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Original Article

The characteristics of fetal central nervous system abnormalities in prenatal magnetic resonance imaging and ultrasonography and their relationship with chromosomal disorders

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Abstract: Objectives: This study aims to evaluate the diagnostic performance of magnetic resonance imaging (MRI) and ultrasound in detecting fetal central nervous system (CNS) abnormalities and to investigate the association between fetal CNS abnormalities and chromosomal disorders. Methods: A cohort of 359 fetuses with suspected fetal CNS abnormalities were included in the study between November 2011 and September 2017. They underwent a fetal head MRI and karyotype analysis within one week after an ultrasonic examination. The diagnostic results of the ultrasound and MRI were compared. The correlation between fetal CNS abnormalities and chromosomal abnormalities were also analyzed. Results: The 359 cases included 271 (75.5%) fetuses with an isolated CNS abnormality and 88 (24.5%) with multiple abnormalities. Diagnostic concordance between MRI and ultrasound occurred in 68.0% (244/359) of the cases. MRI provided additional clinical information in 24.0% (86/359). Completely different diagnoses between MRI and ultrasound were reached 4.7% of the cases (17/359). Abnormal ultrasound findings but normal MRI findings were manifested in 3.3% of the cases (12/359). The prevalence of chromosomal abnormalities was 14.2% (51/359) overall, 4.8% (13/271) for isolated CNS abnormalities, and 43.2% (38/88) for non-isolated CNS abnormalities. A Chi-square test showed a statistical difference in chromosomal abnormalities between the fetuses with isolated CNS abnormalities and non-isolated CNS abnormalities (χ^2=80.3, P<0.001). Conclusion: MRI can improve the diagnostic accuracy and provide more information when fetal CNS abnormalities are detected by ultrasound. Chromosomal abnormalities are more associated with non-isolated CNS abnormalities rather than isolated abnormalities.

Keywords: Magnetic resonance imaging, central nervous system, fetus, chromosome disorders, ultrasound

Introduction

Fetal central nervous system (CNS) abnormality is one of the most common congenital malformations, with a prevalence of 2.6/1000 births [1]. Several prenatal diagnostic techniques, such as prenatal ultrasound, magnetic resonance imaging (MRI), and genetic tests based on amniocentesis or chorionic villus sampling, have improved the detection rate of fetal CNS abnormalities. The early and accurate diagnosis of fetal CNS abnormalities is essential for appropriate and timely management.

Ultrasound is the first-line imaging method used to evaluate the anatomic morphology of the fetal brain. Three-dimensional (3D) prenatal ultrasound has several advantages, including real-time imaging, non-invasiveness, ease of use, low cost, and good reproducibility. However, prenatal ultrasound is affected by the ossification of the fetal skull, amniotic fluid volume, and unsatisfactory fetal position [2]. Thus, supplementary diagnostic techniques are needed for some fetal abnormalities that cannot be adequately assessed by ultrasound alone.

Prenatal MRI can be used as a complementary technique to ultrasound and can provide additional diagnostic information. Prenatal MRI has been reported to have a higher sensitivity than ultrasound for diagnosing fetal CNS abnormalities (89-93% vs. 67-68%) [3, 4]. Furthermore, in

a large minority of cases, MRI provides additional information and affects the final diagnosis and prognosis. However, some unanswered questions remain regarding the diagnostic and clinical impacts of MRI, and there are few published studies comparing the diagnostic performance of MRI and ultrasound for the diagnosis of fetal CNS abnormalities.

The aim of this retrospective study was to compare the values of MRI and ultrasound for the diagnosis of fetal CNS abnormalities. In addition, a karyotype analysis of the fetal chromosome was performed to investigate the associations between fetal CNS abnormalities and chromosomal abnormalities.

Materials and methods

Study subjects

In this retrospective study, pregnant women who underwent prenatal examination in our hospital between June 2011 and August 2017 were screened for inclusion.

The inclusion criteria were as follows: 1) the fetus was suspected or confirmed to have a CNS abnormality based on the ultrasonic findings; and 2) a fetal head MRI and a prenatal karyotype analysis of the fetus had been performed within one week after the ultrasonic examination.

The exclusion criteria were as follows: 1) major pregnancy complications, such as heart disease, hypertension, and so on; or 2) data required for the analysis could not be retrieved from the medical records.

This study was approved by our hospital's Institutional Review Board. Due to the retrospective study design, written consents for inclusion in the study were waived.

Ultrasound

A Voluson 730 Expert 3D color Doppler ultrasound system (GE Healthcare, Chicago, IL, USA) was used with abdominal (3-5 MHz), 3D (4-8 MHz) and intracavitary (5-9 MHz) probes. The fetal organs were scanned through the women's abdomens in a supine position. The examinations focused on the malformations of the fetal heads and spines. Repeated multi-section acquisitions were performed at suspicious sites. If necessary, a 3D or transvaginal ultrasound was undertaken with a 5-9 MHz probe. The examinations were performed by radiologists with more than 3 years of experience.

MRI

A 1.5T superconductive MR scanner with an 8-channel phased-array coil was used (Signa HDxt, GE Healthcare, Milwaukee, WI, USA). The entire uterus was scanned (inferior to superior) with the women in a supine position. Coronal, horizontal, and sagittal T2-weighted imaging (T2WI) were acquired using a fast-imaging employing steady-state acquisition (FIESTA) sequence and a single-shot fast spin-echo (SSFSE) sequence with the fetal head as the center. A T1-weighted imaging (T1WI) was used to detect intracranial hemorrhage. The scanning parameters for the FIESTA sequences were as follows: echo time (TE), 2.0-2.7 ms; repetition time (TR), 5.2-9.6 ms; flip angle (FA), 55°; matrix, 192×192; number of excitation (NEX), 1-2; thickness, 4.0-5.0 mm; and spacing, 0-1 mm. The scanning parameters for the SSFSE sequences were as follows: TE, 92-127 ms; TR, 737-883 ms; matrix, 320×224; NEX, 1-2; thickness, 4.0-5.0 mm; and spacing, 0.5 mm. The scanning parameters for the T1-weighted imaging (T1WI) were as follows: TE, 24 ms; TR, 1709 ms; matrix, 192×192; NEX, 1-2; thickness, 4.0-5.0 mm; and spacing, 0.5 mm. The acquisition time for all sequences required about 20 min. The images were interpreted by two professional associate radiologists who were blinded to the ultrasonic results.

Karyotype analysis

Genetic counseling was offered in the cases of suspected fetal CNS abnormality. Amniocentesis (20 mL) was performed after 16 gestational weeks for routine cell culture, production and G-banding. Twenty karyotypes were observed, and three were analyzed using an Axio Imager Z2 microscope (Carl Zeiss, Oberkochen, Germany), BX51 microscope (Olympus, Tokyo, Japan) and Karyotyping System. A chromosomal karyotype was counted if chromosomal abnormalities were noted.

Follow-up

In order to confirm the final diagnoses, telephone follow-ups were undertaken for the live-born infants, and imaging (ultrasound, MRI or computed tomography) was performed six months after delivery. Autopsy or MRI was per-

formed on the dead fetuses after the termination of the pregnancy.

Data collection and analysis

The following data were collected: ultrasound and MRI findings (e.g. fetal intracranial structures), results of the karyotype, other relevant clinical information (e.g. presence of possible causative infection), and imaging or autopsy results after delivery (live birth or termination of pregnancy).

The ultrasound and MRI diagnoses for each fetus were categorized as: (1) concordant diagnoses; (2) partly concordant diagnoses but the MRI provided additional diagnostic information; (3) completely different diagnoses; or (4) ultrasound detected a CNS abnormality but the MRI findings were normal. Fetal CNS abnormalities in combination with other malformations were classified as non-isolated abnormalities, while those without malformations were classified as isolated. The diagnostic data were mainly presented as a percentage. SPSS 13.0 (Chicago, IL, USA) was used for the statistical analysis. A Chi-square test was used to compare the differences of the chromosomal abnormalities between the fetuses with isolated CNS abnormalities and non-isolated CNS abnormalities. $P<0.05$ was considered statistically significant.

Results

Fetal CNS abnormalities diagnosed with ultrasonography

Ultrasound detected fetal CNS abnormalities in 359 pregnant women, aged 19-48 years (average age, 28.9 years). The gestational age was 20^{+2}-38^{+6} weeks (average, 29.7 weeks). There were 355 cases of singleton pregnancy and 4 cases of twin pregnancy: one case was monochorionic diamniotic (MCDA) twins, and three cases were dichorionic diamniotic (DCDA) twins. There were 116 cases of lateral ventricular enlargement (internal diameter of lateral ventricle trigone <15 mm; unilateral in 83, bilateral in 33), 36 cases of posterior fossa enlargement, 32 cases of arachnoid cysts, 23 cases of holoprosencephaly, 20 cases of subependymal cysts, 19 cases of the absence or agenesis of the corpus callosum (including 1 case of DCDA twin pregnancy), 17 cases of a cavum septum pellucidum (CSP) abnormality, 14 cases of cavum vergae, 12 cases of choroid plexus cysts, 11 cases of bilateral hydrocephalus (internal diameter of lateral ventricle trigone ≥15 mm), 10 cases of microcephaly, 7 cases of Black's cysts, 7 cases of anencephaly, 6 cases of intracranial hemorrhage, 5 cases of Dandy-Walker malformation, 5 cases of cytomegalovirus infection, 5 cases of sacrococcygeal space-occupying lesions, 3 cases of open spina bifida, 2 cases of cerebellar vermis dysplasia, 2 cases of intracranial space-occupying lesions, 2 cases of porencephaly, 2 cases of encephalocele, and 2 cases of tethered cord syndrome (**Table 1**).

Comparison of the diagnoses made by ultrasound and MRI

A diagnostic concordance between MRI and ultrasound occurred in 68.0% of the cases (244/359), and MRI provided additional clinical information in 24.0% of the cases (86/359). MRI and ultrasound yielded completely different diagnoses in 4.7% of the cases (17/359). Abnormal ultrasound findings but normal MRI findings were reported in 3.3% of the cases (12/359). Representative ultrasound and MR images illustrating some of these abnormalities are shown in **Figure 1**. A typical case in which MRI provided additional imaging characteristics for the diagnosis of tuberous sclerosis is shown in **Figure 2**.

The association of chromosomal abnormalities with fetal CNS abnormalities

Among the 359 cases with fetal CNS abnormalities, 51 (14.2%) fetuses also had the following chromosomal abnormalities: trisomy 21 (13 cases), trisomy 18 (8 cases), trisomy 13 (8 cases), and other chromosomal abnormalities (22 cases). The ultrasound features of these 51 cases with their chromosomal abnormalities are shown in **Table 2**. The prevalence of chromosomal abnormalities was 4.8% (13/271) in the 271 cases of isolated fetal CNS abnormalities and 43.2% (38/88) in the 88 cases of non-isolated fetal CNS abnormalities. The Chi-square test showed a statistical difference of chromosomal abnormalities between the fetuses with isolated CNS abnormalities and non-isolated CNS abnormalities ($\chi^2=80.3$, $P<0.001$, **Table 3**).

Discussion

Fetal MRI has high tissue specificity and advantages over ultrasound that include clearer

Table 1. Results of the ultrasound and MRI examinations of the 359 fetuses included in the study

US diagnosis	Cases	Consistency between US and MRI (cases)	Supplementary information provided by MRI (cases)	Different diagnosis provided by MRI (cases)	Abnormal US but normal MRI (cases)
Lateral ventricular enlargement	116	67 cases	43 cases: partial gyrus compression (20); cerebellar atrophy (15); partial gyrus dysplasia (5); cerebellar vermis and right cerebellar hemisphere dysplasia (1); 'banana' sign, 'lemon' sign, cerebellar tonsillar hernia and suspicion of lumbar spina bifida (1); 'banana' sign, 'lemon' sign and suspicion of myelomeningocele (difficult to detect due to obesity) and spinal bifida (1)	6 cases: hypoplasia or absence of corpus callosum (4); cerebral hemorrhage (1); parenchymal dysplasia (1)	0
Posterior fossa enlargement	36	13	14 cases: posterior fossa arachnoid cysts (8); compression of surrounding brain tissue (5); cerebellar dysplasia (1)	7 cases: Dandy-Walker malformation (3); arachnoid cysts (2); corpus callosum hypoplasia (2)	2
Dandy-Walker malformations	5	3	1: corpus callosum hypoplasia	0	1
Vermis hypoplasia	2	2	0	0	0
Blake's cysts	7	6	1: local brain compression	0	0
Arachnoid cysts	32	25	6 cases: partial corpus callosum dysplasia	0	1
Choroidal cysts	12	8	1 cases: enlargement of right lateral ventricle and trigone with changes in the right hemisphere; dysplasia of the other hemisphere could not be excluded	0	3 (missed diagnosis by MRI in 1 case)
Subependymal cysts	20	20	0	0	0
Webster's cavity	14	14	0	0	0
Dysplasia or absence of corpus callosum	19	10	6 cases: Dandy-Walker malformations (3); microcephaly (2); arachnoid cysts (1)	0	3
Suspicion of microcephaly	10	7	2 cases: cortical dysplasia (1); corpus callosum dysplasia (1)	0	1
Cavum septum pellucidum abnormality	17	14	2 cases: malaria-associated malformation (1); anterior perforation of lateral ventricle (1)	0	1
Intracranial hemorrhage	6	5	0	1 case: intracranial tumor with cerebral dysplasia	0
Intracranial space-occupying lesions	2	1 cases: lipoma in brain midline	1 case: ventricular hemorrhage	0	0
Hydrocephalus	11	7	4 cases: third ventricle enlargement and subacute ventricular hemorrhage (1); third ventricle enlargement and interhemispheric cysts interlinked with the ventricle (1); third ventricle enlargement and interhemispheric cysts (1); cysts in brain midline (1)	0	0
Holoprosencephaly	23	17	3 cases: alobar holoprosencephaly (1); absence of cavum septum pellucidum (1); body stalk anomaly (1)	3 cases: correction of semi-lobar to lobar holoprosencephaly (1); correction of lobar to alobar holoprosencephaly (1); incorrect revision of semi-lobar holoprosencephaly (combined with long nose, Dandy-Walker malformation and enhanced echoes in bilateral kidneys) to alobar holoprosencephaly with long nose, since autopsy indicated semi-lobar holoprosencephaly, long nose and bilateral polydactyly (1)	0
Porencephaly	2	1	1 case: absence of cavum septum pellucidum	0	0
Cytomegalovirus infection of brain	5	5	0	0	0
Anencephalus	7	7	0	0	0
Encephalocele	2	2	0	0	0
Open spina bifida	4	3	1 case: posterior fossa cysts	0	0
Tethered cord syndrome	2	2	0	0	0
Sacrococcygeal occupying lesions	5	5	0	0	0
Total	359	244	86	17	12

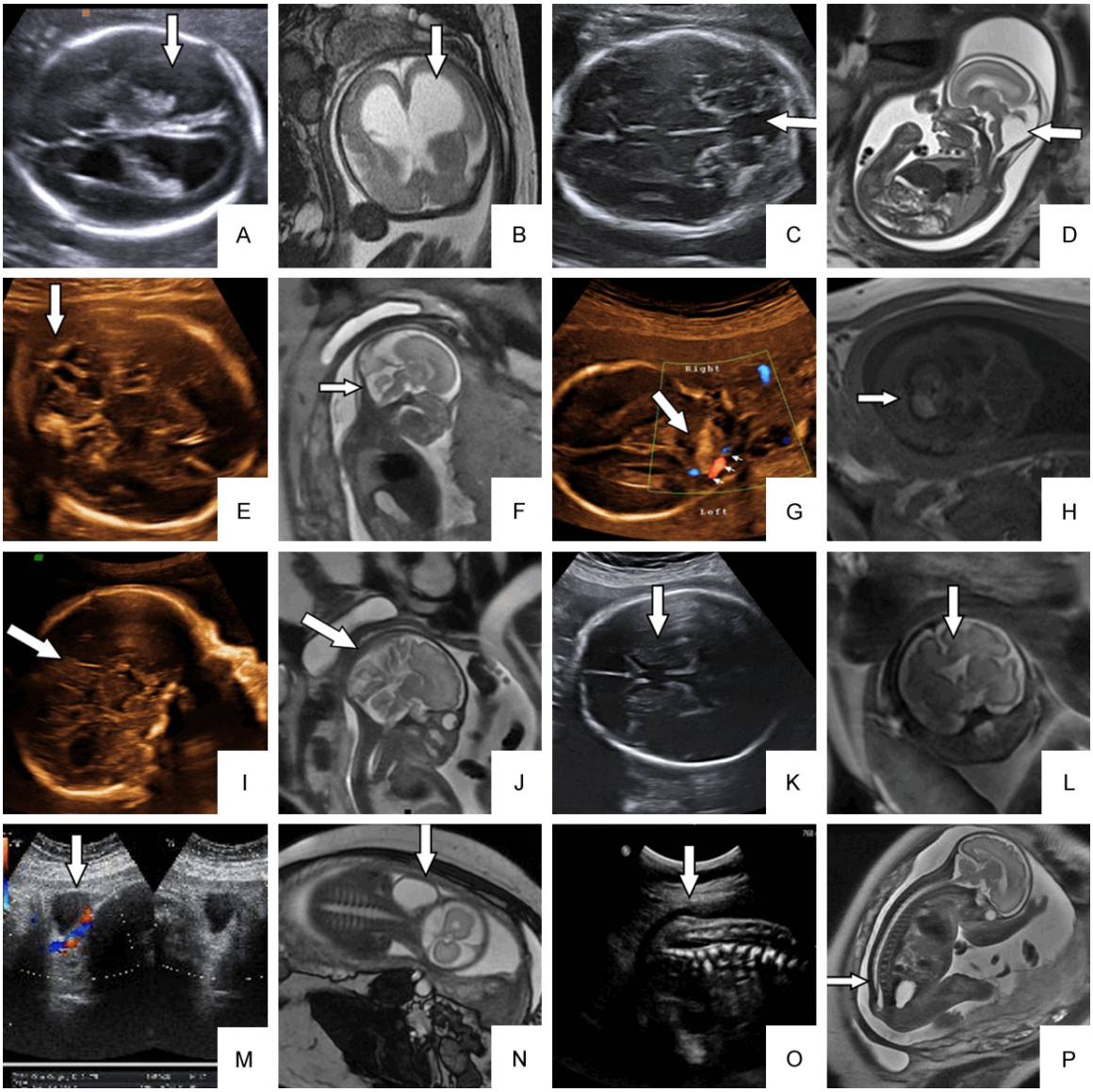

Figure 1. Examples of fetal cerebral abnormalities detected by ultrasonography and magnetic resonance imaging (MRI). (A, B) Hydrocephalus detected by ultrasonography (A) and MRI (B). The ultrasonography and T2WI showed significant supratentorial ventricular expansion and hydrocephalus, as well as thinning of the parenchyma of the cerebral hemispheres. (C, D) Dandy-Walker malformation detected by ultrasonography (C) and MRI (D). The bilateral cerebellar hemispheres and cerebellar vermis volume were small with partial absence and supination. The fourth ventricle was widened with cystic dilatation. Posterior fossa enlargement and uplift of the tentorium and transverse sinus were evident. (E, F) Blake's cysts detected by ultrasonography (E) and MRI (F). The development of the vermis was normal, but the fourth ventricle formed capsules that protruded into the posterior fossa. (G, H) Intracranial hemorrhage detected by ultrasonography (G) and MRI (H). There was left lateral ventricular enlargement, particularly in the inferoposterior aspect, combined with a local hematocele. (I, J) Absence of the corpus callosum detected by ultrasonography (I) and MRI (J). The sagittal image shows absence of the corpus callosum, cavum septum pellucidum and cingulate gyrus. The gyrus was arranged in a radial pattern. (K, L) Holoprosencephaly detected by ultrasonography (K) and MRI (L). The brain midline was broken at the cavum septum pellucidum, and there was interlinking of the anterior cornua. (M, N) Meningocele detected by ultrasonography (M) and MRI (N). (A) cystic mass filled with cerebrospinal fluid protruded from the left side of the neck. The spinal cord tissue protruding into the cyst was closely adhered to the cyst wall. (O, P) Tethered cord detected by ultrasonography (O) and MRI (P).

images, higher resolution, and a wider field of view. Thus, MRI is a good technique for confirming CNS abnormalities detected by ultrasound [5] and for providing additional information regarding these abnormalities, including the effects on surrounding brain tissue and the

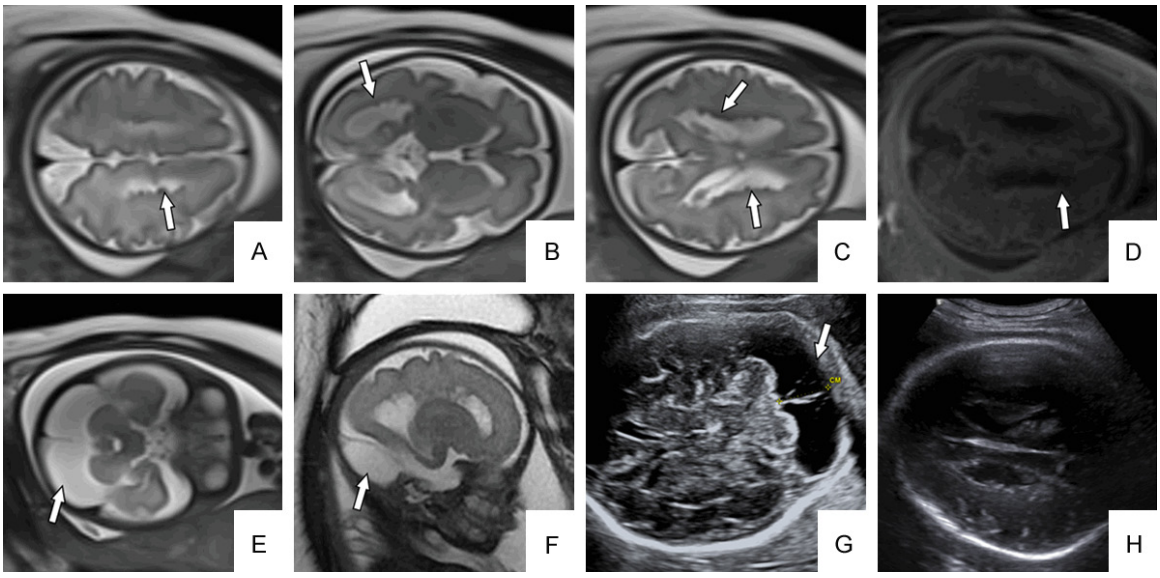

Figure 2. A fetus diagnosed with arachnoid cyst and tuberous sclerosis at 26 gestational weeks. Prenatal MRI demonstrated multiple small nodules at bilateral subventricular zones (A-D, arrows) and a large arachnoid cyst at posterior cranial fossa (E and F, arrows). However, only a large arachnoid cyst could be found on ultrasound image (G). The nodules were difficult to identify and were easily missed on the ultrasound image (H).

extent of any intracranial hemorrhage (**Figure 1G** and **1H**). Obstetric MRI is best performed after 20 gestational weeks [6], and in this study was conducted at 22^{+2}-38^{+6} gestational weeks. Our data are in good agreement with previous studies reporting that MRI provided additional clinical information in 22% [4], 25% [7] and 26% [8] of the cases. However, it should also be noted that in this study, autopsy identified CNS abnormalities missed by MRI in 1.9% of cases, and MRI showed false positive results in 2.5%.

Lateral ventricular enlargement is one of the most common fetal intracranial structural abnormalities identified by prenatal ultrasound screening [9]. In 70-85% of cases, lateral ventricular enlargement is combined with dysplasia of the CNS or other systems. We found that MRI provided supplementary information or corrected the diagnosis in 42.2% (49/116) of the lateral ventricular enlargement cases, consistent with a previously reported value of 51% [10]. In this study, there were 10 cases of lateral ventricular enlargement with an altered pregnancy outcome due to the MRI diagnosis (two decided to continue the pregnancy while eight chose termination of the pregnancy). Ultrasound in these cases demonstrated a moderate lateral ventricular enlargement combined with a fetal sacrococcygeal vertebral fusion, intestinal canal enlargement and chromosomal abnormality 46,XX,der(6)t(6;20)(q27;p11.2). MRI and autopsy after delivery confirmed that the ultrasound diagnosis was correct (**Figure 1A** and **1B**). Therefore, idiopathic lateral ventriculomegaly should not be assumed if prenatal ultrasound detects lateral ventricular enlargement, especially moderate-to-severe and bilateral enlargement. Instead, MRI should be undertaken to identify the cause and exclude other CNS abnormalities.

Posterior fossa abnormalities are also common fetal CNS disorders. MRI is superior to other imaging modalities in displaying the morphology and size of the entire posterior fossa, including cerebellar hemispheres, cerebellar vermis, fourth ventricle and subarachnoid spaces [11]. Among the 36 cases of posterior fossa enlargement identified by ultrasound in the present study, MRI detected additional features in 14 cases and corrected the diagnosis in 7 cases, including finding a Dandy-Walker malformation in 1 case (**Figure 1C** and **1D**) and no abnormality in 2 cases.

The pathogenesis of Dandy-Walker malformation is thought to involve genetic and environmental factors [12]. Agenesis/hypoplasia of the cerebellar vermis, a characteristic feature of Dandy-Walker malformation, is associated

Table 2. Imaging characteristics of 51 cases with fetal central nervous system abnormalities combined with chromosomal abnormalities

No.	Age of mother (years)	Gestation (weeks)	Ultrasound diagnosis	MRI diagnosis	Final diagnosis	Sample	Karyotype analysis
1	28	29+4	Mild enlargement of bilateral lateral ventricles, 'banana' and 'lemon' signs	Mild enlargement of bilateral lateral ventricles, cerebellar tonsillar hernia, suspicion of spinal bifida	Mild enlargement of bilateral lateral ventricles, cerebellar tonsillar hernia, spinal bifida	Umbilical cord blood	46,XY,dup(1)(q11q21) pat
2	25	24+1	Mild enlargement of bilateral ventricles, enlargement of posterior fossa, abnormal heart, thickening of posterior cervical skin	Mild enlargement of bilateral ventricles, enlargement of posterior fossa, abnormal heart, thickening of posterior cervical skin	Mild enlargement of bilateral ventricles, enlargement of posterior fossa, abnormal heart, thickening of posterior cervical skin	Amniotic fluid	47,XY,+der(21;21)(q10;q10)[22]/46,XY[5]
3	31	22+1	Moderate enlargement of bilateral lateral ventricles, fetal sacrococcygeal vertebral fusion, enlargement of intestinal canal	Moderate enlargement of bilateral lateral ventricles	Moderate partial enlargement of bilateral lateral ventricles, fetal sacrococcygeal vertebral fusion, intestinal dilatation	Amniotic fluid	46,XX,der(6)t(6;20)(q27;p11.2)mat
4	19	24+1	Moderate enlargement of bilateral lateral ventricles, polyhydramnios	Moderate enlargement of bilateral lateral ventricles, partial gyrus compression	Moderate enlargement of bilateral lateral ventricles, partial gyrus compression	Amniotic fluid	46,XX,der(9)add(9)(p21)
5	34	23+5	Mild enlargement of bilateral lateral ventricles, duodenal obstruction	Mild enlargement of bilateral lateral ventricles, duodenal obstruction	Mild enlargement of bilateral lateral ventricles, duodenal obstruction	Amniotic fluid	47,XX,+21
6	24	24+3	Enlargement of left lateral ventricle, nasal bone dysplasia	Mild enlargement of left lateral ventricle	Enlargement of left lateral ventricle, nasal bone dysplasia	Amniotic fluid	46,XY,der(5;11)(p15;q23)
7	39	24+6	Enlargement of bilateral lateral ventricles, nasal bone absence, dysplasia of long bones, polyhydramnios	Enlargement of bilateral lateral ventricles	Enlargement of bilateral lateral ventricles, celiac effusion, dysplasia of long bones, polyhydramnios	Amniotic fluid	47,XY,+21
8	30	30+5	Mild enlargement of left lateral ventricle	Mild enlargement of left lateral ventricle, cerebellar atrophy	Mild enlargement of left lateral ventricle, cerebellar atrophy	Umbilical cord blood	47,XY,+21
9	24	23+3	Mild enlargement of bilateral lateral ventricles	Mild enlargement of bilateral lateral ventricles	Mild enlargement of bilateral lateral ventricles	Amniotic fluid	47,XX,+21
10	29	23+2	Mild enlargement of bilateral lateral ventricles, enlarged cavum septum pellucidum, enlargement of posterior fossa, polyhydramnios	Mild enlargement of bilateral lateral ventricles	Mild enlargement of bilateral lateral ventricles, enlarged cavum septum pellucidum, enlargement of posterior fossa	Amniotic fluid	46,XY,del(13)(q12.3q14.11)
11	30	23+4	Mild enlargement of right lateral ventricle, short femur	Mild enlargement of right lateral ventricle	Mild enlargement of right lateral ventricle, short femur	Amniotic fluid	46,XY,der(19)1(14;19)(q32.2;p13.3)pat
12	33	32+4	Moderate enlargement of bilateral lateral ventricles	Moderate enlargement of bilateral lateral ventricles, partial gyrus compression	Moderate enlargement of bilateral lateral ventricles, partial gyrus compression	Umbilical cord blood	46, XY, dup(1) (q11 q21) pat
13	28	25+0	Enlargement of lateral ventricle, left pelvic ectopic kidney, atrioventricular abnormality, absence of nasal bone, thickening of posterior cervical skin	Enlargement of lateral ventricle, thickening of posterior cervical skin	Enlargement of lateral ventricle, left pelvic ectopic kidney, atrioventricular abnormality, absence of nasal bone, thickening of posterior cervical skin	Amniotic fluid	46,XX,inv(q)(p11 q13)
14	33	25+2	Enlargement of left lateral ventricle	Enlargement of left lateral ventricle	Enlargement of left lateral ventricle	Amniotic fluid	47,XY,+21
15	27	30+1	Moderate enlargement of bilateral lateral ventricle	Moderate enlargement of bilateral lateral ventricle, partial gyrus compression	Moderate enlargement of bilateral lateral ventricle, partial gyrus compression	Umbilical cord blood	47,XY,+21
16	32	25+4	Mild enlargement of bilateral lateral ventricles, enlargement of posterior fossa, coarctation of aorta, overlapping fingers, sandal gap, edema of anterior nasal skin, nasal fold thickening	Mild enlargement of bilateral lateral ventricles, enlargement of posterior fossa	Mild enlargement of bilateral lateral ventricles, enlargement of posterior fossa, coarctation of aorta, overlapping fingers, sandal gap, edema of anterior nasal skin, nasal fold thickening	Amniotic fluid	47,XY,+der(21;21)(q10;q10)[22]/46,XY[5]
17	29	33+1	Enlargement of posterior fossa	Enlargement of posterior fossa, posterior fossa arachnoid cysts	Enlargement of posterior fossa, posterior fossa arachnoid cysts	Umbilical cord blood	47,XY,+18

18	38	23+4	Enlargement of posterior fossa, thickening of posterior cervical skin	Enlargement of posterior fossa	Enlargement of posterior fossa	Amniotic fluid	47,XY,+21
19	30	29+4	Enlargement of posterior fossa	Enlargement of posterior fossa	Enlargement of posterior fossa	Umbilical cord blood	46,XY,?inv(5)(p13p15.1)
20	30	26+5	Dandy-Walker syndrome, lung dysplasia, small thoracic cavity, right ventricle double outlet, single umbilical artery	Cerebellum, Dandy-Walker syndrome, lung dysplasia, small thorax, right ventricle double outlet, single umbilical artery	Dandy-walker syndrome, lung dysplasia, small thoracic cavity, right ventricle double outlet, single umbilical artery	Amniotic fluid	47,XX,+18
21	25	34+2	Partial hypoplasia of cerebellar vermis, bilateral cleft lip, cardiac malformation, single umbilical artery	Partial hypoplasia of cerebellar vermis	Partial hypoplasia of cerebellar vermis, bilateral cleft lip, cardiac malformation, single umbilical artery	Umbilical cord blood	47,XY,+18
22	26	22+5	Bilateral choroidal cysts, nasal bone absence	Bilateral choroidal cysts	Bilateral choroidal cysts, nasal bone absence	Amniotic fluid	47,XY,+21
23	34	23+1	Left choroid cyst, enhanced intestinal echo	Left choroid cyst	Left choroid cyst	Amniotic fluid	47,XX,+21
24	29	22+4	Left choroid cyst, diaphragmatic hernia	Left choroid cyst, diaphragmatic hernia	Left choroid cyst, diaphragmatic hernia	Amniotic fluid	47,XX,+18
25	33	21+2	Left choroid cyst	Left choroid cyst, enlargement of right lateral ventricle and trigone, right hemisphere changes; possible contralateral hemisphere dysplasia could not be excluded	Left choroid cyst, enlargement of right lateral ventricle and trigone, right hemisphere changes; possible contralateral hemisphere dysplasia could not be excluded	Amniotic fluid	47,XY,+21
26	31	22+4	Right choroid cyst, fist abnormalities	Right choroid cyst	Right choroid cyst, fist abnormalities	Amniotic fluid	47,XX,+18
27	25	23+6	Left choroid cysts, thickening of posterior cervical skin	Left choroid cysts	Left choroid cysts, thickening of posterior cervical skin	Amniotic fluid	47,XY,+21
28	31	22+4	Bilateral choroid cysts, widening of bilateral renal pelvis	Bilateral choroid cysts, widening of bilateral renal pelvis	Bilateral choroid cysts, widening of bilateral renal pelvis	Amniotic fluid	47,XX,+21
29	28	24+1	Right choroid cysts, cleft lip	Right choroid cysts	Right choroid cysts, cleft lip	Amniotic fluid	47,XY,+18
30	28	32+1	Craniotomy, bowel dilatation	Craniotomy, bowel dilatation	Craniotomy, bowel dilatation	Umbilical cord blood	46,X,inv(X)(p21.1p11.4)mat
31	25	31+3	Craniotomy	Craniotomy	Craniotomy	Umbilical cord blood	47,XX,+21
32	24	32+6	Hydrocephalus, ascites, substantial shortening of long bones, polyhydramnios	Hydrocephalus, ascites, substantial shortening of long bones, polyhydramnios	Hydrocephalus, ascites, substantial shortening of long bones, polyhydramnios	Umbilical cord blood	47,XY,+21
33	27	22+1	Bilateral hydrocephalus, polyhydramnios	Bilateral hydrocephalus, enlargement of third ventricle, subacute ventricular hemorrhage	Bilateral hydrocephalus, enlargement of third ventricle, subacute ventricular hemorrhage	Amniotic fluid	47,XX,+21
34	39	26+5	Hydrocephalus, encephalocele	Hydrocephalus, encephalocele	Hydrocephalus, encephalocele	Umbilical cord blood	47,XY,+18
35	36	24+4	Bilateral hydrocephalus	Bilateral hydrocephalus	Bilateral hydrocephalus	Amniotic fluid	46,XY,der(5;11)(p15;q23)
36	21	22+3	Holoprosencephaly	Holoprosencephaly	Holoprosencephaly, beaked nose, hydrocephalus	Amniotic fluid	47,XX,+13
37	28	21+4	Holoprosencephaly, facial cleft, absence of nasal bone, right heart dysplasia	Holoprosencephaly	Holoprosencephaly, facial cleft, absence of nasal bone right heart dysplasia	Amniotic fluid	46,XX,del(7)(q32)[32]/46,XX,del (7)(q32::?)[7]
38	34	22+0	Holoprosencephaly, microphthalmus, ocular hypotelorism, absence of nasal bone, single umbilical artery (left absence)	Holoprosencephaly	Holoprosencephaly, microphthalmus, ocular hypotelorism, absence of nasal bone, single umbilical artery (left absence)	Amniotic fluid	47,XX,+13

39	28	21+6	Holoprosencephaly, absence of nasal bone, right ventricle double outlet, absence of ventricular septum, umbilical swelling (bowel), giant bladder, single umbilical artery (right absence)	Holoprosencephaly, umbilical swelling (bowel), giant bladder	Holoprosencephaly, absence of nasal bone, right ventricle double outlet, absence of ventricular septum, umbilical swelling (bowel), giant bladder, single umbilical artery (right absence)	Amniotic fluid	47,XY,+13
40	28	22+5	Holoprosencephaly, absence of nasal bone, absence of ventricular septum, umbilical swelling (bowel), edema	Holoprosencephaly, absence of nasal bone, absence of ventricular septum, umbilical swelling (bowel), edema, absence of cavum septum pellucidum	Holoprosencephaly, absence of nasal bone, absence of ventricular septum, umbilical swelling (bowel), edema, absence of cavum septum pellucidum	Amniotic fluid	47,XY,+18
41	27	25+4	Holoprosencephaly, central cleft lip, ocular hypotelorism, tetralogy of Fallot, single umbilical artery (left absence)	Holoprosencephaly	Holoprosencephaly	Amniotic fluid	47,XX,+13
42	30	22+5	Holoprosencephaly	Holoprosencephaly, body stalk anomaly	Holoprosencephaly, body stalk anomaly	Amniotic fluid	47,XX,+13
43	34	22+6	Holoprosencephaly, beaked nose, absence of nasal bone, umbilical bulging (bowel), single umbilical artery (left), multiple umbilical cord cysts	Holoprosencephaly, umbilical bulging (bowel)	Holoprosencephaly, beaked nose, absence of nasal bone, umbilical bulging (bowel), single umbilical artery (left), multiple umbilical cord cysts	Amniotic fluid	47,XX,+13
44	34	24+6	Holoprosencephaly, cleft lip, single atrium, single ventricle, bilateral renal dysplasia	Holoprosencephaly, bilateral renal dysplasia	Holoprosencephaly, cleft lip, single atrium, single ventricle, bilateral renal dysplasia	Amniotic fluid	46,XX,dup(4)(q13.1 q35.2)
45	35	22+4	Holoprosencephaly, beaked nose	Holoprosencephaly	Holoprosencephaly, beaked nose	Amniotic fluid	47,XY,+13
46	36	22+3	Holoprosencephaly, beaked nose, microphthalmus, polyhydramnios	Holoprosencephaly, microphthalmus	Holoprosencephaly, beaked nose, microphthalmus, polyhydramnios	Amniotic fluid	47,XY,+13
47	32	21+3	Holoprosencephaly, beaked nose, absence of nasal bone, left ventricular dysplasia	Holoprosencephaly	Holoprosencephaly, beaked nose, absence of nasal bone, left ventricular dysplasia	Amniotic fluid	46,XX,der(13;13)(q10;q10)
48	30	24+0	Holoprosencephaly, beaked nose, microphthalmus, ocular hypotelorism, flattened face, low binaural auricular position, absence of ventricular septum, microcephaly, rachiterata, overlapping fingers of left hand	Holoprosencephaly, microcephaly, rachiterata	Holoprosencephaly, beaked nose, microphthalmus, ocular hypotelorism, flattened face, low binaural auricular position, absence of ventricular septum, microcephaly, rachiterata, overlapping fingers of left hand	Amniotic fluid	47,XY,+18
49	29	25+2	Strawberry skull, small mandible, flat cerebellum, absence of ventricular septum, persistent left superior vena cava, tethered cord, recessive spina bifida (furus sinus), slightly small kidneys, overlapping fingers of both hands, left single umbilical artery	Strawberry skull, tethered cord	Strawberry skull, small mandible, flat cerebellum, absence of ventricular septum, persistent left superior vena cava, tethered cord, recessive spina bifida (furus sinus), slightly small kidneys, overlapping fingers of both hands, left single umbilical artery	Amniotic fluid	47,XX,+18
50	28	24+2	Sacrococcygeal teratoma, heart enlargement, polyhydramnios, absence of nasal bone	Sacrococcygeal teratoma	Sacrococcygeal teratoma	Amniotic fluid	47,XX,+21
51	25	30+3	Sacrococcygeal teratoma, scalp edema, nuchal fold thickness	Sacrococcygeal teratoma, scalp edema	Sacrococcygeal teratoma, scalp edema	Umbilical cord blood	47,XY,+21

Table 3. Comparison of chromosomal abnormalities between isolated fetal CNS abnormalities and non-isolated fetal CNS abnormalities

	Isolated CNS abnormalities	Non-isolated CNS abnormalities	Total
Chromosomal abnormalities	13 (25.5%)	38 (74.5%)	51
Without chromosomal abnormalities	258 (83.8%)	50 (16.2%)	308
Total	271	88	359

CNS, central nervous system.

with recessive genetic diseases (e.g. Jubert, Walker-Warburg and Meckel-Gruber syndromes) and chromosomal abnormalities (e.g. 18-triosmy and 13-triosmy syndromes) [13]. Among 5 cases of Dandy-Walker malformation detected by ultrasound in this study, MRI confirmed the diagnosis in 3 cases, revealed corpus callosum hypoplasia in 1 case and found no abnormality in 1 case. Two cases of isolated posterior fossa enlargement were diagnosed with 21-trisomy and 46,XY,?inv(5)(p13p15.1), and 1 case of posterior fossa had multiple abnormalities (18-trisomy). The diagnosis of Dandy-Walker malformations (especially variants) should be performed after 20 gestational weeks because development of the cerebellar vermis is not complete before 18 gestational weeks.

In the present study, ultrasound identified 10 cases of absent corpus callosum (**Figure 1I** and **1J**), which can result from environmental insults and chromosomal abnormalities [14-16]. Since corpus callosum hypoplasia leads to lateral ventricular enlargement, an MRI should be performed as a supplementary investigation when lateral ventricular enlargement is detected by prenatal ultrasonography to exclude malformations of the corpus callosum and other intracranial structures. MRI is superior to ultrasound at diagnosing corpus callosum abnormalities since it can display the features of the entire corpus callosum [17].

Abnormal cystic echoes are common manifestations of fetal CNS dysplasia. MRI has significant advantages in localizing intracranial cysts and detecting compression of surrounding brain tissue. In this study, ultrasound diagnosed arachnoid cysts in 32 cases, and MRI confirmed partial corpus callosum dysplasia in 6 of these. The detection rate for choroidal cysts during the second trimester is 0.6-2.0%; the cysts have fixed locations and can be diagnosed by ultrasound as echo-free dark areas within the choroidal plexus. In this study, ultrasound identified 12 cases with choroidal cysts. MRI misdiagnosed 3 of these 12 cases as normal, possibly because MRI is not real-time imaging and was impacted by cerebrospinal fluid in the lateral ventricle. Moreover, MRI is known to be poor at displaying blood flow signals.

Microcephaly is usually correlated with intrauterine infection and congenital dysplasia of intracranial tissues. Clinically, the diagnostic criteria include a head circumference less than two standard deviations of normal fetuses in the corresponding gestational age, a reduction in brain parenchyma, cortical hypoplasia, and a small cranial cavity. MRI examination may be negative for mild microcephaly. Ultrasound identified 10 cases with suspected microcephaly, but MRI subsequently altered the diagnosis in 3 of these (normal intracranial structure, cerebral cortex dysplasia and corpus callosum dysplasia). Hence, MRI should be performed if ultrasound suggests the presence of microcephaly, particularly during the last trimester.

The CSP has a normal width of 0.2-0.9 cm [18], and its absence is usually a manifestation of septo-optic dysplasia or absent corpus callosum. Isolated CSP absence is considered a normal physiologic variation, and CSP simple enlargement usually has no clinical significance. In the present study, pregnancy was continued in 5 cases of CSP enlargement after MRI had excluded other intracranial abnormalities. There were 17 cases of isolated CSP enlargement, including 1 with pachygyria and 1 with interlinked anterior cornua revealed by MRI. In addition, one case was found to have no abnormality on MRI.

MRI can directly display the spinal cord and facilitate the diagnosis of spina bifida, meningomyelocele, meningocele, and vertebral tumors. MRI has been reported to accurately determine the location of meningomyelocele and provide information in 80% of patients that guides management [19]. By contrast, ultrasound is not specific for spinal cord abnormali-

ties that manifest as an irregular arrangement of the spine, local enlargement of the spinal canal, and abnormalities of spinal curvature. Thus, ultrasound alone cannot definitively diagnose some diseases. In this study, MRI successfully diagnosed four cases of meningocele with a bulging of spinal cord tissues (**Figure 1M** and **1N**).

An important finding of the present study was that diagnostic agreement between MRI and ultrasound was found in only 68.0% of the cases, with MRI providing additional clinical information in a further 24.0%. Moreover, MRI and ultrasound yielded differing diagnoses in 4.7% of the cases. The prevalence of chromosomal abnormalities was markedly higher for non-isolated CNS abnormalities (43.2%) than for isolated CNS abnormalities (14.2%). These data supported the theory that MRI may be superior to ultrasound in the diagnosis of fetal CNS abnormalities. Although ultrasound cannot accurately diagnose all fetal CNS abnormalities, as a first-line imaging modality, it still has value for prenatal screening and early detection of intracranial structural abnormalities. However, we recommend that MRI be used as an additional tool to confirm the diagnosis when ultrasound screening suspects a fetal CNS abnormality. Furthermore, we suggest that karyotype is necessary when non-isolated CNS abnormalities are identified.

There are several limitations in this research. First, due to severe malformations found in routine screening around 11-13 weeks, most pregnant women have induced labor at 16 weeks and have no chance to undergo further MRI in our hospital. Second, some pregnant women refused chromosome examinations considering the risk of puncture, so the study cannot show the chromosomal abnormalities in all cases. Whether there are other chromosomal abnormalities, such as microdeletions and balanced translocations, remains unclear. Third, the interpretations of ultrasound and MRI results largely rely on the experience and proficiency of the operators, which may cause discrepancies between the ultrasound and MRI findings. Therefore, the expertise of the physician may greatly affect the accuracy of these final diagnoses.

In conclusion, MRI is superior to ultrasound in the diagnosis of fetal CNS abnormalities. We suggest that MRI should be used as a supplementary tool to confirm the diagnosis after 20 weeks of gestation when ultrasound suspects a fetal CNS abnormality. In addition, chromosomal abnormalities have a close relation with non-isolated CNS abnormalities.

Disclosure of conflict of interest

None.

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