ABSTRACT

Background: Compared with ultrasound, magnetic resonance imaging (MRI) offers superior visualization of the fetal brain. It confirms and characterizes brain abnormalities detected by prenatal ultrasound, particularly in late pregnancy when acoustic windows are difficult or fetal position is inaccessible. Prior to July 2008, only two studies were attempted at our institution as local technical expertise was unavailable. Following collaboration with a neuroradiologist at an expert centre, images of sufficient quality for diagnosis were obtained.

Objective: The study objective is to evaluate the initial experience with fetal brain MRI and its effects on patient counselling and management in a resource limited healthcare system.

Method: In seven fetuses with abnormal ultrasound neuroimaging, fetal MRI was performed with T2-weighted single-shot fast spin-echo (SSFSE) sequences using a 1.5T magnet (GE Medical Systems, Milwaukee, WI).

Results: Magnetic resonance imaging did not alter ultrasound diagnosis in two patients (28%); however, it changed the diagnosis in three (43%), provided additional information in one (14%) and changed management in two (28%) patients.

Conclusion: Magnetic resonance imaging availability further elucidated brain pathology, aided patient counselling, parental decision-making and multidisciplinary management.

Keywords: Fetal brain, Fetal MRI, neurosonogram
the potential outcomes in the neonate and child and to make informed decisions regarding future pregnancy management (9). Counselling is important for parents to obtain knowledge of accurate information on which to base reliable counselling.

The leading indication to perform fetal MRI is the suspicion of CNS abnormalities (2, 7). Studies have indicated that MRI is contrast, a larger field of view and multiplanar capability (6). The approach to overcome the hindrance of fetal motion and refined the ability to diagnose malformations of the CNS. The advent of new software and hardware for MRI imaging has made it possible to overcome the hindrance of fetal motion and perform examinations with images obtained in about 400 ms. Compared with ultrasound, MRI offers superior visualization of the fetal brain as it has advantages of enhanced tissue contrast, a larger field of view and multiplanar capability (6). The leading indication to perform fetal MRI is the suspicion of CNS abnormalities (2, 7). Studies have indicated that MRI is most useful in confirming and further characterizing fetal CNS anomalies detected by prenatal ultrasound (3, 5, 8).

Congenital malformations of the CNS account for 40% of deaths of all children in the first year of life. In survivors, they cause a variety of neurological disorders, mental retardation or drug-resistant epilepsy (2). Fetal CNS imaging gathers accurate information on which to base reliable counselling. Counselling is important for parents to obtain knowledge of the potential outcomes in the neonate and child and to make informed decisions regarding future pregnancy management (9). Accurate, early diagnosis is thus imperative.

Prior to July 2008, only two studies were attempted at the University Hospital of the West Indies (UHWI) as local technical expertise was unavailable and obtained images were of too poor a quality for diagnostic evaluation. Following collaboration with a neuroradiologist at an expert centre, images of sufficient quality for diagnosis were obtained. The cost of MRI is prohibitive to a large proportion of the patient population and this hospital has the only magnetic unit in the island’s public health system. We herein report the initial experience with MRI imaging of seven cases of fetal CNS malformations detected by routine screening sonography. We sought to determine if MRI findings correlated with ultrasound diagnosis and if additional information gleaned affected patient counselling and management in a resource limited healthcare system.

INTRODUCTION

Ultrasoundography is the main screening tool used for prenatal diagnosis as it is safe, easily accessible and relatively inexpensive. However, imaging may be suboptimal in cases of oligohydramnios, large maternal body habitus, complex fetal anomalies or in late gestation (1–3). Particularly during evaluation of the fetal central nervous system (CNS), ultrasound is additionally limited by the technical difficulties inherent in imaging through bone (4), and findings are occasionally inconclusive or insufficient for prenatal diagnosis (5).

Antenatal fetal magnetic resonance imaging (MRI) has refined the ability to diagnose malformations of the CNS. The advent of new software and hardware for MRI imaging has made it possible to overcome the hindrance of fetal motion and perform examinations with images obtained in about 400 ms. Compared with ultrasound, MRI offers superior visualization of the fetal brain as it has advantages of enhanced tissue contrast, a larger field of view and multiplanar capability (6). The leading indication to perform fetal MRI is the suspicion of CNS abnormalities (2, 7). Studies have indicated that MRI is most useful in confirming and further characterizing fetal CNS anomalies detected by prenatal ultrasound (3, 5, 8).

Congenital malformations of the CNS account for 40% of deaths of all children in the first year of life. In survivors, they cause a variety of neurological disorders, mental retardation or drug-resistant epilepsy (2). Fetal CNS imaging gathers accurate information on which to base reliable counselling. Counselling is important for parents to obtain knowledge of the potential outcomes in the neonate and child and to make informed decisions regarding future pregnancy management (9). Accurate, early diagnosis is thus imperative.

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SUBJECTS AND METHODS

Seven cases with abnormal ultrasound neuroimaging seen at the UHWI between July 2008 and March 2010 were imaged after obtaining informed consent. Fetal MRI was performed using a 1.5-T magnetic unit (General Electric, Milwaukee, WI, USA). The body phased-array coil was used in all cases. T2-weighted (T2-W) images were the mainstay of the examination. Imaging sequences included a multiphase single-shot fast spin-echo sequence (repetition time msec/echo time msec, 2015/90; field of view 34 x 34 cm; section thickness 4 mm; spacing 5 mm; matrix 512 x 512). Magnetic resonance images were assessed independently by a radiologist at the UHWI as well as the paediatric neuroradiologist at the collaborating centre who was blinded to the ultrasound diagnosis.

The seven patients had been referred to the maternal–fetal medicine specialist for further evaluation of fetal anomalies detected by screening sonography performed on the hospital’s antenatal clinic patients or in community clinics. Prior to MRI examination, obstetric sonography including detailed neurosonography was performed using either a GE Voluson 730 or GE Voluson E8 system (General Electric, WI, USA) with 3.5- to 5-MHz curvilinear transducers and 5.0 to 9-MHz endovaginal transducers. Analysis of the cases included sonography findings (gestational age at diagnosis, the morphologic abnormality and associated anomalies), in utero and postnatal MRIs, and clinical evaluation at birth and at follow-up. Institutional review board approval was not required as this was a small case series.

RESULTS

The clinical data regarding the seven cases are detailed in the Table. Imaging time ranged from 45 to 60 minutes per patient. All patients were able to tolerate the procedure in the supine position with no complaints of claustrophobia. Images of case one were of too poor a quality for diagnosis (Fig. 1), however postcollaboration, images of sufficient quality for diagnosis were obtained from future patients (Figs. 2–7). Magnetic resonance imaging did not alter ultrasound diagnosis in two patients (28%); however, it changed the ultrasound diagnosis in three patients (43%) and provided additional information in one (14%). Additionally, MRI aided multidisciplinary management with the paediatric neuroradiologists and neurosurgeons who were more comfortable interpreting MRI rather than ultrasound images for patient counselling and prognostication.
<table>
<thead>
<tr>
<th>Case</th>
<th>Maternal demographics (weeks)</th>
<th>Sonography diagnosis</th>
<th>MRI findings</th>
<th>GA at birth (weeks)</th>
<th>Mode of delivery</th>
<th>Outcome/Postnatal follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24, G1P0</td>
<td>Bilateral ventriculomegaly, ? Intracerebral haemorrhage, Duodenal stenosis</td>
<td>Images of too poor quality for diagnosis. Ventricleomegaly</td>
<td>22, TOP</td>
<td>Vaginal</td>
<td>Autopsy – duodenal stenosis, right aortic arch, ventriculomegaly. Fetal brain not adequately fixed for pathologic examination</td>
</tr>
<tr>
<td>3</td>
<td>27, G3P2</td>
<td>Hydranencephaly</td>
<td>Hydranencephaly</td>
<td>30</td>
<td>Vaginal</td>
<td>Comfort care at birth. Neurology follow-up</td>
</tr>
<tr>
<td>4</td>
<td>17, G1P0</td>
<td>Ventricleomegaly, possible IVH. Imaging difficult</td>
<td>Porencephaly</td>
<td>39</td>
<td>Vaginal</td>
<td>Died within 24 hours</td>
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<tr>
<td>5</td>
<td>36, G3P2</td>
<td>Ventricleomegaly, occipital encephalocele</td>
<td>Occipital meningocoele, ventriculomegaly, Callosal dysgenesis</td>
<td>26</td>
<td>Vaginal</td>
<td>Stillbirth. No pathological examination</td>
</tr>
<tr>
<td>6</td>
<td>41, G3P1A1</td>
<td>Inconclusive. ? Subdural/ subarachnoid haemorrhage</td>
<td>Arachnoid cyst</td>
<td>34</td>
<td>Caesarean Section</td>
<td>Postnatal MRI confirmed arachnoid cyst. Neurosurgery follow-up</td>
</tr>
<tr>
<td>7</td>
<td>26, G3P1</td>
<td>Ventricleomegaly, DWV, Small stomach with polyhydramnios</td>
<td>Ventricleomegaly, callosal dysgenesis, DWV</td>
<td>36</td>
<td>Caesarean Section</td>
<td>Admitted NICU, Seizures, RDS. Maternal CMV IgG positive. Neonate CMV IgM negative, IgG positive.</td>
</tr>
</tbody>
</table>

GA, Gestational age; IVH, Intraventricular haemorrhage; DWV, Dandy-Walker variant; RDS, Respiratory distress syndrome; NICU, Neonatal intensive care unit; CMV, Cytomegalovirus.

Fig. 1: Only the Sagittal T2-W series in case 1 was of reasonable quality.

Fig. 2A: Axial T2-W image of case 2 showing an occipital encephalocele containing neural elements. Arrow points to skull defect.
Fig. 2B: Sagittal image of case 2.

Fig. 3A: Sagittal T2-W image of case 3 showing hydranencephaly with residual posterior fossa contents.

Fig. 3B: Coronal T2-W image of case 3 showing the falx cerebri.

Fig. 4A: Axial T2-W image of case 4 showing porencephaly.
Fig. 4B: Coronal T2-W image of case 4 showing porencephaly.

Fig. 4C: Sagittal T2-W image of case 4 showing porencephaly.

Fig. 5A: Axial T2-W image of case 5 showing ventriculomegaly and posterior callosal dysgenesis (arrow head).

Fig. 5B: Coronal T2-W image of case 5 showing ventriculomegaly.
Fig. 5C: Sagittal T2-W image of case 5 showing an occipital meningoecele.

Fig. 6A: Axial T2-W image of case 6 showing an arachnoid cyst.

Fig. 6B: Coronal T2-W image of case 6 showing an arachnoid cyst.

Fig. 7A: Sagittal T2-W image of case 7 showing increased size of the cisterna magna and posterior callosal dysgenesis (arrow head).
Sonography (including transvaginal imaging) was very difficult in cases 4 and 6. In case 4, there was great difficulty visualizing the hemisphere proximal to the probe secondary to reverberations of the sound waves from the skull and in case 6, images were suboptimal due to maternal body habitus and the advanced fetal gestation. In these two cases, the new diagnosis prompted change in perinatal management. Case 4 was at too advanced a gestational age at diagnosis to termination to be offered and thus was offered compassionate care at delivery. The neonate demised on day one of life. Patient 6 was delivered by Caesarean section at 34 weeks gestation by her primary obstetrician despite the benign nature of the arachnoid cyst.

Case 7 was somewhat of a diagnostic dilemma as her previous pregnancy had been complicated by anencephaly. Magnetic resonance imaging of the index pregnancy revealed ventriculomegaly, a Dandy-Walker variant (DWV) and callosal dysgenesis. Thus the possibility of a genetic syndrome was entertained. Her blood serology was positive for cytomegalovirus (CMV) IgG. The neonate suffered from severe respiratory distress at birth and blood serology was negative for CMV IgM but IgG positive at six weeks of life. He demised before confirmatory urine cultures for CMV, cranial ultrasound or computed tomography (CT) of the brain could be done. The parents refused autopsy. Genetic amniocentesis had revealed a normal karyotype. Karyotype was also normal in case 5.

DISCUSSION

Sonography of the fetal CNS is valuable as a primary screening tool. However, numerous limitations are recognized such as the non-specific appearances of some abnormalities, subtle parenchymal changes, operator variability, fetal positional problems, oligohydramnios and in late gestation, the reverberation artefact caused by the calvarium obscuring parenchymal detail proximal to the transducer and limiting the view of the posterior fossa (5, 10, 11). Almost all publications dealing with CNS abnormalities have stated MRI predominance over ultrasound (1), especially in the assessment of posterior cranial fossa defects, corpus callosum malformations, complex brain and spine anomalies, ventriculomegaly, brain and spine tumours, cortical maturation and dysplasia, neuronal migration, ischaemic lesions, intracerebral haemorrhage and evaluation of neural tube defects contents (12).

Thus, despite its attendant cost, particularly in a resource limited health system, as reported by Simon et al, the value of an additional noninvasive technique to confirm sonographically suspected CNS abnormalities cannot be overstated, especially when this information aids in making pregnancy management decisions (10). The crucial decisions made with the additional information documented in this series underscored the importance of the local radiologist collaborating with an expert neuroradiologist to acquire the technical expertise necessary for image acquisition and interpretation.

Magnetic resonance imaging did not alter ultrasound diagnosis in two patients (28%); however, it changed the ultrasound diagnosis in three patients (43%), provided additional information in one (14%) and changed management in two (28%). Though this case series is too small to make statistical inferences, a much larger study by Levine reported somewhat similar findings; of 125 fetuses with ultrasound detected abnormalities, MRI made a major new finding in 45 (36%) cases.
and provided additional information in 54 (43%) cases that either changed diagnosis or clearly changed counselling (13). Management changes occurred in 21 (16%). Santos et al reported in their review of 224 patients that a new diagnosis was found in 43% of cases and additional findings were noted for another 29% of cases (4). Whitby et al and Wagenvoort et al also reported alterations in diagnosis and patient management (11, 14). Despite the poor prognosis associated with hydranencephaly, porencephaly and the large occipital encephalocele with a Chiari malformation, due to the late gestational age at diagnosis, opportunities for significant changes in management were reduced; however, obstetric management was altered with the use of delivery plans avoiding Caesarean section and provision of neonatal comfort care at birth with no active resuscitative measures.

Decisions about continuing or terminating a pregnancy are common in fetuses with encephaloceles such as cases 2 and 5. The most important information for the parents is to know the appearance of the underlying brain (13). In both these cases, MRI contributed to patient care. In case 5, MRI confirmed the presence of ventriculomegaly, demonstrated the additional finding of callosal dysgenesis and excluded the presence of cortical tissue in the sac. In case 2, MRI better demonstrated the size and contents of the cephalocele and the Chiari malformation. These findings worsened the prognosis and were thus important for patient counselling.

Three cases had an abnormal corpus callosum. Case 2 had complete callosal agenesis detected both with ultrasound and MRI. However, in 2 cases, dysgenesis was only detected with MRI and not ultrasound. In cases of complete agenesis, ultrasound is usually sufficient; however, in fetuses with partial agenesis, missed diagnosis often occurs because the contour of the lateral ventricles may not have the typical appearance seen in complete agenesis. Magnetic resonance imaging allows direct evaluation of the length and configuration of the dysgenetic corpus callosum, especially on midline sagittal image (2, 8, 13). In case 7 (ventriculomegaly and DWV) as well as case 5 (occipital meningocele and ventriculomegaly) in our series, callosal dysgenesis was additionally found on MRI. This information was important in patient counselling as agenesis/dysgenesis of the corpus callosum with other associated abnormalities has a poor prognosis (13, 15, 16).

Case 6 was diagnosed with an arachnoid cyst. These occur in about 1% of neonates. Primary cysts are benign cerebrospinal fluid cisterns between dura and brain surface, not communicating with the subarachnoid space. Secondary cysts are the result of haemorrhage, perinatal injury or intrauterine infection. Prenatal MRI examinations allow additional evaluation for aqueduct of Sylvius compression, cyst lumen communication with the ventricular system and corpus callosum dysgenesis. None of these were present in the index case. Such information allows forthright evaluation of the character of the cyst and exclusion of other developmental CNS anomalies, which on sonograms may seem similar to arachnoid cysts (2).

As the cyst was benign, perhaps the patient could have been delivered at term thus avoiding the complications of prematurity.

Porencephalic cysts result from local destruction of the cerebral parenchyma by a vascular, infectious or traumatic cause. These clastic lesions carry a poor prognosis, varying from fetal death in utero to major psychomotor handicap (16). Multifocal porencephalic encephalopathy was hard to visualize on ultrasound in case 4, but was easily seen on MR images (2, 17). Similar to other reports, we found that while ultrasound identified ventriculomegaly with an irregular ventricle contour, MRI better demonstrated the amount of cortical destruction (13). In contrast, hydranencephaly, an extreme form of porencephaly caused by insults occurring after 12 weeks gestational age, was clearly visualized with ultrasound and MRI added no additional information (2). The absence of normal cerebral hemispheres and cerebrospinal fluid covered by meninges above the brain stem was easily visualized with both sonography and MRI.

Ultrasound evaluation of the posterior fossa can be difficult. With MRI, the cerebellar hemispheres, vermis, subarachnoidal space, and fourth ventricle are visible. For diagnosis of Dandy-Walker syndrome and its variants, MRI significantly outstrips ultrasound imaging (9, 10, 18). Puva-banditsis et al reported on fetal CMV infection presenting with ventriculomegaly and a severely destructive change of the cerebellum resulting in a large cyst of the posterior fossa leading to Dandy-Walker malformation being suspected in the fetus (19). They also reported severe respiratory distress in the neonate. A similar picture was seen in case 7 and although we were unable to definitively confirm CMV infection, it could possibly have resulted in the pathology seen. Cytomegalovirus infection produces lesions in the CNS in 55% of fetuses; however, hydranencephaly, cerebral calcifications, gyration disorders and ischaemic lesions are the most common findings.

Prenatal counselling was performed by paediatric specialists – paediatric neurosurgeons and neonatologists – who had experience reading MRI examinations but had limited ability to interpret prenatal sonograms. These specialists felt more confident about a specific diagnosis after viewing the fetal MRI and were therefore better able to counsel the patient. Thus patient and provider management decisions were facilitated (13). The confirmatory technique provided a measure of confidence that was not previously available and was thus extremely valuable.

Magnetic resonance imaging is useful prior to termination or after a stillbirth as brain autopsy may not reflect the antenatal changes due to cerebral destruction from autolysis (11). This would have been useful in case 1, however, the images were of too poor a quality for diagnosis. Difficulty was encountered in removing the brain in total and in formalin fixation. Fetal imaging could have revealed additional pathology not detected at fetal autopsy. As there were also additional abnormalities present in that fetus, it might also have been helpful for genetic counselling.
Fetal karyotype assessment confirming or excluding chromosomal anomalies is useful in fetuses with CNS anomalies and was normal in the two cases performed. Case 5 denied autopsy after stillbirth, however, the prior MRI perhaps reduced the need for autopsy.

CONCLUSION
In this report, we presented the initial experience with MRI of the fetal CNS. Magnetic resonance imaging is a noninvasive, safe diagnostic modality which may be performed as a supplementary examination when sonographic abnormalities are suspected. Its limitations are non-real time imaging, limited availability, cost and contraindications such as claustrophobia. Nevertheless, despite the associated significant expense, in a resource limited healthcare system, MRI was a valuable contributor to patient counselling. Improved prenatal diagnosis led to changes in perinatal management. Collaboration thus led to the local availability of a previously unavailable and valuable tool to aid prenatal diagnosis.

REFERENCES

Erratum
“The Effects of Mild Hypothermia on Coagulation Tests and Haemodynamic Variables in Anaesthetized Rabbits” by C Staikou, A Paraskeva, I Donta, T Theodossopoulos, I Anastassopoulou and M Kontos was published in the October 2011 issue of the West Indian Medical Journal. Under Results in the Abstract, on page 513, the authors stated that “Prothrombin time and activated partial thromboplastin time decreased at hypothermia....” However, it should be “increased”.