

Fetal Magnetic Resonance Imaging in the Evaluation of Fetuses Referred for Sonographically Suspected Abnormalities of the Corpus Callosum

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Objective. Fetal magnetic resonance imaging (MRI) has been shown to be useful in assessing the developing central nervous system. However, its utility in specific brain disorders has not been well investigated. We hypothesized that fetal MRI can better assess the integrity of the brain in cases with sonographically suspected callosal abnormalities. **Methods.** We retrospectively reviewed fetal MRI and prenatal sonographic studies of 10 fetuses referred for MRI for sonographically suspected callosal abnormalities. **Results.** An abnormal corpus callosum was identified on fetal MRI in 80% of cases. The type of callosal abnormality (complete or partial agenesis) was similar on both prenatal sonography and fetal MRI in all cases. All sonographically identified additional brain abnormalities were detected on fetal MRI, with the exception of choroid plexus cysts. Furthermore, in 63% (5 of 8) of cases with a callosal abnormality on both sonography and fetal MRI, additional brain abnormalities were detected on fetal MRI that were not apparent on sonography. These sonographically occult findings were confirmed on postnatal MRI or autopsy in 3 of 5 patients. **Conclusions.** Fetal MRI is an important adjunct to sonography in assessing the corpus callosum and other aspects of brain development when agenesis of the corpus callosum is suspected. It can identify frequent additional findings that are not visible on sonography such as abnormal sulcation. In light of the association between additional brain abnormalities and worse neurodevelopmental outcome, the potential of fetal MRI as an important adjunctive prognostic imaging test in fetuses with callosal agenesis can now be tested. **Key words:** corpus callosum agenesis; fetal magnetic resonance imaging; sonography.

Abbreviations

LMP, last menstrual period; MRI, magnetic resonance imaging; SSFSE, Single-shot fast spin echo

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The corpus callosum is 1 of 3 major commissures that connect the cerebral hemispheres. It develops from the lamina reunions of His between 8 and 20 weeks' gestation.^{1,2} Abnormalities of the corpus callosum include hypoplasia, hyperplasia, agenesis, hypogenesis (also called partial agenesis), dysgenesis, and destruction. Callosal abnormalities can result from genetic factors, metabolic disorders, or insults such as infection to the developing brain. The prevalence of callosal agenesis is estimated at 0.1% to 0.7% in the general population and 2.3% in the developmentally disabled population.³⁻⁸ Isolated agenesis of the corpus callosum is uncommon, with additional abnormalities present in most cases.^{7,9-13} Although the prognostic implications of prenatally detected callosal agenesis are

not fully understood, evidence suggests that the presence of additional abnormalities imparts a worse prognosis.^{1,2,7,10,12,14-17}

With the advent of ultrafast T2 imaging techniques, fetal magnetic resonance imaging (MRI) has been increasingly used to evaluate brain abnormalities that are suspected on prenatal sonography. Fetal MRI affords more detailed visualization of normal brain development¹⁸⁻²⁶ as well as abnormalities of brain development, including callosal agenesis.^{21,22,27-34} Although sonography often relies on indirect signs of callosal agenesis such as colpocephaly, a high-riding third ventricle, and widening of the interhemispheric fissure, fetal MRI also allows better direct visualization of the corpus callosum on a midline sagittal image. Moreover, the increased contrast resolution of fetal MRI allows identification of more subtle brain abnormalities that can be difficult to detect on prenatal sonography and are often seen in the setting of callosal agenesis. We therefore hypothesized that fetal MRI could better assess the degree of brain dysgenesis in fetuses in whom a callosal abnormality was suspected on prenatal sonography.

Materials and Methods

We retrospectively identified all cases referred for fetal MRI for suspected abnormalities of the corpus callosum based on prenatal sonography from November 1997 to June 2002. During this period, all patients at our institution with sonographically suspected callosal abnormalities in the fetus were routinely offered MRI for further evaluation. Fetuses with Chiari II malformations were excluded from this study. Fetal sonographic images were retrospectively reviewed by a sonologist (R.B.G.) with expertise in fetal sonography. In 1 case, the sonographic examination was performed at an outside hospital, and images were reviewed by a perinatologist with expertise in fetal sonography (J.D.G.). Both sonogram reviewers were blinded to the exact clinical history and fetal MR results at the time of review. All fetal MR images were retrospectively reviewed by 2 pediatric neuroradiologists (O.A.G. and A.J.B.). Fetal MRI readers were blinded to the exact clinical history and initial imaging results at the time of review, although they were aware that all cases had a suspected callosal abnormality. A finding was considered "suspicious" on fetal MRI if it could not be confirmed in more than 1 plane.

Ventriculomegaly was not considered an additional finding because dilatation of the posterior lateral ventricle can be attributed to callosal agenesis. Gestational age was based on last menstrual period (LMP).

All fetal MR examinations were performed with a 1.5-T magnet (GE Healthcare, Milwaukee, WI) and a torso phased array coil. Single-shot fast spin echo (SSFSE) T2-weighted images were acquired in the axial, sagittal, and coronal planes. Whenever possible, imaging was repeated in each plane until at least 2 adequate axial, coronal, and sagittal sets of images were obtained. Parameters varied somewhat because studies were done over a 4-year period. All patients had images that were 3 mm in thickness with no skip, and some had additional 4- or 2-mm-thick slices. The field of view ranged from 20 to 28 depending on gestational age. One patient also had SSFSE T2-weighted images acquired via a new technique known as Real-Time SSFSE imaging for the fetus, which allows the MR technologist to interactively control imaging parameters such as slice position, orientation, field of view, and thickness.³⁵ Fetal sonographic examinations at our institution were performed with Acuson Sequoia sonographic equipment (Siemens Medical Solutions, Mountain View, CA) and sector or curved array multifrequency (4- to 8-MHz) multifocused transducers. Endovaginal scanning (with 5- to 10-MHz vaginal probes) was used when visualization of fetal brain anatomy was suboptimal transabdominally and the fetus was in the vertex position.

Follow-up information about the outcome of the pregnancy was obtained in all cases. In cases of a live birth, information about the child's neurodevelopment was obtained when possible. Postnatal MRI studies and autopsy results were reviewed when available. This study was approved by our Institutional Review Board.

Results

Of the 220 patients referred for fetal MRI of the brain, spine, or both from November 1997 to June 2002, 11 were referred for confirmation of suspected anomalies of the corpus callosum. On reanalysis of the sonographic images, 1 patient was no longer thought to have findings suspicious for callosal agenesis and instead was interpreted as having borderline enlarged ventricles. The remaining 10 patients constituted the basis

for our analysis. The median gestational age based on LMP for these 10 patients was 22.6 weeks (range, 19.3–29.9 weeks) at the time of sonography and 23.0 weeks (range, 19.7–32.4 weeks) at the time of fetal MRI. The difference in gestational age based on LMP versus composite sonographic measurements was within 1 week for 8 of 10 patients and greater than 1 week in 2 patients because of discrepant head size measurements (range, 0–19 days; median, 4.5 days). The median number of days between sonography and fetal MRI was 1.5 days (range, 0–17 days), and 7 patients had an MRI within 2 days of the fetal sonography. All pregnancies were singleton, with the exception of a twin pregnancy in which 1 fetus was suspected to have a callosal abnormality on the basis of a sonographic examination performed at 29.9 weeks.

Of the 10 patients with a sonographically suspected callosal abnormality, the callosal finding was concordant on fetal MRI and sonography in 8 (Table 1). In particular, in 2 patients in whom only the anterior corpus callosum was visualized and partial agenesis was suspected on sonography, fetal MRI was in agreement with the suspected sonographic diagnosis of callosal hypogenesis with absence of a posterior body and splenium. Five patients had suspected complete callosal agenesis on the basis of obstetric sonography; fetal MRI findings were in agreement with complete callosal agenesis in all. In 1 case, there was extensive parenchymal destruction, and the corpus callosum was visualized on neither sonography nor MRI either because of agenesis, thinning or destruction of the corpus callosum.

Two of the 10 patients referred for a sonographically suspected callosal abnormality had a normal corpus callosum visualized on fetal MRI. One case was referred for suspected callosal hypogenesis with sonographic visualization of only the anterior corpus callosum and a suspected midline dorsal cyst (Figure 1). Another case was referred for suspected callosal agenesis with ventriculomegaly and distention of the interhemispheric fissure. In this case, fetal MRI demonstrated mild ventriculomegaly while identifying a normal corpus callosum and also showed a focal area of increased T2 signal adjacent to the frontal horn of the lateral ventricle, consistent with parenchymal injury (Figure 2).

Additional brain findings were seen on prenatal sonography in 5 patients with callosal agenesis, and these findings were also identified by fetal

MRI in 4 of the 5 patients. These consisted of parenchymal destruction, ventricular irregularity, cerebellar dysgenesis, and periventricular nodular heterotopia. In 1 patient, fetal MRI did not show choroid plexus cysts. In another case, periventricular heterotopia was suspected on both sonography and MRI, although this could not be confirmed in more than 1 plane on MR images. A total of 5 patients also had ventriculomegaly, which measured from 10.5 to 33 mm on sonography, although this was not considered an additional abnormality in our study because it can be seen in the setting of isolated callosal agenesis.

Additional sonographically occult abnormalities of the brain were identified on fetal MRI in a total of 5 of the 8 patients with a callosal abnormality on fetal MRI. One patient with suspected isolated callosal hypogenesis also had abnormally shallow sylvian fissures and an abnormal appearance of the brain parenchyma (Figure 3). Another patient with suspected isolated callosal agenesis also had a delay in sulcation (only the sylvian fissures were formed) as well as a small pons on fetal MRI (Figure 4). Two patients with sonographic findings of callosal agenesis, ventriculomegaly, and posterior fossa abnormalities also had additional abnormalities on fetal MRI. In particular, ventricular irregularity identified on sonography in 1 case was thought to represent either a destructive process or a neuronal migrational disorder; fetal MRI identified extensive periventricular nodular heterotopia and bilateral schizencephaly as well as a diffusely abnormal cortical pattern that was not apparent on sonography (Figure 5). In the second case, fetal MRI demonstrated additional findings, including kinking of the pontomesencephalic junction and lissencephaly consistent with the diagnosis of Walker-Warburg syndrome (Figure 6). Another patient was referred for fetal MRI because of sonographically suspected callosal agenesis, periventricular heterotopia, and choroid plexus cysts; fetal MRI showed additional findings of underdeveloped sylvian fissures, focal areas of cortical malformation in the left frontal and temporal lobes, a diffusely abnormal morphology of the cerebral hemispheres most marked in the frontal lobes and suggestive of more diffuse cerebral dysgenesis, a dysgenetic cerebellum with abnormal morphology of the fourth ventricle, and unilateral microphthalmia (Figure 7). The constellation of these MRI findings favored the prenatal diagnosis of Aicardi syndrome.

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Table 1. Findings on Prenatal Sonography and Fetal MRI

Case	GA at MRI, wk	Interval Between Sonography and MRI, d	Prenatal Sonographic Findings	Fetal MRI Findings	Follow-up
1	25	0	Callosal agenesis VM	Callosal agenesis VM Delay in sulcation Small pons	Postnatal MRI Callosal agenesis VM Small pons Diffusely abnormal sulcal pattern with too many sulci and lack of secondary and tertiary sulci Diminished white matter volume
2	21	1	Callosal agenesis Suspicious for PVNH VM	Callosal agenesis Suspicious for PVNH VM	Termination without autopsy
3	23	16	Callosal agenesis vs thinning/ destruction Diffuse parenchymal destruction VM	Callosal agenesis vs thinning/ destruction Diffuse parenchymal destruction VM	Autopsy Absent corpus callosum Diffuse parenchymal destruction
4	22	0	Callosal hypogenesis VM	Callosal hypogenesis VM	Postnatal MRI Callosal hypogenesis VM PVNH
5	23	0	Callosal hypogenesis	Callosal hypogenesis Shallow sylvian fissures Poor visualization of parenchymal layers	Autopsy Callosal hypogenesis Unable to confirm or exclude frontal lobe dysplasia
6	23	0	Callosal agenesis Small cerebellum Absent vermis Small midbrain	Callosal agenesis Small cerebellum Absent vermis Small brain stem Kinking at pontomesencephalic junction Absent sylvian fissures (lissencephaly) Homogeneous, thin parenchyma Dysplastic DGN	Autopsy Callosal agenesis Small cerebellar hemispheres Absent vermis Kinked brain stem with acute angle at the pons Flat cerebral surface except for areas of colloblestone appearance and rudimentary sylvian fissures Thin cortical mantle
7	32	17	Callosal agenesis PVNH VM Small cerebellum	Callosal agenesis PVNH VM Small cerebellum Bilateral open and closed lip schizencephalic defects Diffusely abnormal sulcal pattern	Postnatal MRI Callosal agenesis PVNH VM Small cerebellum Bilateral open and closed lip schizencephaly Diffusely abnormal sulcal pattern
8	19	2	Callosal agenesis PVNH Choroid plexus cysts	Callosal agenesis PVNH Shallow sylvian fissures Abnormal sulcation and parenchymal thinning in the frontal and temporal lobes Cerebellar dysgenesis Microphthalmia	Termination without autopsy
9	20	9	Callosal hypogenesis Suspected midline cyst	Normal corpus callosum	Normal neurodevelopment at 23 months
10	25	7	Callosal agenesis VM Prominent interhemispheric fissure	VM Normal corpus callosum Focal periventricular parenchymal injury	Normal neurodevelopment at 10 months

DGN indicates deep gray nuclei; GA, gestational age; PVNH, periventricular nodular heterotopia; and VM, ventriculomegaly. Findings detected only on fetal MRI are indicated in bold.

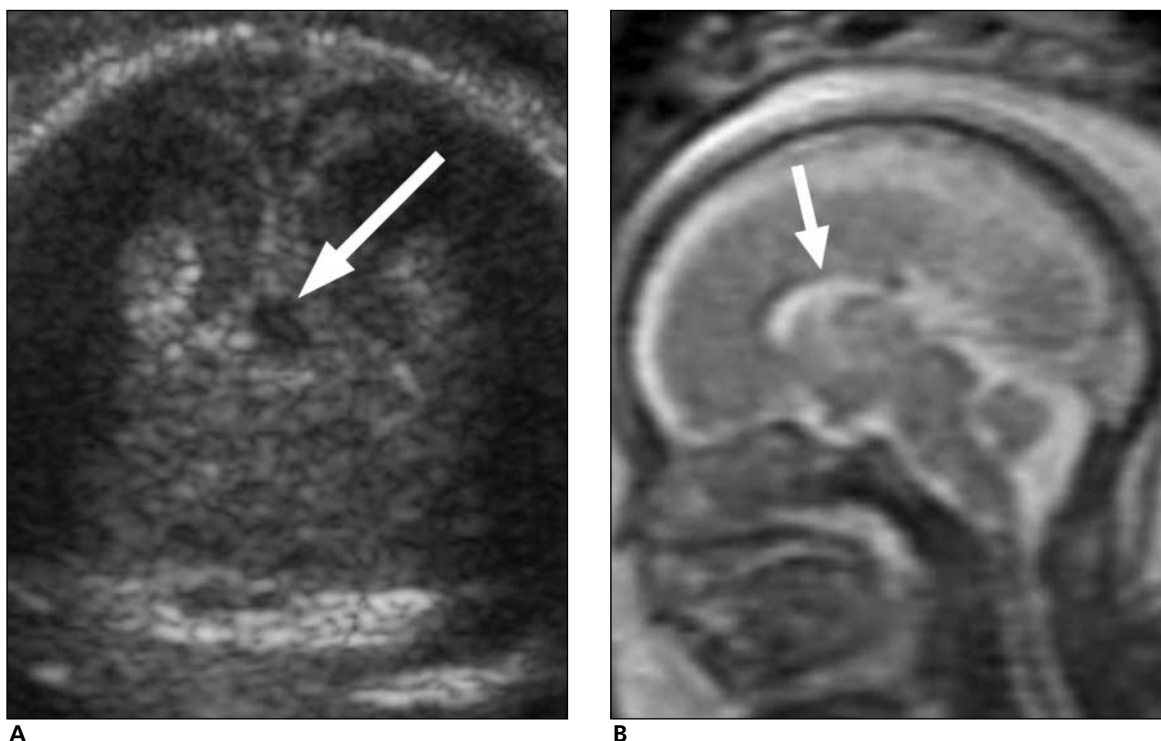


Figure 1. Images from a fetus at 20 gestational weeks with a suspected callosal abnormality on sonography (case 9). **A**, Coronal sonogram showing a midline dorsal cyst (arrow) at 19 weeks' gestation. Only the anterior corpus callosum was visualized on other images. **B**, Sagittal SSFSE T2-weighted image showing an intact corpus callosum (arrow) on MRI performed at 20 weeks' gestation.

Figure 2. Images from a fetus at 25 gestational weeks with a suspected callosal abnormality on sonography (case 10). **A**, Normal corpus callosum on midline sagittal SSFSE T2-weighted image obtained with Real-Time imaging (arrow). **B**, Coronal SSFSE T2-weighted image showing a focus of hyperintensity adjacent to the left lateral ventricle (arrow) and confirmed in the axial plane (not shown).

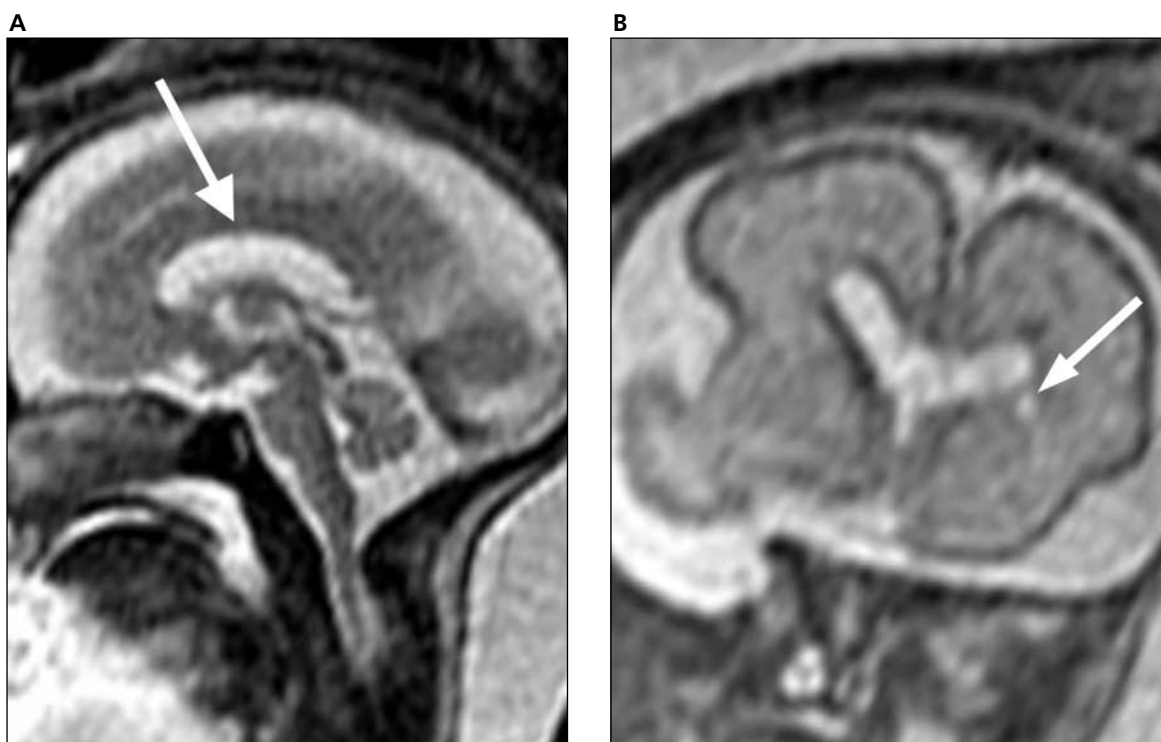
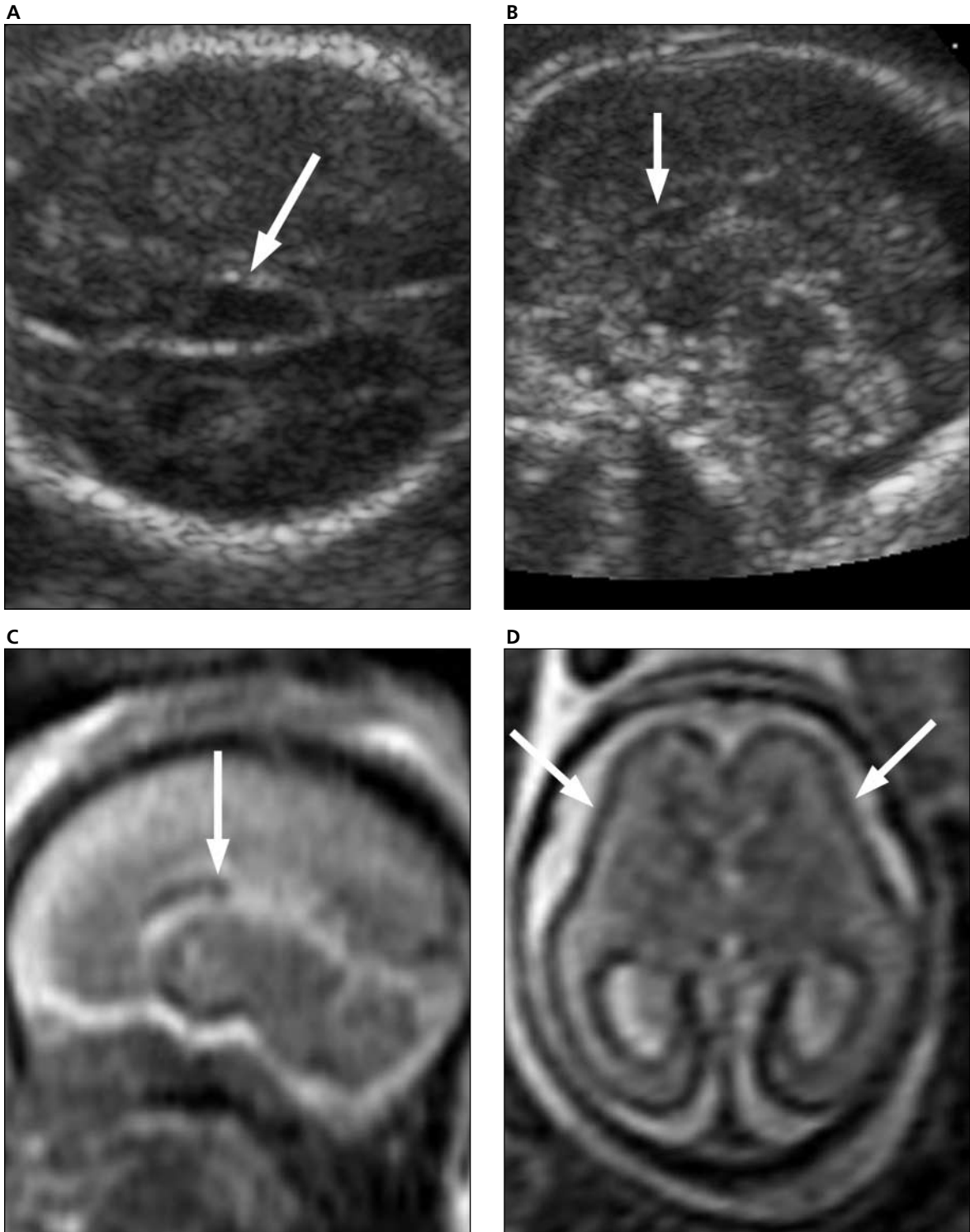
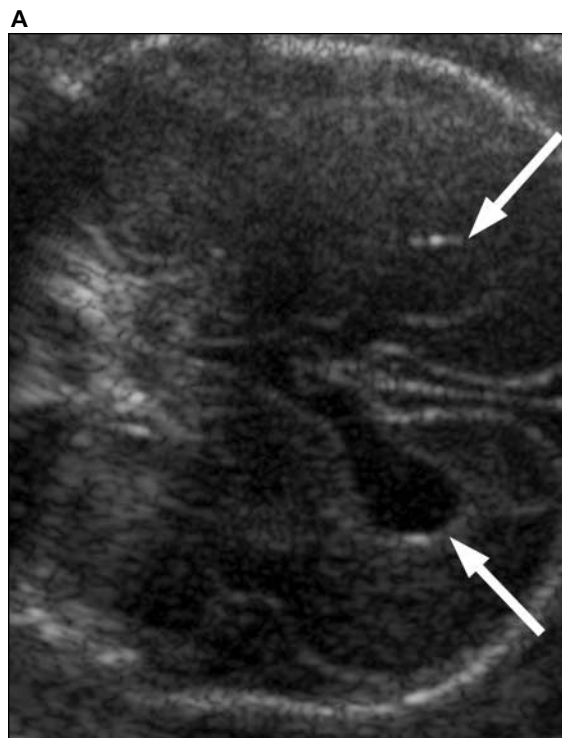


Figure 3. Images from a fetus at 23 gestational weeks with callosal hypogenesis (case 5). **A**, Oblique coronal sonogram showing a high-riding posterior third ventricle (arrow). **B**, Sagittal sonogram showing an intact anterior corpus callosum (arrow) with no posterior callosum identified, consistent with callosal hypogenesis. **C**, Hypogenesis of corpus callosum confirmed on sagittal SSFSE T2-weighted image (arrow). **D**, Axial SSFSE T2-weighted image showing additional MR findings of shallow sylvian fissures for gestational age (arrows) and poor distinction of parenchymal layers.



Autopsy or postnatal MRI confirmation was available in 3 of the 5 patients in whom fetal MRI revealed sonographically occult findings. In the fourth case, autopsy confirmed callosal hypogenesis but could not exclude or confirm any frontal lobe dysplasia. In the fifth case, the pregnancy was terminated, and an autopsy was not performed. The pregnancy was continued in 2 of the 4 cases, and follow-up clinical evaluation showed severe global developmental delays in both children at 2 and 4 years of age. Developmental outcome for both fetuses identified as having callosal agenesis on sonography but found to have a normal corpus callosum on fetal MRI was also available; both children had no developmental or neurologic abnormalities at 10 and 23 months of age.

Figure 4. Images from a fetus at 25 gestational weeks with callosal agenesis (case 1). **A**, Coronal sonogram showing absence of the cavum septi pellucidi and “steer horn” morphology of the lateral ventricles (arrows). This suggested the diagnosis of callosal agenesis. **B**, Sagittal SSFSE T2-weighted image showing an absent corpus callosum and small pons (arrow). **C**, Axial SSFSE T2-weighted image showing additional MR findings of shallow sylvian fissures for gestational age (arrows) as well as ventriculomegaly.

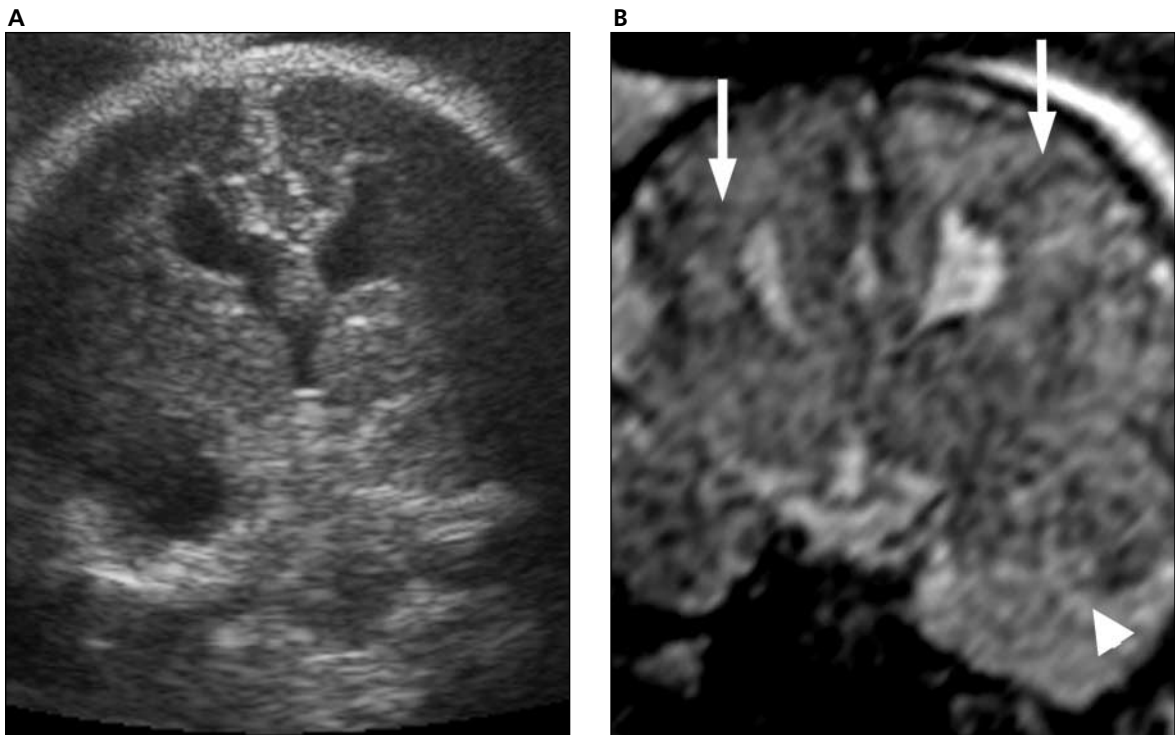


Discussion

Fetal MRI was useful in further evaluating the corpus callosum in patients in whom a callosal abnormality was suspected on sonography. Fetal MRI was able to demonstrate a normal corpus callosum in 20% of cases with a suspected callosal abnormality. This has important implications for prenatal counseling because callosal agenesis is typically associated with neurodevelopmental disability. The corpus callosum was so well seen on MRI in both these cases that there is no question that the sonogram, and not the MR image, was in error despite the fact that, because this was not a prospective study, parents were not obligated to agree to postnatal imaging. However, the callosal abnormality was confirmed in the 6 patients who were examined by postnatal MRI or autopsy, and both patients with a normal corpus callosum visualized on fetal MRI (and consequent lack of intervention) have had normal development. The ability of fetal MRI to better evaluate the structural integrity of the corpus callosum is most likely due to

direct visualization of the corpus callosum on a midline sagittal MR image, whereas sonography has historically relied on indirect signs of callosal agenesis, such as absence of the cavum septi pellicidi and ventricular morphology. It is interesting to note that both cases with a normal corpus callosum on fetal MRI had prominent midline cerebrospinal fluid spaces on prenatal sonography, which may have contributed to the misdiagnosis of callosal agenesis. Fetal MRI can be helpful in showing an intact corpus callosum in such cases. Although fetal MRI identified a normal corpus callosum in cases of sonographically suspected callosal agenesis, this study does not address the sensitivity of sonography for the diagnosis of callosal abnormalities because only patients with a sonographically suspected callosal abnormality were included in this study. Of note, in the 8 cases in which the diagnosis of callosal abnormality was concordant on both fetal sonography and fetal MRI, the type of callosal abnormality was similar on both MRI and sonography. Thus, whereas fetal MRI was helpful in confirming or refuting the sonographic diagnosis

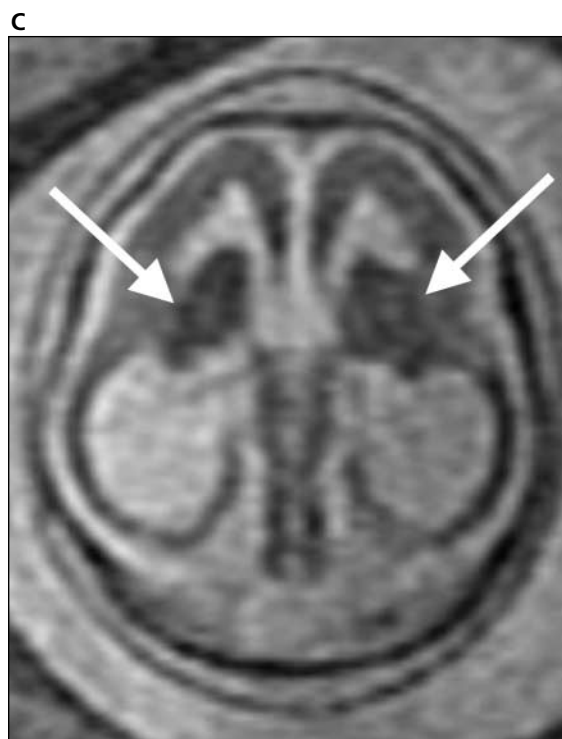
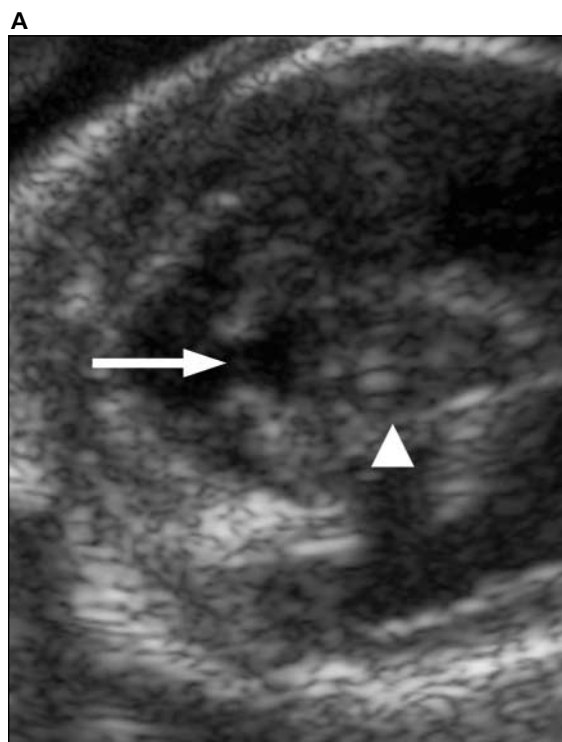
Figure 5. Images from a fetus of a twin pregnancy at 32 gestational weeks with callosal agenesis (case 7). **A**, Coronal sonogram showing ventriculomegaly with irregularity of ventricular margins, consistent with periventricular heterotopia or a destructive process. **B**, Coronal SSFSE T2-weighted image confirming periventricular nodular heterotopia. Bilateral closed lip schizencephaly (arrows), open lip schizencephaly (partially shown; arrowhead), and a diffusely abnormal gyral pattern are only apparent on fetal MRI.



of a callosal abnormality, it did not add to the sonographic findings in assessing the extent of the callosal abnormality in this study of 10 cases.

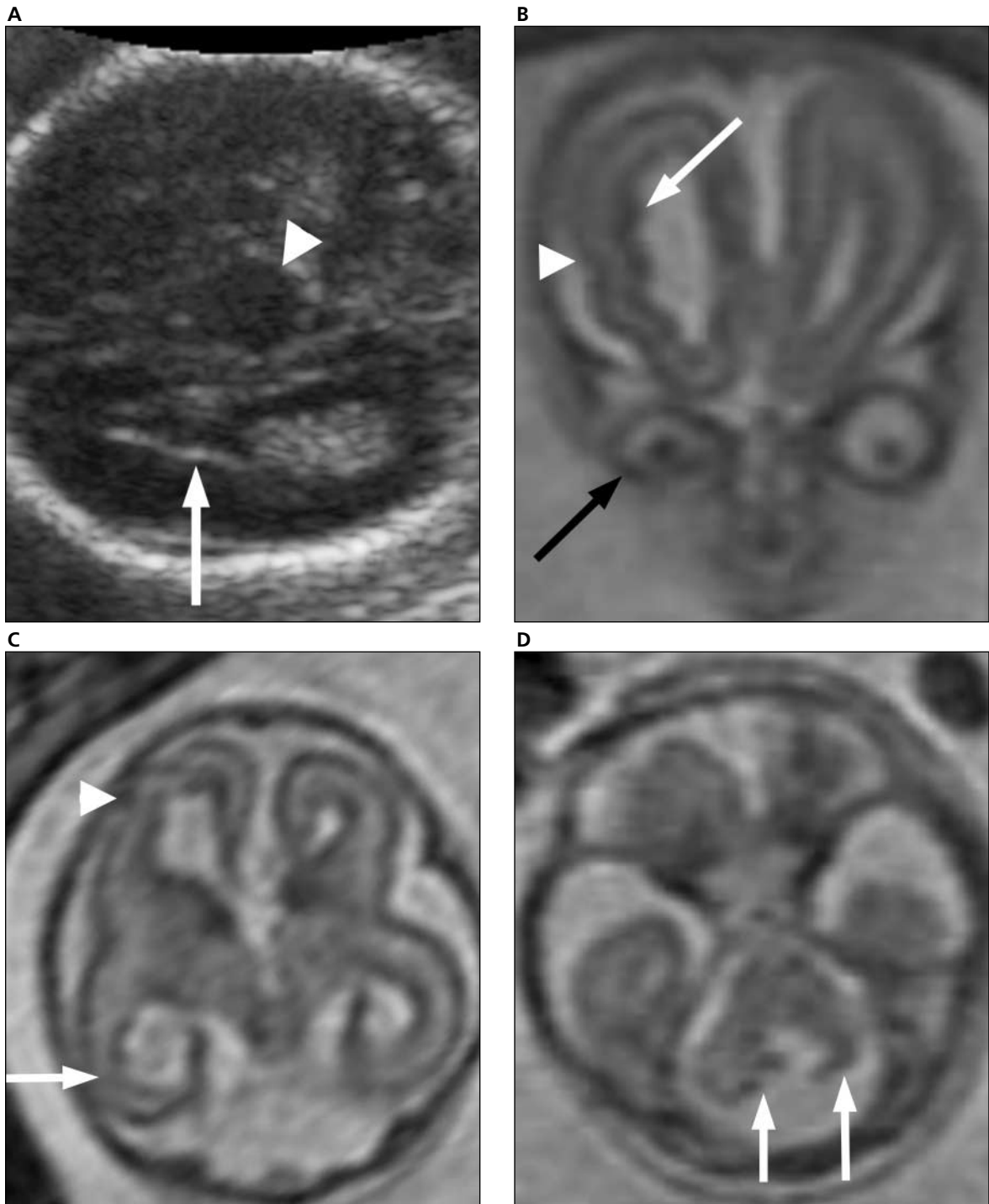
Recent technical advances also contributed to the improved ability of fetal MRI to visualize the corpus callosum in 1 case that was imaged with Real-Time SSFSE for the fetus, software recently developed in collaboration with GE Healthcare that allows interactive control of slice orientation and results in more precise and rapid imaging of midline structures such as the corpus callosum.³⁵ This feature is so easy to use and reliable in allowing us to clearly visualize the corpus callosum on all fetal MR images that visualization of the corpus callosum is a routine part of our fetal MRI examination.

Figure 6. Images from a fetus at 23 gestational weeks with callosal agenesis (case 6). **A**, Axial sonogram showing an abnormally small cerebellum with a cleft between the hemispheres, consistent with an absent vermis (arrow). The midbrain appears small (arrowhead). **B**, Sagittal SSFSE T2-weighted image allowing additional visualization of the brain stem abnormality that can now be characterized as abnormally thin with kinking at pontomesencephalic junction (arrow). Findings of callosal agenesis, a small cerebellum, and vermian agenesis are also present. **C**, Axial SSFSE T2-weighted image showing abnormally thin and homogeneous parenchyma with dysplastic deep gray nuclei (arrows) and absent sylvian fissures, findings not apparent on sonography. The constellation of findings on fetal MRI led to prenatal diagnosis of Walker-Warburg syndrome.



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Figure 7. Images from a fetus at 19 gestational weeks with callosal agenesis (case 8). **A**, Axial sonogram showing teardrop-shaped ventricles with irregular margins (arrow) and an interhemispheric cyst (arrowhead), all consistent with callosal agenesis. **B**, Coronal SSFSE T2-weighted image confirming heterotopia with nodularity seen along the dilated frontal horn (white arrow). Additional sonographically occult findings include abnormal sulcation of the developing frontal lobe (arrowhead), consistent with cortical dysgenesis, and unilateral microphthalmia, confirmed on multiple images (black arrow). **C**, Thinning and abnormal sulcation of the overlying frontal parenchyma is also visualized on an axial SSFSE T2-weighted image (arrowhead) in addition to abnormally thin temporal lobe parenchyma (arrow). The corpus callosum is not visualized. **D**, Axial SSFSE T2-weighted image showing abnormal morphology of the fourth ventricle, with small, dysgenetic cerebellar hemispheres bilaterally (arrows), not detected on sonography. The constellation of findings on fetal MRI led to prenatal diagnosis of Aicardi syndrome.



Fetal MRI was also important in detecting additional brain abnormalities in patients in whom a callosal abnormality was identified on both sonography and fetal MRI. In 75% (6 of 8) of patients in whom both MRI and sonography agreed on the diagnosis of callosal agenesis, there were additional abnormalities recognized on sonography, MRI, or both. Interestingly, there were no cases of heterotopia detected on fetal MRI that had not been suspected on prenatal sonography, an observation that differs from that reported in the literature by others.^{11,33,36} This may be attributed to a considerable experience comparing sonograms and MR images in fetuses with abnormalities that has accrued at our center before and during this period, increasing sonologists' awareness of the frequency and findings associated with this abnormality. Fetal MRI was able to identify all abnormalities that were seen on sonography with the exception of choroid plexus cysts, which are considered incidental. All cerebellar and brain stem abnormalities detected on prenatal sonography were also identified on MRI, although MRI was able to better characterize these findings and to suggest a specific diagnosis.

Importantly, fetal MRI identified brain abnormalities that were not detected on sonography in 63% (5 of 8) of cases with a callosal abnormality. All these cases had at least 1 abnormality of sulcation that could not be detected on sonography. Some of these abnormalities were focal and some were diffuse; they included delays in sulcation (when accounting for both the sonographic and LMP gestational age) in addition to more frankly dysplastic gyral patterns such as polymicrogyria and schizencephaly. Moreover, all these cases had more than 1 additional structural brain abnormality on fetal MRI. In addition, fetal MRI was able to identify 1 cerebellar, 1 brain stem, and 1 deep gray nuclear abnormality that were not apparent on sonography in 3 of these 5 fetuses. All fetal MRI findings that were sonographically occult were confirmed with either postnatal MRI or autopsy in all but 2 cases. This illustrates the importance of performing fetal MRI in cases with a callosal abnormality. Precise delineation of additional abnormalities is important for better understanding the etiology as well as postnatal clinical significance of fetal callosal agenesis.

The identification of sonographically occult abnormalities on fetal MRI led to the diagnosis of a specific syndrome in 25% of our cases (2 of 8

with callosal agenesis on both fetal MRI and sonography). In particular, the diagnosis of Aicardi syndrome, in which there are no known inherited cases, was suggested in 1 case, and the diagnosis of Walker-Warburg syndrome, an autosomal recessive disorder, was suggested and confirmed on autopsy in another case. These diagnoses have important implications for the counseling of parents with regard to future pregnancies and genetic risk.

Our experience in fetuses with callosal agenesis further confirms the ability of MRI to detect additional brain anomalies not evident on sonography.^{13,28,36} Sonigo et al²⁸ identified more than 3 times as many additional abnormalities with fetal MRI compared with prenatal sonography in fetuses with callosal agenesis. Additional sonographically occult abnormalities were also identified on fetal MRI in 36% and 21% of fetuses with callosal agenesis in studies by d'Ercole et al³⁶ and Rapp et al,¹³ respectively. These abnormalities included neuronal heterotopia, gyral abnormalities, posterior fossa abnormalities, interhemispheric cysts, brain stem hypoplasia, cerebellar hypoplasia, and destructive parenchymal lesions.^{13,28,33,36} It is interesting to note that gyral abnormalities were the most common sonographically occult abnormalities in our experience rather than neuronal heterotopia, as reported by others.^{28,36} As mentioned earlier, this may reflect the extensive clinical collaborative experience at our institution in comparing sonographic and MR images and the consequent increased sensitivity of our sonographers to ependymal irregularities.

The incidence of additional brain abnormalities in fetuses with callosal agenesis was greater than in many other studies and, not surprisingly, greater than in studies using prenatal sonography.^{10,12-14,16,36} It is possible that the use of a 1.5-T magnet, thinner sections, and a smaller field of view compared with other fetal MRI studies allowed detection of more associated brain abnormalities. Another factor might be our acquisition of at least 2 sequences in each of the axial, coronal, and sagittal planes. Although our slices have no skip, it is our experience that fetuses move during the acquisition of each single series, resulting in gaps in the coverage of the brain. Acquiring at least 2 sets of images in each of the 3 planes increases the likelihood of visualizing the entire brain and, thus, of detecting small focal abnormalities.

Our finding that 75% of fetuses with callosal agenesis had additional brain abnormalities is similar to findings in studies of postnatal autopsy or MRI results after the prenatal diagnosis of ACC.^{9,11} Brisse et al¹¹ detected additional brain abnormalities on autopsy and postnatal MRI in 75% of infants with prenatally diagnosed callosal agenesis. The most common associated findings were cerebellar hypoplasia and gyral anomalies. These additional abnormalities, however, were only diagnosed by fetal MRI in 55% of their patients, which may be because their imaging studies were performed with a 0.5-T magnet. Gyral anomalies and cerebellar hypoplasia were also the most common additional findings seen on fetal MRI.

In a review of the autopsy literature as well as their own experience, Parrish et al⁹ reported additional brain abnormalities in 85% of cases. Of interest, gyral anomalies and heterotopia were the most common, occurring in more than half of their cases. Additional abnormalities included cerebellar vermian hypoplasia, absence of the pyramidal tracts, and hypoplasia of the olfactory lobes or tracts.

The exact clinical relevance of callosal agenesis is still not well understood. Although there are published cases of incidentally noted callosal agenesis in adults with no other apparent abnormalities,^{37,38} this is in contrast to studies on children with postnatally diagnosed callosal agenesis in which most (65%–83%) have developmental delay and about half develop epilepsy.^{7,17,39,40} These studies on children, however, are subject to referral bias because children without neurodevelopmental abnormalities are not routinely imaged. Thus, it is difficult to extrapolate these results to the fetal population.

However, postnatal studies strongly suggest a relationship between additional brain abnormalities and outcome. Shevell¹⁷ found that the presence of cerebral dysgenesis on postnatal imaging was predictive of a more severe developmental abnormality in children with callosal agenesis. In a review of the literature of callosal agenesis cases as well as their own experience, Jeret et al⁷ also reported an association between other central nervous system abnormalities and mental retardation. Thus, although the exact prognosis of isolated callosal agenesis is still not fully understood, it appears fairly clear that the presence, and perhaps type, of additional brain abnormalities is associated with a guarded prog-

nosis. The use of fetal MRI, therefore, may allow more accurate counseling of the parents if a callosal anomaly is identified.

There are several limitations to our study. The small size of our cohort and the lack of extensive developmental follow-up limit our assessment of the clinical importance of the additional anomalies detected by fetal MRI. Good data in this area await a large prospective study with long-term postnatal follow-up. Another limitation is the lack of postnatal imaging or autopsy confirmation for all patients. However, the additional sonographically occult findings detected on fetal MRI were confirmed by either autopsy or postnatal MRI in 3 of 5 patients. Moreover, the incidence of additional abnormalities detected with fetal MRI in our study is in general agreement with other autopsy and postnatal imaging data. Our study, however, did not address the sensitivity of fetal MRI for the detection of additional abnormalities in callosal agenesis. It is interesting to note that in 1 case of callosal hypogenesis, periventricular nodular heterotopia was only identified on the postnatal MRI. Studies on the diagnostic accuracy of fetal MRI for specific brain abnormalities are needed. In addition, the excellent correlation of our MRI findings with the sonographic findings in terms of the extent of the callosal anomaly shows that MRI is certainly no worse than sonography, and our unequivocal identification of a corpus callosum in 2 patients with a sonographic diagnosis of callosal agenesis suggests that MRI has increased specificity compared with sonography. Our study is also limited by the variable time interval between sonographic and MRI examinations in each patient. Imaging the fetal brain with MRI at a later gestational age could theoretically allow better visualization of certain abnormalities because the brain is larger and the abnormalities might, therefore, be more easily seen. In 6 of the 8 patients with callosal abnormalities, however, MRI was performed within 2 days of sonography, and additional sonographically occult findings were detected in 66% (4 of 6) of these cases. Finally, the comparison of sonography and MRI is compromised by the fact that the neuroradiologists who reviewed the MR images knew that the sonograms had shown callosal abnormalities and, therefore, were focused on the corpus callosum. In our practice, however, direct visualization of the corpus callosum is a fundamental aspect of fetal brain MRI; sagittal images are

acquired again and again until the corpus callosum, cerebellum, and brain stem are adequately evaluated. Therefore, it seems very unlikely that the MRI results would have differed if the sonographic findings had not been known.

In conclusion, our findings show that fetal MRI, when compared with sonography, can better delineate the integrity of the corpus callosum as well as identify coexisting brain abnormalities, such as those of sulcation. In light of the association between additional brain abnormalities and worse neurodevelopmental outcome, the increase in detection of such findings suggests that fetal MRI may be an important prognostic adjunctive imaging test in fetuses with callosal agenesis. Long-term outcome studies of these fetuses imaged with MRI are needed to confirm this hypothesis.

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