

The Role of Fetal MRI in the Diagnosis of Agenesis of Corpus Callosum (ACC) and other Associated Cerebral Anomalies

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Abstract: The corpus callosum is the main transverse tract of fibers that connects the two cerebral hemispheres. In rare conditions an absence of fusion of the main commissural pathway connecting the cerebral hemispheres is observed. This malformation develops in utero and is classified as partial and complete agenesis or hypoplasia of corpus callosum. The condition is found in 3 to 7: 1000 live births. Fetal ultrasound (US) is first-line modality in evaluating corpus callosum by 18-20 weeks of gestation. Fetal magnetic resonance imaging (MRI) is useful for exact assessment of the degree of malformation as well as for detecting frequently associated anomalies. This pictorial review aims to present the role of fetal MRI as a valuable adjunct to US in various abnormalities of corpus callosum in fetuses, which is an important issue for prognostic counseling.

Keywords: Agenesis of corpus callosum, Antenatal ultrasound, Fetal MRI, Associated cerebral anomalies.

INTRODUCTION

The Corpus callosum is the main commissural pathway that connects the cerebral hemispheres. It is composed by four segments: the rostrum, genu, body and splenium. The narrowed space between the body and splenium is called the isthmus. Agenesis of corpus callosum (ACC) could be either partial or complete. Most commonly partial agenesis affects the splenium, especially in Chiari II malformation and this condition is also seen in patients with holoprosencephaly. MRI is suitable for evaluation of both isolated (without any coexisting anomaly) or complex type of ACC, associated with interhemispheric cysts, neuronal migration anomalies, intracranial lipomas etc. [1, 2]. Clinical presentation of ACC encompasses mental retardation (60%), visual problems (33%), seizures (35%); although, in most patients with isolated agenesis no neurological deficit is observed [3]. Antenatal US is usually diagnostic, but fetal MRI is a preferred method for detection of associated cerebral anomalies.

CASE 1

Patient at 26-gestational week with suspicion of ACC is referred for fetal MR examination. The MR examination is performed on 1,5T GE Signa MR unit using single-shot fast spin echo (SS-FSE) and Fiesta sequences in coronal, axial and sagittal plane, FOV 24x18, slice thickness 5mm and matrix 512x256.

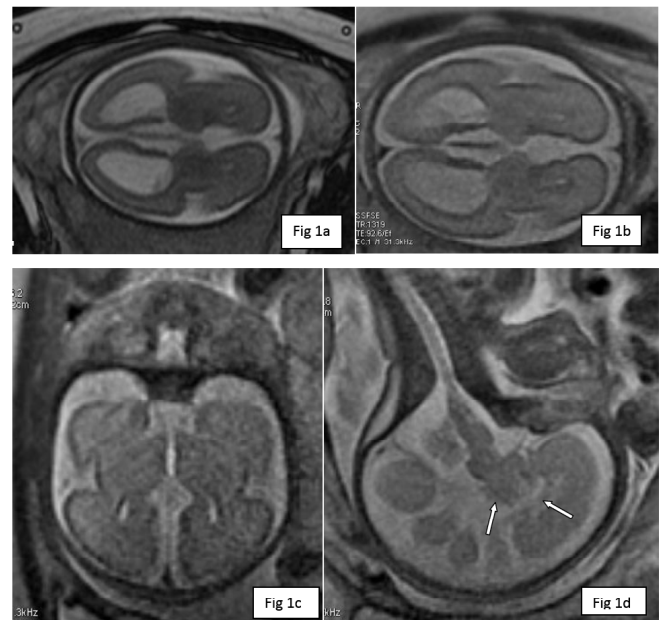


Figure 1: Axial T2 SS-FSE and FIESTA images show parallel configuration of the lateral ventricles with dilatation of the occipital horns (colpocephaly) and non-visualization of cavum septum pellucidum (Figure 1.a, b). Coronal and sagittal images display absent corpus callosum and cingulate gyrus with central gyral radiation (arrows) and low-riding, wide interhemispheric fissure (Figure.1c, d).

CASE 2

Patient at 32 weeks' gestation referred to MRI with suspected agenesis of corpus callosum (ACC). Fetal MR exam confirms the diagnosis and demonstrates the complete callosal agenesis, lack of cavum septum pellucidum and dilatation of the occipital horns of the lateral ventricles. The right occipital horn is slightly larger and the left frontal horn is hypoplastic. Both frontal horns are with parallel orientation. Fetal MRI

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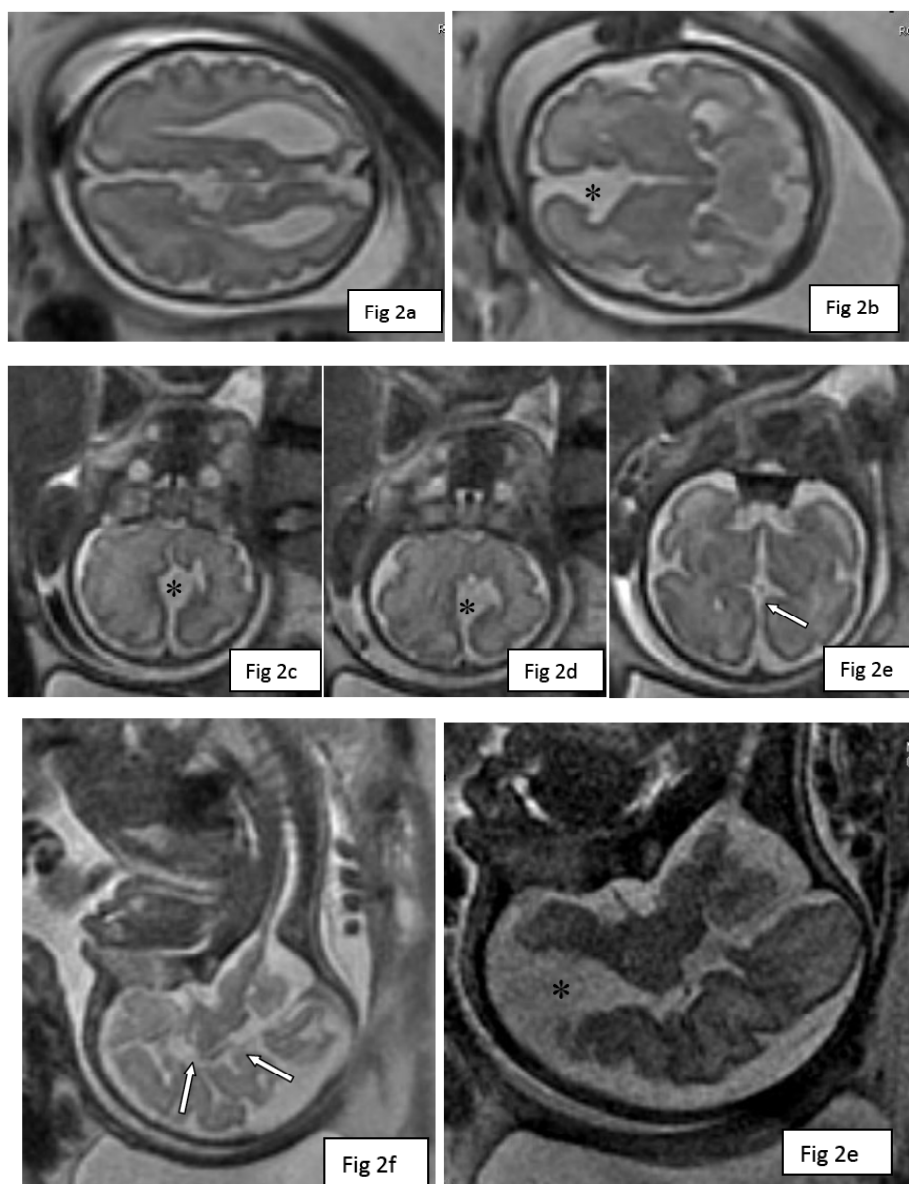


Figure 2: MR images presenting a case of agenesis of corpus callosum with associated interhemispheric cyst. Axial (Figure 2.a, b), coronal (Figure 2.c, d, e) and sagittal (Figure 2.f, g) fetal MR images confirming the sonographic data of ACC (arrows) additionally identifying the presence of interhemispheric cyst (*) and abnormal sulci.

also reveals the presence of an interhemispheric cystic structure with abnormal frontal sulci on the inner border of the left hemisphere in comparison with normal contralateral hemisphere. No additional cerebral anomaly is found close to the interhemispheric cyst. The MR examination is performed on 1,5T GE Signa MR unit using SS-FSE and Fiesta sequences in coronal, axial and sagittal plane, with FOV 24x18, slice thickness 5mm and matrix 512x256.

CASE 3

Patient at 36 week of gestation with severe hydrocephalus and non-visualization of corpus

callosum on ultrasound due to abnormal presentation of the fetus. Fetal MRI using SingleShot-FastSpinEcho and Fiesta sequences is done in order to confirm suspected callosal agenesis. MRI shows highly dilated occipital horns of the lateral ventricles, more pronounced on the left side, absence of cavum septum pellucidum and absence of corpus callosum. The interhemispheric sulcus is slightly wider. There is also higher than usual positioning of the third ventricle. No other associated cerebral and cerebellar pathology of the fetus is evident. The MR examination is performed on 1,5T GE Signa MR unit using same scanning parameters as in case 1 and 2.

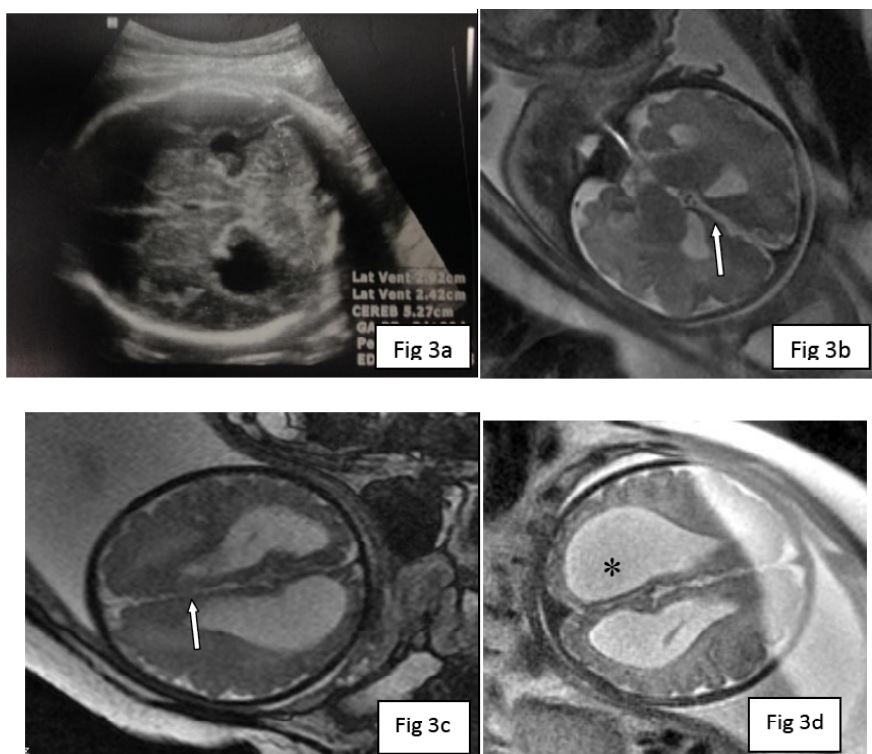


Figure 3: Prenatal ultrasonography (Figure 3a) and fetal MRI images in coronal (Figure 3b) and axial plane (Figure 3c, d) showing the absent corpus callosum (arrows) and marked dilatation of the occipital horns of the lateral ventricles (*).

CASE 4

Patient at 31 week of gestation with suspected isolated agenesis of corpus callosum on ultrasound examination. Cavum septum pellucidum is not evident on ultrasonography. 3T MR using SingleShot – TurboSpinEcho sequences reveals the absence of corpus callosum with “racing car sign” of frontal horns in association with dilatation of the occipital horns of the lateral ventricles which presents with parallel orientation. No other cortical defects or associated brain anomalies are found on MR images. SS-TSE sequences were performed with TR=15000 and TE=120 with FOV 24x18, slice thickness 5mm and matrix 256x1169, flip angle 90.

DISCUSSION

Fetal MR is useful in the evaluation of anomalies of corpus callosum suspected on ultrasound. This anatomical entity can be visualized directly in the sagittal plane as a curvilinear, C-shaped T2 hypointense structure located at the superior margin of the lateral ventricles and the cavum septum pellucidum, above the fornices [4, 13]. The midsagittal fetal MR image enables direct visualization of the corpus callosum and diagnosis of complete or partial

agenesis anomalies [14]. Axial and coronal MR images provides indirect signs of complete agenesis of corpus callosum such as absent cavum septum pellucidum, straight parallel lateral ventricles, dilated occipital horns of lateral ventricles (colpocephaly), high riding third ventricle and unformed cingulate sulcus [15]. Agenesis of corpus callosum is either isolated or associated with other cerebral abnormal conditions. Clinically isolated agenesis of corpus callosum may be asymptomatic or associated with macrocephaly, epilepsy, development delay and hypothalamic dysfunction [10]. Isolated ACC could be complete, partial or associated with interhemispheric cyst. In cases of associated anomalies the prognosis of ACC is worse and increased risk of epilepsy, development delay and disability could be observed [5]. Other associated intracranial malformations include corpus callosum lipoma, heterotopia, holoprosencephaly, lissencephaly, schizencephaly [10]. Some authors like Cagneaux *et al.* suggest that focal abnormal sulcation may be related to mechanical interferences of the cyst with cortical folding due to its mass effect. The presence of such abnormal sulci in absence of cortical dysplasia is probably of less significance and with small effect on postnatal prognosis [6]. Another study from Tang *et al.* describes low frequency (7%) of pure isolated ACC on fetal MR imaging, while when excluding sulcation delay

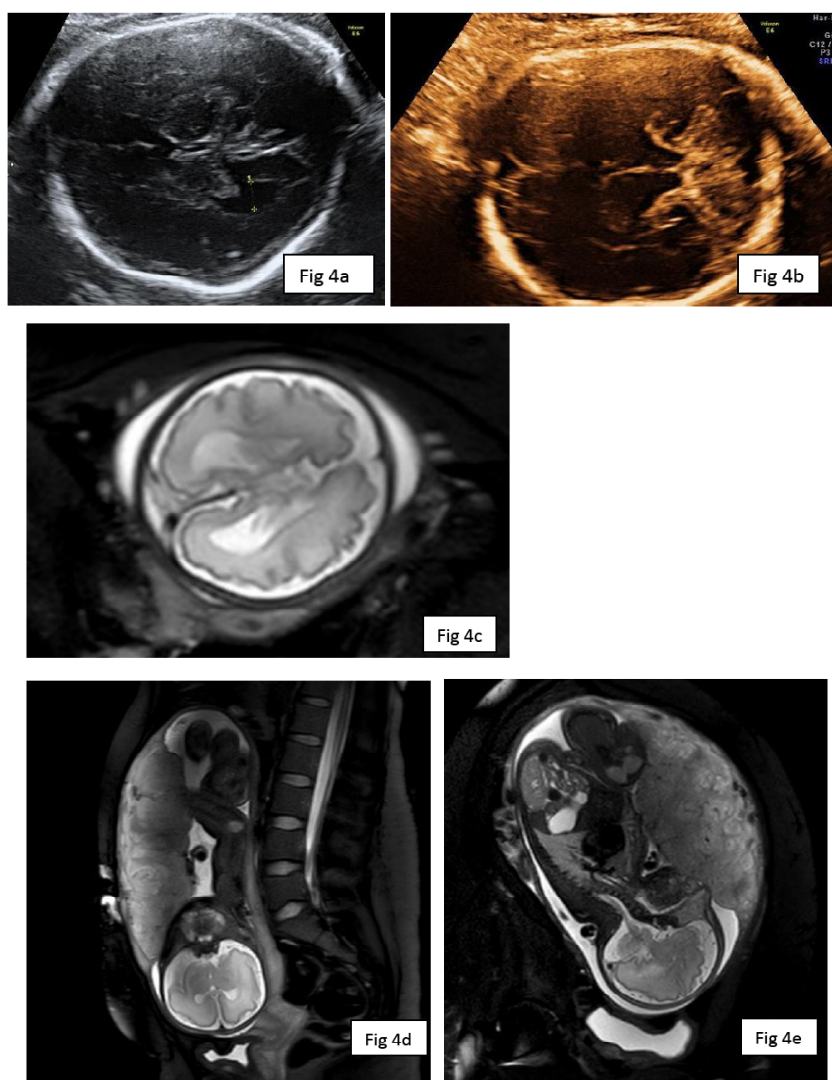


Figure 4: Antenatal ultrasonography (Figure 4a, b) of isolated agenesis of corpus callosum and absent cavum septum pellucidum. 3T MRI in axial (Figure 4c), coronal (Figure 4d) and sagittal (Figure 4e) plane clearly demonstrates the absence of corpus callosum with “racing car sign” of frontal horns in association with dilatation of the occipital horns of the lateral ventricles which have a parallel orientation.

additional findings on fetal MR imaging raises up to 69%. Those authors identify fetal abnormalities on MR imaging not detected by prenatal sonography in 83% of examinations [7]. An important pearl in the diagnosis of partial ACC is that the absence of the splenium is more frequently found than the absence of the genu. As a pitfall it is important to differentiate agenesis of corpus callosum from a thinned corpus callosum in patients with periventricular leucomalacia [12].

The genetics of ACC in humans are variable and reflect the underlying complexity of callosal development of Corpus Callosum. Current evidence suggests that a combination of genetic mechanisms, including Mendelian mutations of single gene, single-gene sporadic mutations and complex genetics

disorders (mixture of inherited and sporadic mutations) might have a role in the etiology of ACC. Approximately 10% of cases present with chromosomal anomalies and 20–35% have a recognizable genetic syndromes. However, if we only consider individuals with complete ACC, then the percentage of patients with recognizable syndromes drops to 10–15%, and thus 75% of cases of complete ACC do not have an identifiable cause [8]. Similar results described by Tang *et al.* report destructive changes in the brain parenchyma, suggesting acquired etiology or genetic/metabolic abnormality, associated with ACC in 10% of fetuses [7]. Other studies conducted by Bedeschi *et al.* describe similar data for chromosomal anomalies in young patients with ACC (11%) and for co-existing specific genetic syndromes (30%) [9]. Most common

syndromes associated with ACC syndromes are Aicardi syndrome, Apert syndrome, morning glory syndrome, Chiari II malformation and Dandy-Walker syndrome. Apart from genetic syndromes, ACC is strongly associated with fetal alcohol syndrome and some metabolic disorders [11].

Fetal MRI is also useful in diagnosing dysplastic/agenetic septum pellucidum and any associated anomalies related to optic chiasm or pituitary gland like septo-optic dysplasia [16]. Although conventional MRI is most commonly used in fetal MRI, advanced MRI techniques such as diffusion-weighted imaging (DWI) and magnetic resonance spectroscopy (MRS) have been applied to fetal MRI [14, 17, 18]. Diffusion imaging of the fetal brain is useful for both developmental and destructive brain processes [14] however, its clinical application is currently limited by its long acquisition times [17]. Future developments and improvements of parallel imaging could be helpful in order to decrease the scan time as well as to increase the signal to noise ratio (SNR) and image resolution [17].

According to our experience fetal MRI is a valuable complementary technique in cases of isolated ACC. The method has further advantages in cases with more complex associated abnormalities due to the better anatomical visualization and to the better tissue resolution.

CONCLUSION

For proper interpretation of fetal MRI, a radiologist and clinician should be familiar with the normal developing fetal anatomy. Fetal gestational age is an important factor for the correct interpretation of fetal MRI. Agenesis of corpus callosum is a rare condition with unknown etiology. It may be diagnosed on direct visualization or suspected in cases when indirect signs and features are present. Careful examination of the fetal head anatomy with ultrasonography including transvaginal approach should be carried out as in some occasions the isolated forms may remain undetected. The advantageous role of fetal MRI is to confirm or reject the US findings and to rule out coexisting anomalies of the brain. Fetal MRI visualization is not significantly limited by maternal obesity, fetal position, or oligohydramnios and especially visualization of the brain is not restricted by the ossified skull. MRI provides multiplanar imaging in a large field of view, facilitating examination of fetuses with large or complex anomalies [19]. However, fetal MRI study may give

limited diagnostic information concerning ACC in early gestational age due to the small size of the fetus and fetal movement [20]. It seems that chromosomal abnormalities are less common in cases where there are no other coexisting structural anomalies. In all fetuses with suspicion of these conditions or established diagnosis both antenatal and postnatal follow-up is highly recommended.

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Received on 13-11-2015

Accepted on 17-11-2015

Published on 25-11-2015

<http://dx.doi.org/10.15379/2408-9761.2015.02.03.01>© 2015 Hadjidekov *et al.*; Licensee Cosmos Scholars Publishing House.

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