenesia, aneuploidy, and oligohydramniosis-hypoplastic nasal bone separately. Two babies followed with multiple fetal anomalia died in neonatal period and a baby who underwent several operations for hydrocephalus died in 9th month of life. Operation for hydrocephalus were performed in three babies, while one baby for neural tube defect (NTD) and another baby for hydrocephalus and NTD were operated. Follow up of 26 newborns (including one twins) continued after birth, three of them had deficiency in motor skills, one had seizure, two had microcephalus, and one had abnormal psychometric assessment. Data of three patients were missing and they also could not be reached by phone, neurodevelopment of other infants were normal. Additional antenatal cranial and extracranial findings of fetuses who had normal neurodevelopment on follow up are shown in Table 5.

Comment

When fetal ventriculomegaly is detected, detailed fetal examination should be performed. Aneuploidy, TORCH infection,

Table 3
Clinical progression of isolated and nonisolated ventriculomegaly(IVM: isolated ventriculomegaly, NIVM: nonisolated ventriculomegaly, NTD: neural tube defect).

	Mild IVM (n:43)	NIVM (n:12)	Moderate IVM (n:12)	NIVM (n:11)	Severe IVM (n:1)	NIVM (n:10)
Termination of pregnancy (n)	0	4	0	1	0	3
Finding at postnatal imaging (n)	4	5	0	5	1	5
Need of neurosurgery(n)	0	1(NTD)	0	0	0	3
Neurodevelopment delay (n)	4	1	0	1	0	4

Table 4
Contribution of MRI (IVM: isolated ventriculomegaly, NIVM: nonisolated ventriculomegaly, MRI: magnetic resonance imaging).

Additional cranial anomalia at MRI	IVM (n:56)	NIVM (n:33)	p
present	2 (3.6%)	22 (66.6%)	<0.001
absent	54(96.4%)	11 (33.3%)	

Table 5
Additional findings in antenatal imaging of fetuses whose neurodevelopment are normal on follow up.

Cranial findings	
Corpus callosum agenesia	10
Bilateral coroid plexus cyst	1
Megacysterna magna	2
Periventricular encephalomalasia	1
Frontal encephalomalasia	1
Interhemispheric cyst	2
Retrovermian cyst	1
Neural tube defect	1
Extracranial findings	
Abdominal ascites	1
Pyelectasia	2
Polidactyly	1
Clinodactyly	1
Club foot	1
Ventricular septal defect	1

other cranial or extracranial anomalies, and presence of intracranial hemorrhage should be inspected. Bilaterality, degree and progression of ventriculomegaly should be followed [4,11].

Although routine detailed obstetric ultrasound was performed at 18–22th gestational weeks, initial examination of most patients in our study were in third trimester according to their referral time from other hospitals.

Ultrasound may not be sufficient due to image artefacts, adipose tissue, or oligohydramniosis, therefore, additional methods of imaging may be necessary [8]. There are studies comparing diagnostic accuracy of ultrasound and MRI in doubt of anomalia especially related to central nervous system. It is shown that both imaging methods may be correlated, or one may be superior to the other in terms of diagnosis [6,8,12]. Studies have reported 5–10% contribution of MRI to diagnosis of ultrasound, with most benefit in third trimester and particularly for cortical anomalies [4,11]. Paladini et al. [6] also notified that in case of ultrasound being performed by an experienced team, MRI contributed little, and this additional benefit especially included huge space-occupying lesions after 24th gestational week. Tercanli et al. [1] emphasized that the utility of both methods was related to the quality of imaging and experience of the physician. Gonçalves et al. [12] depicted that MRI was more sensitive than ultrasound and provided contributory information which affected prognosis at 22% of the patients, however false positivity rate was much more in small findings of central nervous system.

In our study group, most of the major anomalies were detected by ultrasound, however, MRI was used to confirm the diagnosis especially in severe cases of nonisolated group and additional small findings were recorded, therefore, all these patients were considered to benefit from MRI. On the other hand, MRI provided additional contribution at 3.6% of isolated ventriculomegaly group, which produced significant difference between isolated and nonisolated groups. Only one fetus with severe ventriculomegaly was assessed in the isolated group due to ultrasound finding of 16 mm ventricular width, however MRI examination revealed 11 mm ventricular width and a separate connatal cyst adjacent to the ventricle.

When finding of ventriculomegaly is explained to pregnant patients for the first time, their primary anxiety is probable necessity of a surgical intervention and effect of this condition to neurodevelopment of the baby. In case of severe fetal anomalies, options including termination of pregnancy is discussed with the patient. MRI is beneficial in evaluating fetal cranium and vertebrae to decide on termination in earlier weeks, as well as to detect additional anomalies and manage the patient in later weeks. However, leading the patient to MRI in the first visit is debated if there is not any finding other than mild ventriculomegaly at ultrasound which is performed at an experienced center, and the laboratory results are normal. Rather, ultrasound follow up every two weeks and repeating detailed examination at 30-34th gestational week is recommended. It is also emphasized that progression of ventriculomegaly is the most important predictor for prognosis [4,9].

In previous studies, it was reported that 15.7% of mild ventriculomegaly was progressive, and 16.7% of them had neurodevelopmental delay, these prevalances were similar with general population showing 2–3% of neurodevelopmental delay. However it was emphasized that neurodevelopmental delay did not mean permanent neurological injury [4,11].

Our radiological progression rates were 1.8% and 18.2%, and neurodevelopmental delay rates were 7.3% and 18.2% in isolated and nonisolated groups respectively. However, the neurodevelopmental delay was not related to antenatal radiological findings in isolated ventriculomegaly group, and therefore this may be considered as coincidental. Furthermore, progression of ventriculomegaly and additional information provided by MRI was not found to be significantly related in both groups, however, as most of the patients were seen in third trimester, the radiological progression of ventriculomegaly may be hard to evaluate.

Signorelli et al. [5] described ventriculomegaly with 10–12 mm atrial width as 'borderline'. They reported this group to be associated with normal neurodevelopment until ten years of life after birth, and they suggested to consider isolated ventriculomegaly with 10–12 mm width as a variant of the normal.

In our study, only one patient in mild isolated ventriculomegaly group showed progression, which did not cause neurodevelopmental delay. While 43 of our isolated ventriculomegaly patients were in mild subgroup, 12 patients were in moderate isolated ventriculomegaly subgroup with ventricular width $\leq$13 mm in all patients. When the intrauterin exitus mentioned above is excluded in this subgroup, none of the 11 patients showed progression in intrauterine and postnatal imaging, and all babies had normal neurodevelopment in follow up. Ultrasound and MRI measurement differences in isolated ventriculomegaly group did not cause statistical and clinical significance. Also, postnatal imaging and neurodevelopment of babies were significantly much better in isolated ventriculomegaly group when compared to nonisolated ventriculomegaly group, therefore, our results may support the idea of this group being a variant of the normal.

Neurological follow up period of babies varied in our study, however, we did not exclude babies with short follow up as we considered bad prognosis would exhibit signs even in the first year, furthermore, babies needing surgical intervention would have been operated during this time. Follow up period in the previous reports also varied between 2 and 10 years, and there is not a consensus on the subject. However, it is denoted that longer period might complicate the follow up due to contributing factors such as education and socioeconomic environment [11]. Though, as neurodevelopment is a long lasting process, we consider that more accurate results may be obtained by longer follow up.

Heterogenious follow up period is a limitation of our study. Other limitations are that, neonatal imaging was not obtained for all patients, and information of neurodevelopment could only be

achieved via phone calls for patients who were followed in other hospitals in neonatal and childhood period.

Conclusion

Our results did not show significant difference of MRI and ultrasound in isolated ventriculomegaly group in terms of clinical prognosis, therefore, additional diagnostic contribution of MRI is limited in this group especially in early gestational weeks. In our opinion, ultrasound performed by an experienced team is mostly sufficient for follow up of isolated ventriculomegaly, while MRI is helpful in suspicious cases or when progression occurs. Though, large prospective studies are needed to decide necessity and timing of MRI.

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