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REVIEW ARTICLE

Findings and differential diagnosis of fetal intracranial haemorrhage and fetal ischaemic brain injury: what is the role of fetal MRI?

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ABSTRACT

Ventriculomegaly (VM) is a non-specific finding on fetal imaging. Identification of the specific aetiology is important, as it affects prognosis and may even change the course of current or future pregnancies. In this review, we will focus on the application of fetal MRI to demonstrate intracranial haemorrhage and ischaemic brain injury as opposed to other causes of VM. MRI is able to identify the specific aetiology of VM with much more sensitivity and specificity than ultrasound and should be considered whenever VM is identified on obstetric ultrasound. Advances in both fetal and neonatal MRI have the potential to shed further light on mechanisms of brain injury and the impact of chronic hypoxia; such information may guide future interventions.

INTRODUCTION

MRI has become a standard problem-solving tool in fetal imaging with the earliest studies showing utility in evaluation of the brain. Even though there are many diverse applications now, the most common indication is still assessment of brain abnormalities.^{1–4}

Intracranial haemorrhage (ICH) and ischaemic brain injury are rare in the fetus. The true incidence is difficult to ascertain because of underdiagnosis and the varied descriptors used in the literature, including “fetal stroke”, “prenatal cerebrovascular disorder” or inclusion in the series of “perinatal stroke” and “perinatal brain injury”. Dicuonzo et al⁵ defined fetal stroke as an event occurring between the 14th week of pregnancy and the beginning of labour and cited an incidence of approximately 17–35 of 100,000 live births. Other sources report an incidence of 0.5–1.0 per 1000 pregnancies.⁶ In a series published in 1985, 6% of autopsies for stillbirth showed some evidence of fetal ICH.⁷

In this review, we will focus on the use of fetal MRI to demonstrate the features of ICH and ischaemic brain injury illustrated with examples referred to this institution for further evaluation of “ventriculomegaly”, “hydrocephalus” or “abnormal findings on screening ultrasound”. The diagnosis of ICH/ischaemia had not been considered in the

majority of the cases. Lack of prospective diagnosis may be due to the rarity of the condition as well as the fact that while the sonographic findings of ICH are similar to those seen in premature infants and thus familiar to radiologists who interpret neonatal head ultrasound, they may not be as easily recognized by community radiologists, obstetricians or maternal fetal medicine specialists. Outcome is related to the severity of the bleeding and associated brain injury; the grading system for this is discussed in more detail below.

Importance of recognition of fetal intracranial haemorrhage and ischaemic brain injury
ICH in the fetus can be intra-axial or extra-axial.⁶ Recognition is important because of the potential for poor outcome with the consequent implications for pregnancy management as well as the possibility of recurrence in future pregnancies in conditions such as alloimmune thrombocytopenia. In the USA, fetuses with ICH are delivered by caesarean section in order to avoid additional bleeding as a result of head compression during labour and vaginal delivery. Vaginal delivery, rather than operative delivery, is offered in cases where haemorrhage is associated with sufficient brain injury that families elect comfort care only for the infant. The demonstration of a bleed or of ischaemic brain injury prior to the onset of labour proves that birth trauma is not the cause of neurological

Table 1. Causes of fetal intracranial haemorrhage

Idiopathic
Alterations in maternal/fetal blood pressure
Umbilical/placental abnormalities
Gene mutations, e.g. COL4A1 associated with hereditary parenchymal haemorrhage and porencephaly
Maternal
Trauma
Maternal coagulopathy/use of anticoagulants
Infection
Drug use
Medication complications
Seizure disorder
Febrile illness
Cholestasis of pregnancy
Fetal
Thrombocytopenia—NAIT
Congenital Factor X, Factor V deficiency
Vascular malformations
Tumour
Consequence of fetal intervention
Complications of monochorionic twinning

NAIT, neonatal alloimmune thrombocytopenia.

impairment and may prevent medicolegal action for inadequate obstetric care. In countries where termination of pregnancy beyond 20 weeks is illegal unless it is for the benefit of the mother's health, for uniformly lethal fetal conditions or with conditions that carry a "grave prognosis", recognition of high-grade ICH or ischaemic brain injury becomes extremely important. Exclusion criteria for fetal surgery for open neural tube defect and laser therapy for twin–twin transfusion include any fetal abnormality unrelated to the primary diagnosis.⁸ The

authors are aware of a case for which fetal surgery for open neural tube defect was denied based on an erroneous report of ICH on fetal MRI. When the MR images were obtained for review, cerebrospinal fluid (CSF) flow artefact had been misinterpreted as a bleed. The window for fetal surgery (as well as that for pregnancy termination) had passed by the time the error was proven, resulting in considerable distress for the family. This anecdotal case demonstrates the importance of correct interpretation of fetal MRI studies.

Grading and outcome

The grading for fetal intraventricular haemorrhage (IVH) is the same as that used for preterm infants. Grade I is isolated to the germinal matrix at the caudothalamic groove, Grade II implies IVH without ventricular dilatation, Grade III is IVH with ventricular dilatation and Grade IV indicates periventricular haemorrhagic infarction.⁹ Grading is helpful for discussions regarding prognosis. Although there is limited information on outcomes with fetal ICH, higher grade IVH is associated with worse prognosis.^{10,11} Ghi et al¹² reported a series of 16 fetuses and reviewed another 93 reported cases for a total of 109 cases. There were 32 cases each of Grades III and IV IVH, with a 51% loss rate by 1 month of age. Of the survivors, only 52% were judged neurologically normal at 12 months of age. Initial survival and neurologic outcome was associated with grade of haemorrhage. In another series of 33 fetuses diagnosed with haemorrhagic brain lesions, there were 17 terminations of pregnancy, 2 intrauterine fetal demises and 1 death at 2 months of age with 13 live births. Eight neonates had moderate to severe neurological deficit by a mean age of 35 months. These eight cases and the one that died at 2 months had Grade III–IV IVH *in utero*.¹³ Echogenic material in the fetal frontal horns has been shown by both ultrasound and MR; this is not the normal location of the choroid plexus and may represent haemorrhage (*i.e.* Grade II). In the series by Hines et al,¹⁷ some cases resolved without sequelae, but some progressed to ventricular enlargement and porencephaly. In preterm neonates, the severity of IVH clearly correlates with outcome. A meta-analysis among preterm infants found that after a specific abnormality is identified on cranial ultrasound, there was a higher post-test probability for the presence of cerebral palsy or neuromotor impairment for Grade III (26%), Grade IV haemorrhage (53%) and hydrocephalus (27%).^{14–16}

Table 2. Scan parameters for performance of fetal MRI

Single-shot T2WI	Gradient-echo T1WI	Diffusion-weighted imaging/ADC
Three planes	Two planes	<i>b</i> -value = 0, 500, 1000
TR 1000 ms TE 100 ms	TR 100 ms TE 5 ms	
512 × 512 matrix	512 × 512 matrix	
4-mm interleaved	5-mm slice, 1-mm gap	
HASTE (Siemens Healthcare GmbH, Erlangen, Germany) SSFSE (GE, Boston, MA) SSHTSE (Phillips, Andover, MA)	FLASH (Siemens Healthcare GmbH, Erlangen, Germany) SPGR (GE, Boston, MA) T1FFE (Phillips, Andover, MA)	

ADC, apparent diffusion coefficient; FLASH, Fast low angles shot; SPGR, Spoiled Gradient Recalled acquisition; SSFSE, Single Shot Fast Spin Echo; SSHTSE, Single shot turbo spin echo; T1FFE, T1 Fast Field Echo; T1WI, T₁ weighted image; T2WI, T₂ weighted image; TE, echo time; TR, repetition time.

Figure 1. Motion artefact: coronal T_2 weighted MRI in a fetus with Chiari II malformation was interpreted as showing evidence of intracranial haemorrhage because of low signal on the right and a blood-fluid level on the left. The patient was denied *in utero* repair as a result. In fact, the dark signal on the right is an artefact due to fetal and amniotic fluid motion; it can be noted that it extends far beyond the cranial margins (arrowheads). The dark swirl in the left ventricle is cerebrospinal flow artefact not intraventricular clot; it was not reproduced on any other scan plane and there was no high signal on T_1 weighted sequences. A blood-fluid level should be linear and layer dependently in the ventricle.

Aetiology

The various aetiologies of fetal ICH are listed in Table 1.^{6,7} Identification of the specific aetiology is important, as it may change the course of the current pregnancy or may have an impact on future pregnancies. This is especially the case in neonatal alloimmune thrombocytopenia, as treatment with intrauterine transfusions or maternal i.v. immunoglobulin can improve outcomes. There is a 50–100% risk of the mother having another affected child.²⁰ Approximately 20% of offspring develop ICH, of which half occur *in utero*. Therefore, making the diagnosis is essential in order to appropriately counsel mothers and provide appropriate surveillance and detection in future pregnancies.^{6,19} Fetal ICH is most common in the third trimester, as the majority arise from germinal matrix haemorrhage.^{6,13} Those cases associated with causes such as maternal trauma, twin complications etc. will of course be seen at any gestational age; therefore, the diagnosis should not be discounted in a second trimester fetus with appropriate imaging findings.

The work-up of any fetal abnormality requires a thorough history including all forms of trauma; direct questions regarding injury are important, as adverse fetal consequences may be seen with even apparently minor degrees of injury.^{21–24} Complete record of maternal drug use should be obtained, with care to ask about drugs of abuse such as cocaine or methamphetamine usage as well as about over-the-counter medications such as aspirin. Coumadin should rarely be encountered in pregnancy, but heparin is used in patients with thrombophilia. In pregnant females, Factor V Leiden and SSA/SSB antibody positivity and

full-blown systemic lupus erythematosus are causes of thrombophilia as well as the rare but potentially devastating paroxysmal nocturnal haemoglobinuria.^{25,26}

Intrauterine demise of a monochorionic twin may result in severe ischaemic injury and extensive ICH in the surviving twin.^{27,28} Maternal infections can seem mild yet have significant consequences for the fetus. An example of this is primary cytomegalovirus infection which can cause intracranial bleeding as well as the more frequently encountered migrational disorders, brain destruction and calcification. Detection of intracranial bleeding in that setting is unlikely to influence pregnancy management but will, at least, reassure the mother that the recurrence risk is low in future pregnancies.^{29–31} Recent work has identified genetic mutations that may predispose to ICH.³²

ADVANTAGES OF MRI FOR DIAGNOSIS OF FETAL INTRACRANIAL HAEMORRHAGE AND ISCHAEMIC BRAIN INJURY

Ultrasound is the initial screening modality for fetal anatomy. The differential diagnosis of some of the sonographic findings in ICH is broad and MRI is helpful in exclusion of ICH as well as in confirmation of its presence; but, it is an expensive imaging modality and is not always locally available. However, studies of the fetal brain are relatively simple with respect to sequence selection and scan plane and a single MR scan may provide a specific diagnosis with regard to the presence or absence of intracranial bleeding. A study could be performed at the mother's convenience with images sent for expert interpretation *via* secure cloud computing. Maternal sedation is not required, nor is administration of i.v. contrast agents. There is no known risk to mother or fetus.^{33–35}

Only a few standard sequences are used; the parameters are listed in Table 2. Orthogonal images are obtained through the fetal brain just as they are in paediatric or adult scans. The fetal orbits are a useful landmark to set up the scan plane when first starting to perform fetal MRI.³⁶ A combination of the anterior body phased-array coil and the posterior spinal coils are used to obtain a uniform field. Sequences are scanned in as little as 30–60 s.³⁷

Diffusion-weighted imaging is now being implemented into many fetal MRI protocols and can be used to detect acute

Table 3. Sonographic findings in fetal intracranial haemorrhage

Loss of normal cerebral landmarks
Variable echogenicity, avascular intracranial mass
Hyperechoic acute clot adherent to bulky/nodular choroid plexus
Hyperechoic clot outlining cerebral cortex
Hyperechoic nodular ependyma
Increased periventricular white matter echogenicity
Porencephaly
Hydranencephaly

Clot and infarcted brain parenchyma change in echogenicity over time becoming less echogenic and undergoing eventual resorption.

Figure 2. Typical ultrasound findings in fetal intracranial haemorrhage: (a) axial ultrasound is showing a large avascular, mixed echogenicity mass (long arrows) associated with ventriculomegaly (VM) (arrowheads) and porencephaly (short arrows). (b) Axial ultrasound is showing VM; echogenic clot in the third ventricle (arrow) is the clue to the underlying diagnosis. (c) Axial ultrasound is showing dilated frontal horns and nodular ependyma (arrowheads). The porencephaly (arrows) adjacent to the downside ventricle is the clue to haemorrhage as the cause; this was not appreciated on initial sonographic review. (d) A magnified view of the occipital horn is showing thick, echogenic, nodular ependyma with intraventricular echogenic debris (arrowheads) that was separate from the choroid plexus in real time. Initial diagnosis was grey matter heterotopia and cortical dysplasia with VM attributed to aqueductal stenosis.

cytotoxic and/or vasogenic oedema, especially with the use of low b -value T_2 diffusion imaging. The acute response of the fetal brain to ischaemia is not as well delineated as in the adult brain and the timeline of diffusion changes in fetal intracranial ischaemia is an area for future study. T_2 diffusion imaging has the potential to display abnormalities in white matter maturation in cases of fetal ICH and may be beneficial in the assessment of prognosis. The value of echoplanar imaging may be in its increased sensitivity for detection (as compared with T_1 and T_2 weighted imaging), as well as in its ability to differentiate between intraparenchymal haemorrhage and infarct.^{38–40} Normative apparent diffusion coefficient values for healthy fetuses have recently been reported.^{41,42} Knowledge of normal apparent diffusion coefficient values may help contribute to early identification of fetal brain abnormalities and assist in follow-up and outcome assessment.

MRI artefacts

Fetal motion can be a challenge when performing fetal MRI. The sequences used provide fast, single-slice acquisition and can be repeated as necessary to obtain sequential slices of the brain in

orthogonal planes. When the ventricles are dilated, the CSF “swirls” with fetal movement; this results in low signal flow artefacts on T_2 weighted sequences. It is important to recognize this and differentiate it from true low signal related to the presence of blood products. Motion artefact will be inconsistent

Table 4. MRI findings in fetal intracranial haemorrhage

T1WI
High-signal intraventricular clot
High-signal parenchymal foci suggest vasculitis or petechial haemorrhage
T2WI
Low signal intraventricular clot
Intraventricular fluid–fluid level
Abnormal cortical signal
Porencephalic cyst formation

T1WI, T_1 weighted image; T2WI, T_2 weighted image.

Figure 3. Suprasellar tumour: (a) an axial ultrasound image is showing an inhomogeneous mass (arrows) distorting the normal anatomy associated with bilateral ventriculomegaly (white arrowheads). Owing to sudden onset of head enlargement in the third trimester and ventricular dilatation in association with a hypovascular mass, the possibility of a large haemorrhage was raised. (b) A sagittal T_2 weighted image is showing that this is in fact a suprasellar mass (black arrowheads), which is elevating and distorting the normal brain. There was no evidence of haemorrhage in or around the tumour on any sequence. The infant expired within minutes of birth and the family declined autopsy.

from plane to plane, whereas low signal clot or blood-CSF levels are reproducible. Also, clot is high signal on T_1 weighted images, but flow artefact is not visible (Figure 1). Positioning of surface coils is important to ensure that the area of interest is in the region of best field homogeneity and counter to most MRI studies small fields of view lead to decreased image quality because of poor signal to noise and wrap artefact.⁴³

ULTRASOUND AND MRI FINDINGS IN INTRACRANIAL HAEMORRHAGE AND ISCHAEMIA

The most common abnormality found on ultrasound in the setting of fetal ICH is ventricular enlargement.^{6,23} Other features are listed in Table 3 and illustrated in Figure 2. Ventriculomegaly (VM) is a non-specific finding on fetal imaging. It is associated with multiple conditions, the specific findings of which may

not be immediately apparent on ultrasound. MRI should be considered a complimentary study for further evaluation and characterization of the brain in the setting of non-specific or inconclusive sonographic findings. In a study of over 700 patients, ultrasound detected additional findings associated with VM 16% of the time, whereas MRI found associated lesions 58% of the time.⁴⁴

Typical imaging findings of fetal ICH are present on the standard rapid T_1 and T_2 weighted sequences used for anatomic assessment; additional information may be gained with the use of diffusion-weighted imaging, T_2^* and echoplanar sequences.^{18,37,38,45–48} The MRI findings of ICH and ischaemia are listed in Table 4. There is little information available regarding changes in signal of fetal intracranial blood products

Figure 4. Differentiation between intracranial lipoma and clot: (a) axial ultrasound is showing an echogenic avascular, mass (arrows) extending to the left of the midline. The cavum septi pellucidi was not visible and the working diagnosis was intracranial lipoma in association with agenesis of the corpus callosum. Maternal obesity limited sonographic evaluation (b) An axial T_1 weighted image is showing ventriculomegaly and high-signal clot (arrows) in the frontal horn and adherent to the choroid plexus (c) An axial T_2 weighted image is showing low-signal clot (arrows) and diffuse increased signal of the cerebral mantle indicating diffuse ischaemic injury. The cavum was visible on MRI. In this case, the MRI also identified a large retroplacental abruption as the cause of fetal hypotension and brain injury. Given the poor prognosis, the patient elected early induction of labour and the infant expired within minutes of delivery.

Figure 5. Porencephalic cyst on fetal MR: coronal T_2 Half-Fourier Acquisition Single-shot Turbo Spin-Echo (HASTE) MR is clearly demonstrating a porencephalic cyst (long arrows) adjacent to the right lateral ventricle. There is internal debris (black arrowhead) in the cyst and clot (asterisk) in the dilated frontal horn. Haemosiderin deposition causes chemical shift artefact (short arrows), which confirms intracranial haemorrhage as the underlying aetiology. The initial ultrasound noted only unilateral ventriculomegaly on the standard views; on review, there was evidence of parenchymal destruction with clot and debris in the developing porencephalic cyst, but the area was obscured by reverberation in the near field.

over time; MRI is used for problem solving in fetal imaging and is not typically used for follow-up. If the pregnancy continues, follow-up imaging is with ultrasound. Live born infants may undergo serial MRI or CT as part of their management.

Some of the alternative diagnoses are illustrated below with specific emphasis on how the MRI findings lead to a correct diagnosis.

Mass: tumour vs clot

Fetal intracranial tumours are rare. They are most often supratentorial as opposed to the more commonly encountered paediatric brain tumours. Teratomas are most common (62%) followed by neuroepithelial tumours (15%) and lipomas. The masses may be both cystic and solid, and internal calcification and haemorrhage are common.¹⁸ VM and macrocephaly are also common. Tumours manifest as space-occupying lesions with mass effect on adjacent brain structures (Figure 3), whereas the avascular mass of the clot seen in association with severe ICH often reflects periventricular haemorrhagic infarction and thus, the clot replaces destroyed brain tissue (Figure 4). Over time, the sonographic features evolve from a solid mass-like structure composed of clotted blood and infarcted brain to eventual porencephalic cyst formation. Mass effect is not a dominant finding. Intraventricular clot also changes in echogenicity over time.

Intracranial lipoma is described in association with agenesis of the corpus callosum; it presents as an echogenic, midline avascular mass on ultrasound and follows fat signal on all MR

sequences. Agenesis of the corpus callosum can be quite subtle on ultrasound and may be missed, but when complete, it is usually associated with absence of the *cavum septi pellucidi* and colpocephaly particularly in later gestation when clot related to ICH is more likely to be in the differential diagnosis of a mass.^{49–51}

Cyst: porencephalic vs arachnoid

In differentiating porencephalic cyst and arachnoid cyst, *ex vacuo* dilatation of the ventricle is seen in the former but mass effect in the latter; ventricular dilatation secondary to obstruction may occur if an arachnoid cyst causes impaired CSF circulation such as by kinking the foramen of Monro. A porencephalic cyst is an intra-axial, avascular cavity in the brain, typically in communication with the ventricular system, which does not reach the inner table of the skull. It can be the result of ICH or other destructive processes such as *in utero* infection or toxin exposure. In cytomegalovirus infection, temporal lobe destruction results in a characteristic distribution of intraparenchymal cystic lesions.^{18,29} Porencephalic cysts are associated with severe developmental delay and seizure disorders due to the underlying brain destruction (Figures 5 and 6). Arachnoid cysts are simple in architecture and, unless associated with mass effect or other brain malformation, have no adverse impact on the infant. Larger cysts with mass effect, or those that obstruct CSF circulation, may be treated with fenestration with good long-term outcome (Figure 7). Thus, differentiation between the two entities is vital for parental counselling. Other cystic lesions

Figure 6. Porencephalic cyst missed on fetal ultrasound: axial postnatal T_2 weighted imaging is showing bilateral porencephalic cysts (white arrows), blood-cerebrospinal fluid level (long black arrow), intraventricular debris (arrowheads) and thick, nodular ependyma (short black arrows). These features were all apparent on fetal MRI, just of somewhat lower resolution owing to the limited type of sequences that are fast enough to image a “moving target” such as a fetus. This is the follow-up of the ultrasound image shown in Figure 1c. The porencephalic cyst was not appreciated on the fetal ultrasound. The infant had abnormal thumbs and the final diagnosis was thrombocytopenia absent radius syndrome.

Figure 7. Arachnoid cyst mistaken for porencephalic cyst: (a) sagittal T_2 HASTE MR is showing a well-circumscribed infratentorial cyst (arrows) with mass effect on the adjacent *vermis* (V) and brainstem. It can be noted that although the tentorium is elevated, the *vermis* is not rotated; rather it is compressed against the brainstem. The supratentorial brain was normal. (b) The fetal ultrasound was misinterpreted as a porencephalic cyst despite the fact that the brain was normal and the mass (arrows) was a simple cyst, and extra-axial in location. The neonatal head CT was misinterpreted as a Dandy-Walker malformation until it was compared with the fetal MRI study (which was under the mother's name).

included in the differential include connatal cysts, which are benign entrapment cysts seen in the frontal horns (Figure 8).^{52,53} These may be confused with subependymal cysts in the setting

Figure 8. Connatal cyst: parasagittal ultrasound in a 36-week twin is showing one of the bilateral well-circumscribed, oval cysts (arrow) anterior to the caudothalamic groove (arrow-head) in an otherwise normal brain. Concern was raised for *in utero* germinal matrix haemorrhage. MRI showed no evidence of blood products; as a result, the patient was allowed to deliver vaginally. Postnatal imaging confirmed simple entrapment cysts also known as connatal cysts. C, caudate nucleus, T, thalamus.

of Grade II germinal matrix haemorrhage, but MRI can exclude bleeding as there will be no blood products visible on any sequence.

Hydranencephaly vs giant open lip schizencephaly or severe hydrocephalus

Hydranencephaly and schizencephaly are often confidently diagnosed on ultrasound. However, in the third trimester, reverberation from the ossified skull vault can obscure detail and obese maternal habitus can further compromise sonographic image quality. Markedly enlarged CSF spaces may be seen with hydrocephalus; recognition of the presence of a thin, stretched cortical mantle in hydrocephalus is important in order to differentiate it from hydranencephaly, which is considered lethal. Whatever the underlying diagnosis is, in hydrocephalus, most cases are non-lethal. Hydranencephaly implies complete destruction of the brain parenchyma thought to be due to a vascular insult. 85% of those born with hydranencephaly die within the first year of life. MRI shows complete destruction of the brain parenchyma perfused by the carotid arteries (Figures 9 and 10).^{54,55} Schizencephaly is an abnormal cleft within the brain parenchyma lined with grey matter. The cleft can be closed or open; only open lip schizencephaly has been detected with confidence on fetal imaging.^{56,57} Bilateral giant open lip schizencephaly can be confused with hydranencephaly (Figure 11). Infants born with schizencephaly often survive, but with severe epilepsy and neurologic deficits. Whether making the decision to terminate a pregnancy or deciding on monitoring/intervention in labour and neonatal resuscitation, parents need the best possible information. Neither hydranencephaly nor giant open lip schizencephaly

Figure 9. Hydranencephaly: (a) an axial T_1 weighted image is showing foci of high-signal haemorrhagic debris (arrows); there is no normal brain. (b) An axial T_2 weighted image is showing fragments of intermediate signal debris (arrows) on either side of the fenestrated falx cerebri (arrowheads); there is no normal brain. (c) An axial T_2 weighted image is showing the cerebellum (long arrows) and the medial portions of the temporal lobes (short arrows), which are perfused by the posterior circulation. All of the brain perfused by the anterior circulation is destroyed. This confirms hydranencephaly (a lethal entity) and excludes severe hydrocephalus.

has a significant recurrence risk. Both have dismal neurological outcomes *vs* the prognosis for hydrocephalus, which has variable neurological outcome and recurrence risk depending on the underlying aetiology.

Figure 10. Severe hydrocephalus: an axial T_2 weighted image in a fetus with severe hydrocephalus due to aqueductal stenosis is showing a thin, continuous rind of temporal lobe cortex (arrows). The patient presented late in the third trimester; skull reverberation and maternal habitus made ultrasound very challenging and it was not clear whether there was a cortical mantle. Hydrocephalus has variable prognosis and neurological outcome cannot be predicted on the basis of parenchymal thickness alone, whereas hydranencephaly is lethal. Hydrocephalus is not a diagnosis; it is an observation that should prompt a thorough search for a specific diagnosis. In this case, the patient had three consecutive children affected by X-linked aqueductal stenosis (X linked recessive inheritance, *L1CAM* gene mutation).

FUTURE DEVELOPMENTS

Ultrasound is the mainstay of fetal imaging. The improvements in resolution with modern equipment are astounding to those of us who have been in the field since the late 1980s. Three-dimensional and four-dimensional imaging and vascular mapping with three-dimensional colour and power Doppler are now widely available. MRI, although not as accessible as ultrasound, is an excellent tool for problem solving particularly in the brain. Fetal MRI is constrained by the need to image a moving target, the size of the structure to be imaged and its location within the maternal uterus as well as by safety concerns regarding energy deposition and noise exposure. Techniques such as diffusion tensor imaging, spectroscopy and functional MR and the use of higher field strengths are appealing in so far as they have the potential to shed further light on mechanisms of brain injury and the impact of chronic hypoxia.^{58–60} Who knows what the future may hold? It may become possible to “see” exactly which tracts are damaged and thus to target early intervention to recruitment of neurons in the area with a view to utilizing the natural plasticity of the young brain to overcome structural deficits.^{61–64} Gene therapy and stem cell therapy are no longer science fiction; perhaps in the future, the skills currently being leveraged on treatment of degenerative diseases such as Parkinson’s disease can be applied to treatment of brain injury. Emerging data suggest that transplantation of umbilical cord blood-derived stem cells may have therapeutic potential for neuroregeneration and improved functional outcome.^{65,66}

CONCLUSION

Fetal ICH is a rare but important diagnosis to make *in utero*, as it has prognostic implications for the current and potentially for future pregnancies. Ultrasound diagnosis of fetal ICH can be difficult particularly in late gestation (when it is most likely to occur), with multiple pregnancies or with maternal obesity. Fetal MRI can overcome the acoustic access issues caused by

Figure 11. Giant open lip schizencephaly: (a) axial ultrasound obtained at presentation at 28 weeks of gestation is showing an intact midline but little in the way of normal cerebral mantle. The working diagnosis is hydranencephaly. (b) A composite image with Sagittal T_1 weighted image superiorly and sagittal T_2 weighted image in the same plane inferiorly is showing residual posterior cortex with no T_1 high signal to indicate haemorrhage. The T_2 weighted image is showing that the edges of the defect are lined by grey matter (arrow); thus, this is a primary brain malformation and not the result of destruction of normal brain. This is not a lethal entity, but it is associated with severe developmental delay.

overlapping fetal parts, challenging fetal position and ossified skull vault. It is also less impacted by maternal obesity than ultrasound is. In most cases, fetal MR allows for a confident diagnosis of fetal ICH and/or ischaemia. With ongoing research and application of

new techniques, it may even become possible to recognize areas at risk allowing intervention to prevent injury. More detailed assessment of injured area may allow specific, targeted therapy to maximize functional outcome for affected children.

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