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FULL PAPER

Analysis of supratentorial cystic abnormalities using *in utero* MR imaging

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Objective: Our anecdotal experience from foetal neuro-imaging studies suggests that there are often significant disagreements between the findings of ultrasonography (USS) and *in utero* MR (iuMR) imaging in cases of antenatally detected supratentorial extra-axial cysts. Although this is a relatively rare clinical situation, it warrants further investigation because of the high risk of other intracranial abnormalities that are likely to cause long-term neurodevelopmental problems.

Methods: We reviewed 957 consecutive referrals for iuMR of the foetal brain over a 3.5-year period and studied all cases where the referral from USS described supratentorial extra-axial cysts in the foetus. The iuMR imaging was reviewed, and a comparison between the results of the two examinations was made.

Results: Supratentorial extra-axial cysts were an unusual referral for iuMR occurring in only 13/957 (1.4%) of cases. The findings on USS and iuMR imaging were conflicting in

all 13 cases with intracranial pathology being excluded on iuMR imaging in 4 cases and more significant pathology being shown in 9 cases. Abnormalities of the corpus callosum were recognized in association with a cyst in eight cases, and this was recognized in only two cases on USS. Six of those cases also had abnormalities of cortical formation.

Conclusion: iuMR imaging should be used in the assessment of pregnancies in which a supratentorial extra-axial cyst has been detected on USS. This is based on the improved primary diagnosis and a high rate of associated brain abnormalities not detected on USS.

Advances in knowledge: Our retrospective observational study examines a range of foetal intracranial abnormalities which are better defined using iuMRI. This is a previously described spectrum of neurodevelopmental anomalies which we suggest would benefit from MRI.

INTRODUCTION

Females in the UK are routinely offered ultrasonography (USS) screening for structural abnormalities of the foetus at approximately 20 weeks' gestational age. If an abnormality is shown on the screening study, a detailed "anomaly scan" is performed by an appropriately trained and experienced foeto-maternal consultant. Intracranial abnormalities are one of the most frequent problems detected on USS and may have potentially serious long-term implications for the foetus after delivery. The role of *in utero* MR (iuMR) imaging to assist in antenatal diagnosis is becoming established, particularly for suspected foetal intracranial abnormalities.¹⁻³ IuMR has many advantages over USS, including multiplanar ability and superior contrast resolution, which is particularly important in the brain. Many of the routine strategies for producing a succinct differential diagnosis in paediatric and adult neuroimaging can be applied to interpreting foetal neuroimaging, either on USS or iuMR. This includes a description of location by defining a mass as either in the brain (intra-axial) or inside the skull but outside the brain (extra-axial) and

supratentorial or infratentorial. This is supplemented by a description of the echo patterns (USS) or signal characteristics (iuMR) in order to predict the contents of the mass. In some circumstances, the imaging findings will lead to a diagnosis of a fluid-filled structure with a thin wall often described as a "cyst". In this article, we describe our experience of performing iuMR imaging in cases in which a cystic extra-axial mass in the supratentorial compartment of the foetus has been described on USS. The impetus for the study was our anecdotal observations that the diagnoses made on USS and iuMR were usually discrepant, and more clinically significant pathology was frequently recognized on iuMR.

METHODS AND MATERIALS

This was a retrospective, observational study of females attending for an iuMR examination of the foetal brain at our institution between January of 2008 and July 2011. All referrals came from experienced foeto-maternal experts working in one of nine regional centres in the UK. The cases in our cohort were research cases and consented as

Table 1. Cases where *in utero* MR (iuMR) imaging demonstrated a less severe abnormality compared with ultrasonography (USS)

Case number	GA at USS (weeks)	GA at iuMR (weeks)	Summary of finding on USS	iuMR findings
1	30	31	Interhemispheric cyst; normal appearance of the corpus callosum	Normal
2	28	29	Interhemispheric cyst	Normal
3	36	37	Supratentorial midline cyst	Normal
4	21	21	Supratentorial midline cyst likely to be an arachnoid cyst	Normal

GA, gestational age.

such under the guidance and approval of the institutional research ethics committee. The females did not have any known or suspected contraindication to MRI, and all iuMR studies were performed at, or after, 20 weeks' gestational age. The females were not paid for their involvement in the study but travel expenses were offered to them and a companion. Relevant

review was sought, and approval obtained, from the Institutional Clinical Effectiveness Unit and Research Department in order to allow cases performed for clinical purposes to be reported in this article as well. For the purpose of this study, we reviewed the department's database to find USS referrals in which (a) a supratentorial, extra-axial cyst was suspected on USS or

Table 2. Cases where *in utero* MR (iuMR) imaging demonstrated more severe features compared with ultrasonography (USS)

Case number	GA at USS (weeks)	GA at iuMR (weeks)	Summary of finding on USS	iuMR findings
5	27	28	Left-sided supratentorial extra-axial cyst, arachnoid cyst	Hypogenesis of the corpus callosum and associated interhemispheric cyst (probably Type 2)
6	19	20	Right-sided parafalcine supratentorial cyst	Hypogenesis of the corpus callosum with an associated interhemispheric cyst (probably Type 2) and a cortical formation abnormality
7, Figure 1	22	26	Widened interhemispheric fissure anteriorly, cyst	Agenesis of the corpus callosum with associated (probably Type 1) interhemispheric cyst
8, Figure 2	35	36	Interhemispheric cyst and ventriculomegaly	Hypogenesis of the corpus callosum, associated interhemispheric cyst (probably Type 2) and a cortical formation abnormality
9, Figure 3	20	21	Supratentorial intracranial cyst, arachnoid cyst	Microencephaly and hypogenesis of the corpus callosum; no definite cyst but widened posterior interhemispheric cistern
10	21	22	Posterior fossa cyst	Dural venous sinus thrombosis involving venous confluence and tributaries reported previously ⁴
11	35	36	Right parafalcine arachnoid cysts with dysgenesis of corpus callosum	Agenesis of the corpus callosum with interhemispheric cyst (probably Type 2) and possible cortical formation abnormality
12	20	20	Twin pregnancy; one twin with agenesis of the corpus callosum, interhemispheric cyst, reduced sulcation and heterotopia	Agenesis of the corpus callosum with associated interhemispheric cyst (probably Type 2), cerebellar hypoplasia and germinal matrix cyst; microencephaly
13	25	26	Twin pregnancy; one twin with three extra-axial masses in the parietal region, arachnoid cysts	Agenesis of the corpus callosum with associated interhemispheric cyst (probably Type 2) and cortical formation abnormality

Figure 1. Interhemispheric cyst on ultrasound shown to be associated with agenesis of the corpus callosum on *in utero* MR (Case 7). Ultrafast T_2 weighted images at 26 weeks' gestation in the coronal plane (a, b) and axial plane (c, d) demonstrate agenesis of the corpus callosum and an interhemispheric cyst that does not appear to communicate with the third ventricle (probably Barkovich Type I).

(b) cases when a referral for an infratentorial cyst was suspected on USS but was shown to be supratentorial on iuMR. Cases referred with suspected choroid plexus or germinal matrix cysts were not included in this analysis.

All iuMR imaging was performed on a whole-body 1.5 T system (either Infinion; Philips Medical Systems, Cleveland, OH, or HDx; GE Healthcare, Waukesha, WI) using a flexible phased-array body coil. Our standard iuMR imaging protocol has been described in detail elsewhere but, in summary, consisted of T_2 weighted single-shot fast spin-echo sequences in the three orthogonal planes, axial ultrafast T_1 weighted imaging and axial diffusion-weighted imaging.⁴ Cases after 2009 also routinely had axial ultrafast fluid-attenuated inversion recovery imaging. The iuMR studies were reported by a radiologist at the time of the original examination, but for the purpose of this study, all cases of supratentorial extra-axial cysts diagnosed were reviewed and rereported by the authors (who were aware of the findings of the antenatal USS examination).

RESULTS

A total of 957 iuMR examinations of the foetal brain were performed over the 3.5-year study period, and 13 referrals for

supratentorial, extra-axial cystic masses were located accounting for 1.4% of all referrals. The gestational age at iuMR imaging ranged from 20 to 37 weeks, and in 12/13 (92%) cases, the iuMR imaging was performed within 5 working days of the referral from USS. In 10/13 cases, the extra-axial cysts were the only intracranial abnormality detected on USS (1 case showed ventriculomegaly and 2 cases described abnormalities of the corpus callosum).

There were no cases (0/13) of complete agreement between the USS and iuMR reports. In 4/13 (31%) cases, the iuMR examination downgraded the severity of the abnormal intracranial findings; specifically, the iuMR examinations were reported as normal in all 4 cases (Table 1). In all of those cases, the USS diagnosis was "interhemispheric cyst" as the only finding. In 9/13 (69%) cases, iuMR imaging diagnosed more severe intracranial abnormalities when compared with USS (Table 2). In 8/9 of those cases, failure of commissuration (agenesis or hypogenesis of the corpus callosum) was recognized in association with an interhemispheric cyst (see Discussion). Two of those cases were recognized on USS, but in both of those cases, other brain abnormalities were shown on iuMR. In 6/8

Figure 2. Interhemispheric cyst and ventriculomegaly on ultrasound shown to be associated with hypogenesis of the corpus callosum on *in utero* MR (Case 8). Ultrafast T_2 weighted images at 36 weeks' gestation in the sagittal plane (a, b), coronal plane (c) and axial plane (d) demonstrate hypogenesis of the corpus callosum and an interhemispheric cyst that does appear to communicate with the third ventricle (probably Barkovich Type II). There is a high suspicion of a cortical formation abnormality in the left cerebral cortex adjacent to the cyst.

of the cases of failed commissuration, cortical formation abnormalities were either confidently diagnosed (5 cases) or suspected (1 case). In two cases, supratentorial extra-axial “cysts” were found in conjunction with lissencephaly. In the other case, the USS diagnosis was of a cystic mass in the posterior fossa, but this was shown to be due to dural venous thrombosis and ectasia involving the venous confluence and its supratentorial tributaries. That case has been reported in a previous paper.⁴

DISCUSSION

Intracranial cystic structures encompass a wide variety of pathological entities and anatomical variants. Arachnoid cysts constitute a significant proportion of supratentorial extra-axial cystic masses in adult and paediatric populations. For example, arachnoid cysts account for approximately 1% of intracranial masses in the adult population and 2–3% of intracranial masses in older children, but supratentorial arachnoid cysts are less commonly seen in children <4 years of age. Arachnoid cysts can present with epilepsy, focal neurologic deficits and/or hydrocephalus⁵ and may rupture, but they are often asymptomatic, being shown as incidental findings on neuroimaging studies performed for other reasons. The differential diagnosis for such

lesions includes epidermoid cysts (0.2–1.8%), dermoid cysts (0.5%), pineal cysts, Rathke’s cleft cysts and neurocysticercosis.⁶ This information appears to be applied to *in utero* cases by foeto-maternal experts because “arachnoid cyst” is given as the most likely cause of an extra-axial cyst before birth. In our present study, “arachnoid cyst” was the leading specific diagnosis on referral from USS (5/13 cases), and it was the implied diagnosis in most of the other cases based on clinical discussions with referrers. It is important to consider if this approach is appropriate for the foetus.

A primary arachnoid cyst is regarded by most authorities as a developmental abnormality of the arachnoid mater, characterized by splitting of the arachnoid membrane.⁷ As such, it might be expected that arachnoid cysts are found as frequently in the foetus as in the older child/adult and in similar locations. This does not appear to be the case. Studies of arachnoid cysts in the foetus are sparse but they are thought to be less common in the neonate and, therefore, probably rare in the foetus as well. One study found only 5 arachnoid cysts in 3000 (0.17%) consecutive neonatal autopsies, 2 cysts in the posterior fossa and 3 cysts supratentorially (2 cysts at the cerebral convexity/interhemispheric fissure and 1 cyst at the anterior temporal

Figure 3. Supratentorial cyst thought to be an arachnoid cyst on ultrasound and shown to be hypogenesis of the corpus callosum and microlissencephaly on *in utero* MR. Ultrafast T_2 weighted images at 21 weeks in the coronal plane (a, b), axial plane (c) and sagittal plane (d) demonstrate a small head and brain with poor sulcation consistent with microlissencephaly. The anterior portion of the corpus callosum is present but it is absent posteriorly. There is marked widening of the interhemispheric distance posteriorly (the feature detected on ultrasound). Please note the presence of the embryologically persistent falcine sinus (arrow on d) draining into a structurally abnormal superior sagittal sinus (arrowhead on d).

pole).⁷ This led Harding to posit “One may then wonder whether the anomalies are overlooked at autopsy in fetuses and neonates, or whether certain cysts develop and become symptomatic after birth”.⁸ There is growing evidence that the latter is correct and, although the abnormality of the arachnoid mater is present in foetal life, arachnoid cysts only become macroscopically apparent and therefore apparent on imaging as a result of progressive accumulation of cerebrospinal fluid (CSF). This most frequently occurs post-natally, as the expansion of the fluid is thought to be produced by secretory activity by the cells lining the defect in the arachnoid mater.⁹ Pathology studies in adults show that approximately 60% of arachnoid cysts are supratentorial, the commonest sites for primary arachnoid cysts being: sylvian fissure (49%), cerebellopontine angle (11%), pericolicular (10%) cerebellar vermis (9%), interhemispheric fissure (5%), cerebral convexity (4%) and periclavicular (3%).¹⁰ Similar distributions were described in early reports of cross-sectional neuroimaging,¹¹ although the introduction of MRI led to a significant increase in the detection of arachnoid cysts in the middle cranial fossa, adjacent to the anterior pole of the temporal lobe.

Our series is in keeping with the findings of previous reports that supratentorial extra-axial cysts of all varieties are uncommon in the foetus and accounted for <2% of referrals for foetal brain iuMR studies to our institution. None of those cases carried a diagnosis of isolated intracranial “arachnoid cyst” after the iuMR examination. We accept that we do not have “reference quality” outcome data in our cases and our analysis merely compares the antenatal USS and iuMR imaging results. A large study is currently in progress that will study the diagnostic accuracy of antenatal USS compared with iuMR in the UK,¹² but there is already a large amount of published data about the improved performance of iuMR.^{1–3} We argue that in the context of a normal iuMR, a large, clinically significant, supratentorial, extra-axial cyst could be confidently excluded as in our Cases 1–4. Small cystic structures may be overlooked on iuMR however, whereas USS may show those because of a better ability to show a cyst wall and septae, which can be difficult on iuMR. There is little doubt that iuMR detects developmental abnormalities of the corpus callosum better than USS,^{1,13} and we maintain that this should now be the reference standard for confirming that abnormality. We accept that the correct

detection of abnormalities of cortical formation in the foetus by iuMR is less certain and requires further research.

The significance of interhemispheric cysts associated with failed commissuration (agenesis or hypogenesis of the corpus callosum) warrants further discussion and has been studied extensively by Barkovich et al¹⁴ in the paediatric population. Those authors make the distinction between interhemispheric cysts that communicate with the ventricular system (Type 1) and those that do not (Type 2). This is an important distinction in terms of the risk of finding other brain abnormalities as discussed below. Barkovich et al¹⁴ stress that it is sometimes difficult to distinguish between those subgroups on cross-sectional studies in children, and we add that it can be even more difficult in fetuses using ultrafast iuMR imaging. Type 1 cysts represent ventricular extensions and diverticulae and are therefore lined by normal ependyma and are often found in conjunction with hydrocephalus and macrocephaly. These cysts are often noted to develop later in gestation in conjunction with developing hydrocephalus or increasing intraventricular pressure which may reflect the communicating nature of these cysts.¹⁵ Type 2 cysts are separate from the ventricular system and their contents often have signal characteristics distinct from the ventricular CSF on MRI (including iuMR), but this is not always the case. The cysts may be multiloculated, often have thick walls and may be lined with ependymal.^{7,14} There is a much higher risk of cortical formation abnormalities with Type 2 cysts, particularly subependymal heterotopia and

polymicrogyria (classified as Type 2b) or subcortical heterotopia (classified as 2c). It is possible that some Type 2 cysts are true arachnoid cysts and those were classified as Type 2d cysts by Barkovich et al.¹⁴

The difficulty in correctly characterizing supratentorial extra-axial cysts is often compounded by ascribing the cystic lesion to an incorrect anatomical location. The differential diagnosis for such lesions is significantly longer, and one must also consider abnormalities or variants of the cavum septum pellucidum, vein of Galen malformations, congenital cysts/ventricular diverticulae, schizencephaly, porencephaly and intracranial haematoma. It should be appreciated that many of these abnormalities and anatomical variants in foetal and paediatric imaging studies are often included under the title of “congenital arachnoid cysts”, e.g. dilated cisterns, cysts of the cavum vergae, cysts of neural origin and ependymal cysts.⁷ The use of iuMR imaging can help demonstrate features that exclude the majority of these lesions and hence considerably narrow the differential diagnosis.

In summary, our results demonstrate that an extra-axial, supratentorial cyst is an uncommon finding in the foetus. It should be appreciated that primary arachnoid cysts are unusual in this site at stage of development and that other intracranial pathology will be found in a high proportion of cases. In this situation, iuMR should be used to supplement antenatal USS, and this approach will allow the counselling clinician to inform patients with an appropriate level of confidence.

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