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Differential diagnosis and outcome of fetal intracranial hypoechoic lesions: report of 21 cases

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ABSTRACT

Our objective was to evaluate the diagnostic and prognostic value of sonography in fetal intracranial hypoechoic lesions. A retrospective study revealed a total of 21 cases diagnosed over a period of 10 years. Most of the diagnoses were made in the third trimester. The presence of fluid-filled lesions within the brain matter always predicted porencephaly and a poor outcome. In most of these cases (nine out of ten), the lesions were seen to communicate with the cavity of the lateral ventricles. Among the 11 cases of hypoechoic lesions that were external to the brain matter, Doppler ultrasound was always able to distinguish between arachnoid cysts (seven cases) and vein of Galen aneurysms (four cases). Arachnoid cysts were associated with a good outcome in four out of five pregnancies that delivered at term. Three of the four cases of vein of Galen aneurysm were associated with distortion of the cerebral architecture and/or hydrops: one pregnancy was terminated and two resulted in early postnatal death. One pregnancy with vein of Galen aneurysm and normal cerebral structures, without signs of hydrops, had a good outcome. It is concluded that current antenatal ultrasound has the capability of accurate differentiation between different clinical entities resulting in fetal intracranial hypoechoic lesions, and that the sonographic findings have practical clinical implications.

INTRODUCTION

Fetal intracranial hypoechoic lesions are rare entities predominantly caused by three conditions: arachnoid cysts, porencephaly or vascular malformations[1]. The distinction between these three entities is clinically relevant, as each one carries different prognostic implications. However, the experience thus far depends mostly upon case reports; the capability of fetal ultrasound to make an accurate differential diagnosis is unclear. Indeed, the use of other methods of antenatal evaluation, including magnetic resonance imaging (MRI) and fetal blood sampling, has been proposed[2–5].

We retrospectively reviewed our experience and herein report 21 cases that were diagnosed at our unit between 1985 and 1995.

MATERIALS AND METHODS

The archives of our ultrasound laboratory between 1985 and 1995 were retrospectively reviewed. Cases with an antenatal diagnosis of intracranial hypoechoic lesions were collected. No attempt at identifying false negatives was made. Twenty-one cases with a detailed follow-up were obtained. In all cases, a systematic neurosonographic examination of the fetus had been performed by the use of axial, coronal and sagittal views[6]. Pulsed Doppler evaluation of cerebral vessels was always performed. Transvaginal sonography was performed in fetuses presented by the vertex from 1987, and color Doppler from 1990 onwards.

The diagnostic criteria were as follows: the demonstration of a sonolucent intracranial lesion, external to the cerebrum and without Doppler evidence of blood flow, suggested the presence of arachnoid cysts[1]. An intracranial lesion internal to the brain mass, whether or not in communication with the cavity of the lateral ventricles, suggested porencephaly[3,7,8]. Demonstration with pulsed and/or color Doppler ultrasound of blood flow within a midline hypoechoic lesion suggested a vein of Galen aneurysm[9,10].

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Table 1 Main clinical data of fetuses diagnosed *in utero* as having arachnoid cysts

Case	*Gestational age at diagnosis* (weeks)	*Prenatal findings*	*Outcome*
1	23	large midline cyst in the anterior–middle third of brain; agenesis of corpus callosum	one termination of pregnancy, two delivered at term: cyst–peritoneal shunt in both, normal development at 6 and 9 years
2	32		
3	22		
4	28	large midline cyst in posterior third of brain	delivery at term, cyst–peritoneal shunt in one case, normal development at 2 and 7 years
5	31		
6	22	small cyst in ambient cistern; double-outlet right ventricle; clenched hands; trisomy 18	termination of pregnancy
7	34	small cysts in ambient cistern; agenesis of corpus callosum	delivery at term, seizures, developmental quotient 70 at 4 years

Table 2 Main clinical data of fetuses diagnosed *in utero* as having porencephaly

Case	*Gestational age at diagnosis* (weeks)	*Prenatal findings*	*Outcome*
8	29	large unilateral cyst communicating with the lateral ventricles; hydrocephalus and macrocrania; blood clot in two cases	delivery at term; encephaloclastic porencephaly; alloimmune thrombocytopenia in one; one perinatal death; postnatal shunt and severe retardation in all four survivors
9	36		
10	33		
11	32		
12	35		
13	25	recipient fetus in twin–twin transfusion; hydrops; large irregular cyst communicating with lateral ventricles; hydrocephalus	intrauterine death of recipient at 26 weeks; donor twin delivered at 31 weeks, alive and well
14	24	twin–twin transfusion; following the death of the recipient twin, the donor developed large subarachnoid spaces and ventricles and multiple cysts in the periventricular area	termination of pregnancy; autopsy not performed
15	22	clefts in parietal lobes, bilateral and symmetric in two cases, unilateral in one case; absence of the cavum septum pellucidum in all; microcephaly in two cases	termination of pregnancy in one case; delivery at term in two cases: schizencephaly and infantile death in one, severe retardation in the other
16	32		
17	34		

Table 3 Main clinical data of fetuses diagnosed *in utero* as having vein of Galen aneurysm (VGA)

Case	*Gestational age at diagnosis* (weeks)	*Prenatal findings*	*Outcome*
18	28	VGA; borderline ventricles; echogenic brain matter	delivery at 35 weeks; perinatal death
19	34	VGA; borderline ventricles; echogenic brain matter; cardiomegaly; hydrops	delivery at term; death at 1 month
20	24	VGA; overt ventriculomegaly; echogenic brain matter	termination of pregnancy
21	26	VGA; normal brain structures; no signs of hydrops	delivery at term; angiographic embolization at 1 year; normal IQ at 7 years

A detailed postnatal follow-up was obtained in each case. One of the cases herein described (Table 1, case 1) has been previously reported[11].

RESULTS

The relevant clinical data are reported in Tables 1–3 and described here in more detail.

Arachnoid cysts

In these cases (Table 1), the lesions were uniformly sonolucent, with thin regular walls and posterior sound enhancement. In some cases, demonstration that the lesion was external to the cerebrum and separate from the lateral ventricles was not obvious in standard axial views of the brain, and required meticulous scanning. The cysts were unilocar in all cases but two, in which a thin intracavitary septum was found (Figure 1). In five cases, the cyst was on the midline. In three of these fetuses, the cyst was in the anterior and/or mid-portion of the cerebrum, was associated with agenesis of the corpus callosum and was found to communicate with the cavity of the third ventricle (Figure 2). In the remaining two cases, the cyst was in the posterior third of the brain, and the corpus callosum was intact. In one fetus, a 5-mm cyst was found in association with multiple malformations and trisomy 18 (Figure 3). In another fetus, two small cysts (5 and 6 mm) were found in association with agenesis of the corpus callosum.

Pulsed Doppler ultrasound examination of the cerebral circulation was always unremarkable. The pulsatility index of the middle cerebral artery was well within the normal range of the chart established in our laboratory (unpublished data). Topography and size of the main cerebral arteries appeared normal in the five fetuses in which color

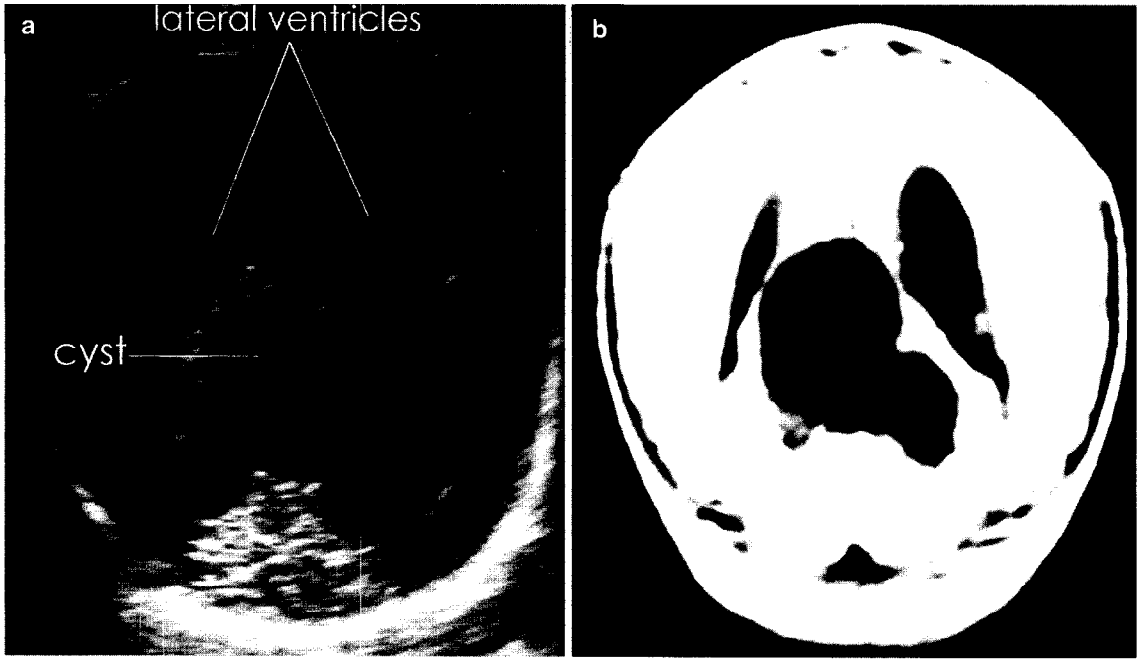

Figure 1 Case 5: coronal scan (a) of a midline arachnoid cyst obtained with transabdominal sonography, compared with the postnatal magnetic resonance image (b). A thin septum is seen within the cyst. It is of note that there was spontaneous regression of ventriculomegaly throughout gestation. The infant was asymptomatic at birth and no surgical treatment was performed

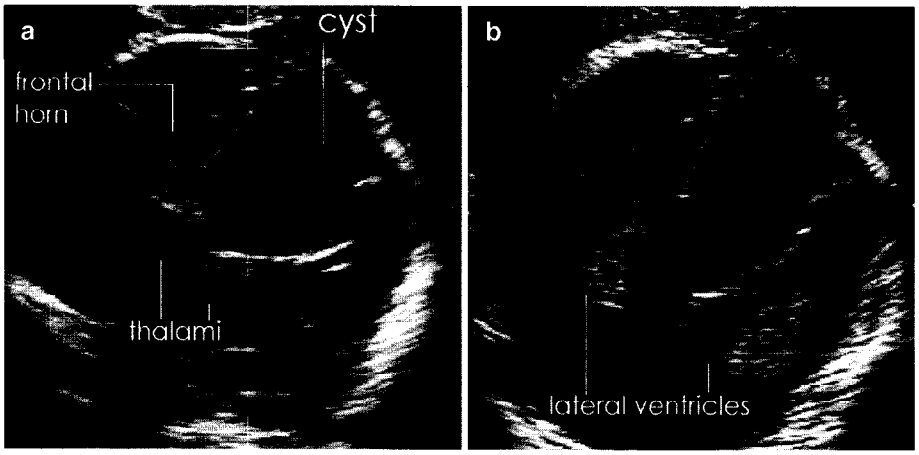

Figure 2 Case 3: anterior (a) and posterior (b) coronal scans obtained by transvaginal sonography, demonstrating a large arachnoid cyst of the midline. The cyst caused lateral dislocation of the cerebral hemispheres and was in continuity inferiorly with the third ventricle. The corpus callosum was obviously absent

Doppler was used – with the remarkable exception of cases with associated agenesis of the corpus callosum, which demonstrated abnormal branching of the anterior cerebral artery[11]. The diagnosis was made in the third trimester in three out of seven cases. All fetuses diagnosed late in pregnancy had undergone mid-trimester examinations, described as normal. In two such cases, satisfactory images of the brain were available, and were found to be unremarkable. Large cysts were always associated with enlargement of the ventricles described as borderline to overt. Two pregnancies with associated anomalies (one trisomy 18, one agenesis of the corpus callosum) were terminated upon request of the couples. The other five fetuses were delivered at term. In three out of four fetuses with large cysts, the lesion was found to increase in size with gestation. The neonates had signs of intracranial hypertension and a cyst–peritoneal shunt was implanted in the first weeks of life. In the remaining case, the lesion was stable and indeed the ventricles diminished spontaneously in size throughout gestation (Figure 1); intervention was not deemed necessary at birth. All these infants are alive and well, and are developing normally at the long-term follow-up. One infant with bilateral small cysts in the ambient cisterns and associated agenesis of the corpus callosum is developmentally retarded at 4 years and has seizures. The antenatal diagnosis of arachnoid cysts was confirmed postnatally in all cases.

Confirmation was based upon dissection of the abortive specimens or upon diagnostic imaging in the surviving infants.

Porencephaly

Porencephaly was diagnosed antenatally in ten cases by demonstrating hypoechoic lesions internal to the brain mass (Table 2). A communication with the cavity of the lateral ventricles was present in nine cases. In six cases, the lesions were unilateral, had an irregular shape with a jagged contour and were associated with absence of a significant portion of the relative cerebral hemisphere, severe hydrocephalus and macrocrania (Figure 4). In two of these cases, echogenic images suggestive of blood clots were found within the cyst (Figure 5). In one of these cases, alloimmune thrombocytopenia was diagnosed after birth (Figure 5). In two cases, porencephalic cysts occurred in the context of twin–twin transfusion syndrome. In one hydropic recipient twin at 25 weeks, a large unilateral porencephalic cyst communicating with the cavity of the lateral ventricle was seen. In another case, enlargement of the subarachnoid spaces and lateral ventricles with multiple small cysts in the periventricular area were seen in the donor twin following the intrauterine death of the recipient (Figure 6). With the exception of the last two cases, in which autopsy was not possible, the diagnosis of porencephaly was always confirmed at birth. Two pregnancies were terminated, and there were two perinatal deaths. All survivors had severe hydrocephalus at birth, underwent shunting and have severe developmental retardation.

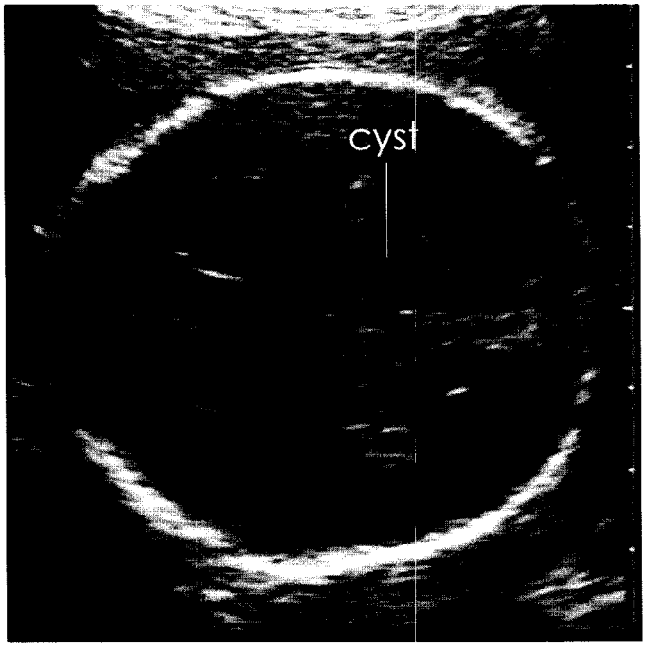

Figure 3 Case 6: transabdominal scan, demonstrating a small cyst in the ambient cistern of a mid-trimester fetus with trisomy 18

In three cases, ultrasound revealed clefts involving the parietal and/or temporal lobes, with a smooth contour (unilateral in one case, bilateral and symmetric in two cases), in association with absence of the septum pellucidum (Figure 7). These findings prompted the diagnosis of schizencephaly[2,12]. Of these fetuses, only one survived, and this one is profoundly retarded at the time of writing.

In two fetuses with encephaloclastic porencephaly, pulsed Doppler studies revealed a similar aberrant finding: the middle cerebral artery supplying the porencephalic hemisphere demonstrated absent or reversed end-diastolic velocities, compared with a normal waveform in the

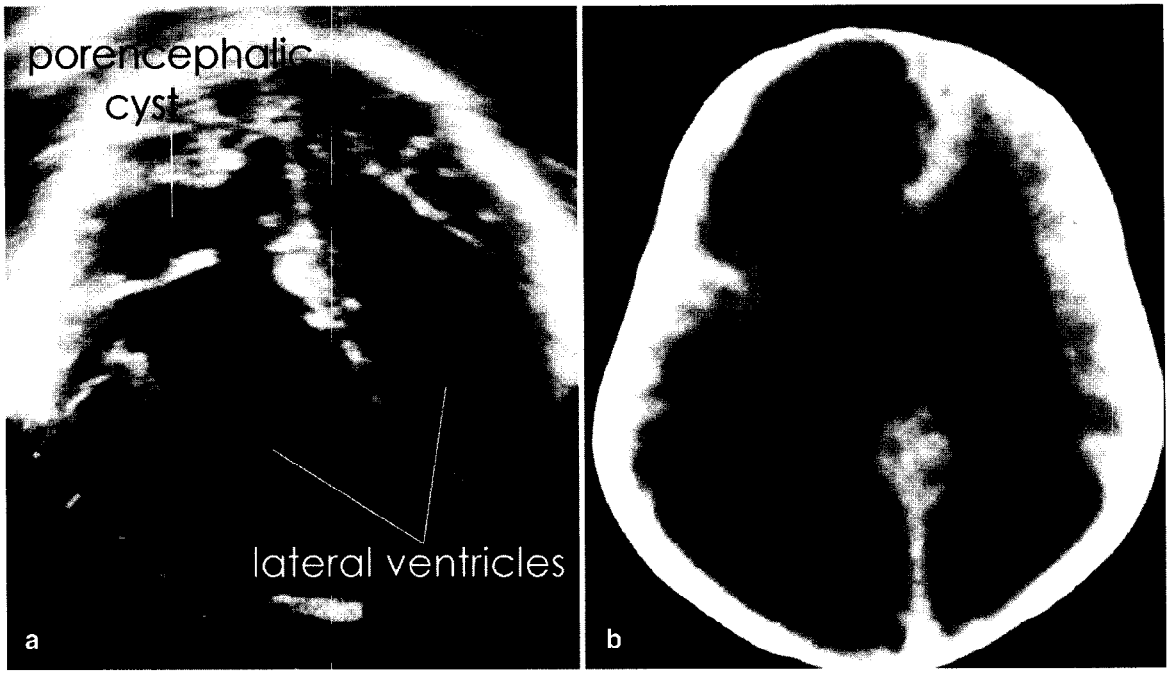

Figure 4 Case 9: in this fetus with asymmetric hydrocephalus, a large cyst with irregular walls, amply communicating with the cavity of one lateral ventricle, suggests encephaloclastic porencephaly. The antenatal scan (a), obtained transabdominally, is compared with an early postnatal computed tomographic image (b)

contralateral vessel (Figure 8). In one fetus with schizencephaly, color Doppler failed to demonstrate the middle cerebral artery supplying the affected portion of the brain.

Aneurysm of the vein of Galen

All these cases (Table 3) had in common the presence of an elongated fluid-filled area in the posterior third of the midline. Similarly to previously reported cases[9,10] pulsatile blood flow was rapidly demonstrated by color and/or pulsed wave Doppler ultrasound (Figure 9). In three cases, the lesion was associated with significant ventriculomegaly, and an increased echogenicity of the brain matter, thought to represent edema. In one of these fetuses, cardiomegaly and hydrops were also present. In one case, termination of pregnancy was performed. In the other two, early infantile death occurred. An infant with a relatively small lesion, and otherwise normal brain structures (Figure 10) was the only survivor. He was successfully treated by angiographic embolization and is doing well at the age of 7 years.

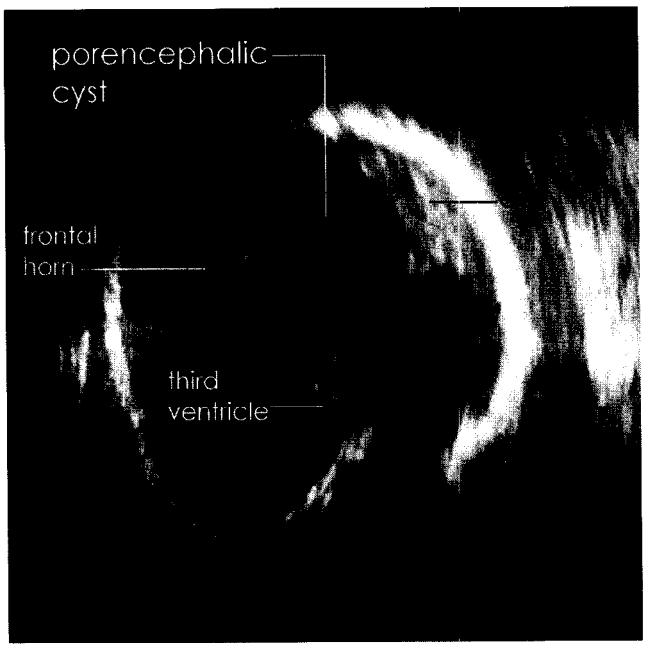

Figure 5 Case 11: a large porencephalic cyst is seen in this coronal plane obtained by transabdominal scanning. Most of one hemisphere is replaced by fluid. The cyst is in ample communication with both the contralateral lateral ventricle and with the inferior third ventricle. A gravity-dependent blood clot is seen within the cyst

DISCUSSION

The sonographic finding of an intracranial hypoechoic lesion is shared by three entities[1]. Arachnoid cysts are fluid-filled cavities lined completely or partially by the arachnoid membrane. It has been postulated that they derive either from an abnormality of the development of the meninges or from exogenous events such as infection or hemorrhage. The most frequent location includes the surface of the hemispheres in the area of the major fissures (sylvian, rolandic and interhemispheric). The outcome is most frequently favorable, although neurosurgery is frequently required[13,14].

Porencephaly (also referred to as encephaloclastic porencephaly or pseudoporencephaly) consists of cerebral cavitations that frequently communicate with the ventricular system[3,7]. It usually derives from local destruction and reabsorption of brain tissue as a consequence of infection, ischemia or hemorrhage. Porencephaly is frequently found in twins, particularly in the context of monochorionic placentation. The pathogenetic mechanisms are probably

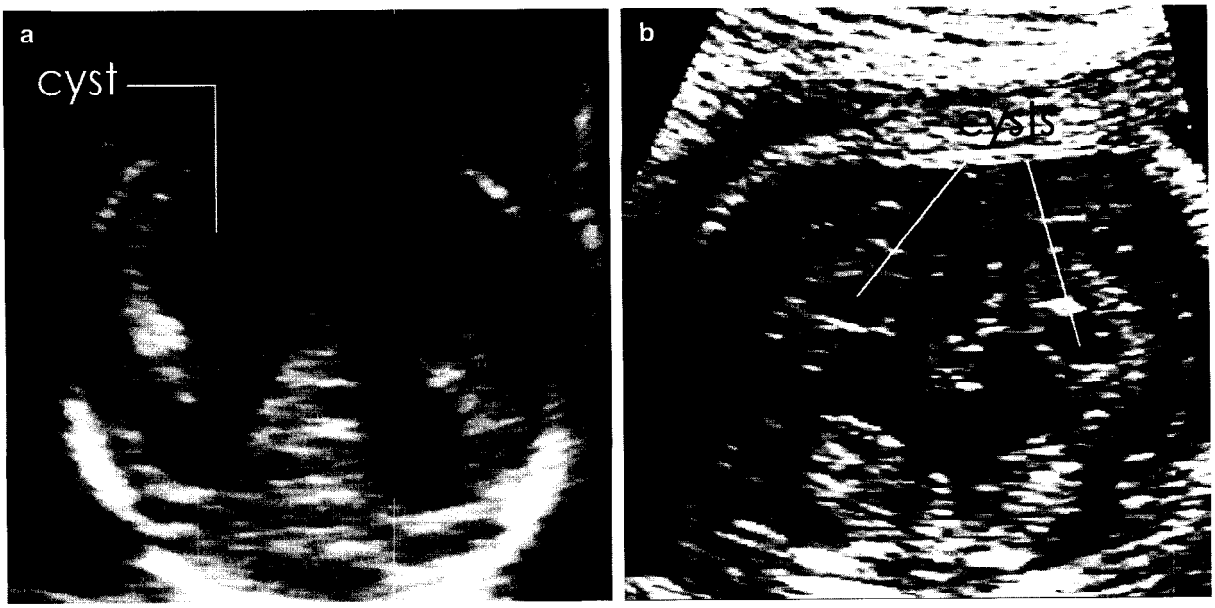

Figure 6 Porencephalic cysts in twin–twin transfusion syndrome. (a) Coronal view of the brain of a hydropic recipient twin (case 13). A large porencephalic cyst communicating with the cavity of one frontal horn is seen. (b) Multiple brain cavitations in the periventricular white matter, separate from the cavity of the lateral ventricles, in a donor fetus, following demise of the recipient co-twin. Enlargement of the lateral ventricles and of subarachnoid spaces is also seen (case 14)

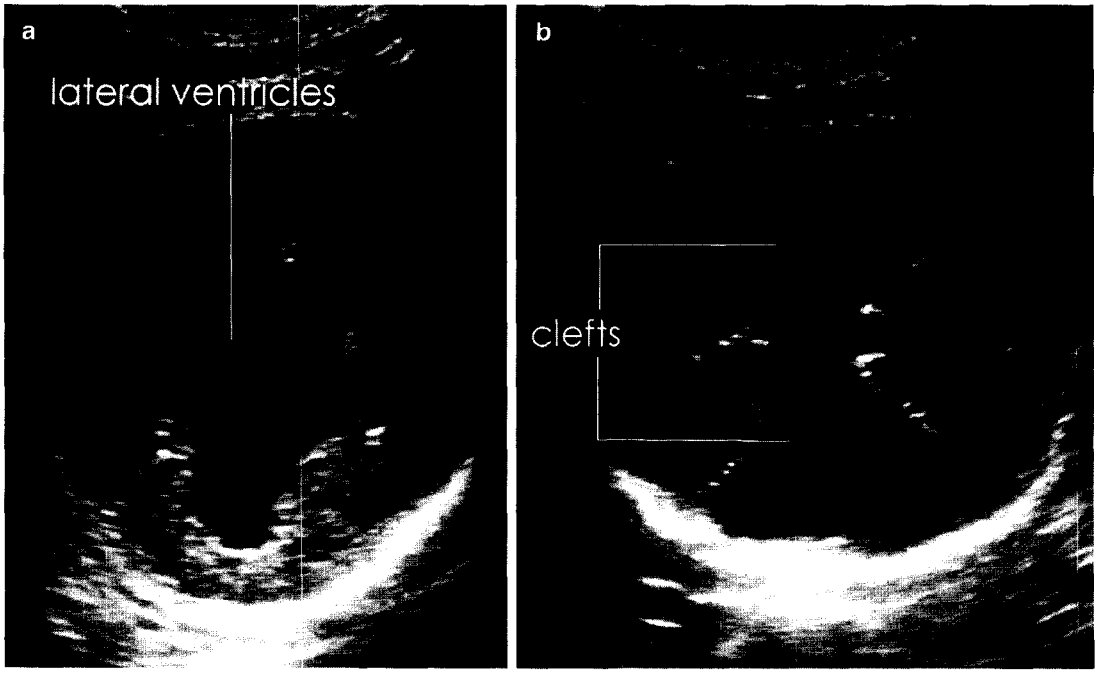

Figure 7 Case 15: schizencephaly. (a) The lateral ventricles communicate with each other because of the absence of the septum pellucidum. At a slightly lower level (b), bilateral and symmetrical clefts involving the parietal and temporal lobes are demonstrated

Figure 8 Case 10: pulsed Doppler ultrasound reveals an abnormal waveform, with reversed diastolic velocities, into the middle cerebral artery supplying the porencephalic hemisphere. The controlateral artery had normal velocimetry

heterogeneous, and the interested reader is referred to specific publications on this subject[15–17].

Schizencephaly or true porencephaly is a rare variant of porencephaly, characterized by loss of brain tissue, most frequently at the level of the parietal and temporal lobes, resulting in typical clefts of the cerebrum[2,12].

The prognosis for porencephaly is heterogeneous. However, extensive lesions tend to be associated with a poor outcome[7,12]. In our experience, all cases had a dismal outcome. We speculate that most small porencephalic cysts will go undetected *in utero*, and that antenatal diagnosis will probably be made only in the presence of large lesions, associated with other abnormal findings, such as hydrocephalus, macrocrania or microcephaly.

Vein of Galen aneurysm is a complex vascular malformation. At times, the alteration of cerebral hemodynamics can result in abnormal brain perfusion, with edema and ventriculomegaly. High-output cardiac failure can develop,

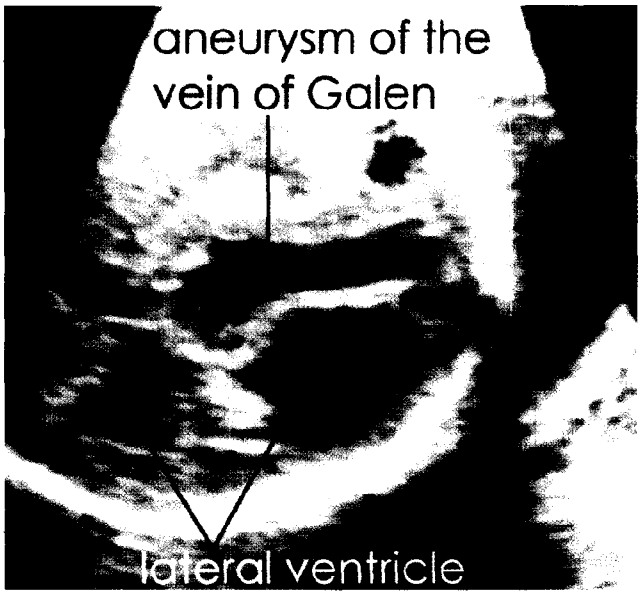

Figure 9 Case 20: aneurysm of the vein of Galen is an obvious diagnosis from color Doppler ultrasound. The lateral ventricles are enlarged. The increased echogenicity of the white matter is thought to represent brain edema

resulting in hydrops and perinatal death. However, in some cases, the lesion is well tolerated[9].

Our study indicates that current sonographic techniques are accurate in the differentiation of fetal intracranial hypoechoic lesions. A lesion that is external to the brain matter and has no evidence of blood flow is compatible with an arachnoid cyst. In our study, the interhemispheric fissure was a favored site for arachnoid cysts. Cysts in the Sylvian fossa, or in the cisterna magna, have been described

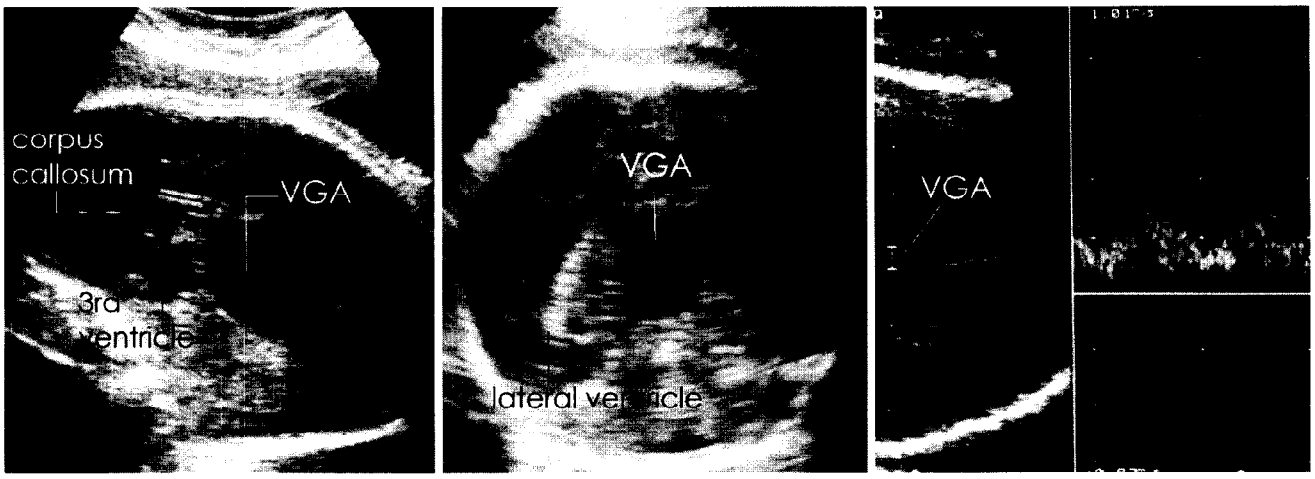

Figure 10 Case 21: in this fetus, sagittal and coronal scans reveal a cystic lesion at the level of the cistern of the vein of Galen. The diagnosis of aneurysm is confirmed by the pulsed Doppler demonstration of pulsatile blood flow within the lesion. The remaining intracranial anatomy appears unremarkable

in other reports[1,13,14]. One fetus with a glioependymal intracranial cyst has recently been reported[18]. The lesion had a sonographic appearance identical to that of an arachnoid cyst. Glioependymal cysts are very rare entities when compared to arachnoid cysts, as only a handful of cases have been described thus far. It is important to stress that our cases lack histological confirmation, and therefore we cannot rule out the possibility that some of our cysts were of glioependymal origin. Indeed, descriptions of infants affected by this condition[19] seem to fit our cases with midline cysts communicating with the third ventricle, and associated with absence of the corpus callosum (Table 1, cases 1–3, Figure 2). At present, it is uncertain whether glioependymal cysts have different prognostic implications from those of arachnoid cysts.

Lesions internal to the brain mass without evidence of blood flow are indicative of porencephaly. In the encephaloclastic variety, additional findings include a jagged contour of the cyst, and the occasional presence of images suggestive of blood clots. In schizencephaly, typical full-thickness clefts of the hemispheres are found. Communication of the cyst with the cavity of the lateral ventricles is a useful clue to the diagnosis, and was present in most of our cases. In one fetus, we were able to recognize porencephalic cysts separate from the lateral ventricles. We are unaware of previous reports of similar cases. As such cavitations tend to be small, we speculate that the diagnosis will be difficult in most cases.

Midline intracranial hypoechoic lesions with Doppler evidence of blood flow are consistent with vein of Galen aneurysm. In most of our cases, alterations of cerebral architecture – including increased echogenicity of brain tissue, presumably due to edema – and ventriculomegaly were documented. However, in at least one case, only Doppler ultrasound allowed a clear-cut distinction from an arachnoid cyst.

Doppler ultrasound was essential for identifying vein of Galen aneurysm, but it provided valuable information in the other cases as well. In encephaloclastic porencephaly, increased pulsatility of the cerebral vessels was noted, suggesting an increase in the peripheral resistances in the vascular tree supplying the affected area. In one case of schizencephaly, the artery supplying the damaged portion of the brain could not be imaged. Both findings are consistent with the well-established vascular pathogenesis of these conditions[7,12]. In all cases of arachnoid cysts, velocimetry of the cerebral circulation was unremarkable, even when significant ventriculomegaly was present.

An algorithm for the prenatal and perinatal management of cases with vein of Galen aneurysm has recently been developed[9]. The diagnostic workup and the management of fetuses with other types of hypoechoic lesions are uncertain. Fetal arachnoid cysts are most frequently isolated, but have occasionally been reported in association with other anomalies. In our series, four fetuses had agenesis of the corpus callosum and one had trisomy 18. At present, therefore, we feel that a targeted examination of the entire fetal anatomy and karyotyping should be offered.

To the best of our knowledge, neither encephaloclastic porencephaly nor schizencephaly have been reported in association with other anatomical or chromosomal anomalies. Encephaloclastic porencephaly, particularly in those cases in which the lesion communicates with the lateral ventricles, is probably the final result of cerebral intraparenchymal hemorrhage. MRI has been successfully used to demonstrate fetal intracranial hemorrhage[4], and fetal blood sampling has been proposed for indirect confirmation, by demonstrating anemia[5]. Fetal blood sampling has also been used to confirm alloimmune thrombocytopenia, a well-established cause of antenatal brain hemorrhage[20]. The clinical relevance of such information in the context of a fetal porencephalic cyst is uncertain. However, the diagnosis of alloimmune thrombocytopenia would be important for counselling the couples and managing the following pregnancies. Infection was never found in our series, but it is a well-established cause of porencephaly[21], and we believe, therefore, that the diagnostic workup of such cases should include laboratory tests for at least cytomegalovirus and toxoplasmosis.

The natural history of congenital intracranial hypoechoic lesions is scarcely known. Most of these lesions (arachnoid cysts and encephaloclastic porencephaly, in particular) are presumed to develop throughout gestation. Our experience confirms that these entities usually go undetected in the mid-trimester.

In conclusion, our study indicates that current sonography allows an accurate differential diagnosis of fetal intracranial hypoechoic lesions. However, multiplanar imaging of the fetal brain was essential in many cases. Pulsed and color Doppler ultrasound provided useful additional information. The clinical value of other investigations, such as MRI and/or fetal blood sampling, remains unproven.

We acknowledge that our study has several limitations, the most important being the relatively limited number of cases. The capability of ultrasound to recognize rare entities, such as cystic tumors, remains untested.

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