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Fetal hydrocephalus

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Abstract
Introduction Hydrocephalus is the most frequent and devastating illness affecting a fetus. The development of both ultrasonography and magnetic resonance, associated with laboratorial tests, has greatly facilitated its diagnosis.
Materials and methods In the Fetal Medicine Service of the Federal University of São Paulo and in the Santa Joana/Pro-Matre Paulista Hospital Complex, in São Paulo, SP, Brazil, repeated cephalocenteses, ventricular-amniotic shunting, and neuroendoscopy were used to treat 57 fetuses with hydrocephalus, all of them at a gestational age under 32 weeks. Another eight fetuses had myelomeningocele and underwent correctional open surgery to prevent hydrocephalus.
Results Thirty-nine patients were followed up for a period longer than 3 years and had their intelligence coefficient assessed: 26 of them were considered normal (IQ above 70); six had mild or moderate handicaps (IQ from 35 to 70), and seven were severely handicapped (IQ below 35). Out of the eight patients operated for correction of myelomeningocele, only two came to require shunting. There were no cases of maternal morbidity, and no infectious condition was observed in any of the patients subjected to intrauterine treatment.
Conclusion Selected cases of isolated, evolutive, non-destructive hydrocephaly diagnosed before 32 gestational weeks may benefit from fetal neurosurgical procedures. With the accuracy improvement of diagnoses, the number of patients fitting into that group has become very small.

Keywords Fetal hydrocephalus · Cephalocentesis · Ventriculo-amniotic shunting · Neuroendoscopy · Myelomeningocele · Viral infection

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Introduction

With the recent technological development, especially as far as diagnosis is concerned, fetal medicine has been privileged with the evolution of ultrasonography (US), the complementation of ultrasound with magnetic resonance imaging (MRI), and a huge evolvement of laboratory tests: Safe diagnosing is assured for central nervous system diseases, including genetic, malformative, and infectious processes affecting the fetus. The use of MRI with T2-weighted sequence is most satisfactory, as it is too fast to be affected by the fetal movements and allows a perfectly accurate observation mainly of the posterior fossa structures such as the brainstem and the cerebellum, thus increasing diagnostic possibilities. Small hemorrhages formerly not visualized by ultrasonography can now be more easily detected by fetal MRI [4, 17, 24, 26, 27, 32].

Fetal hydrocephalus is a serious malformation, which, behind a ventriculomegaly, hides a large number of different defects, each one of them with a different evolution, depending on the type of disease that has given cause to the hydrocephaly [29]. The fetal moment, characterized as the period during which the fetus suffers the insult culminating in hydrocephalus, is also one of the most important factors to consider when establishing a prenatal prognostic. Fetal hydrocephalies beginning in the last trimester of gestation

have a much more satisfactory evolution that those diagnosed at the beginning of gestation. Experimental studies in animal models have demonstrated that the more precocious is the treatment for fetal hydrocephalus, the more it is effective. This type of result is not verified in the daily clinical practice due to the large variety of diseases a fetus is subject to. In the case of malformative hydrocephalus, many patients present with multiple associated malformations, which compromise a good outcome [12, 14, 18, 36].

The real incidence of fetal hydrocephalus is probably underestimated because many cases of fetal death at the beginning of gestation are often discarded without being studied. In fact, it is not even known how often abortions are performed among mothers of hydrocephalic fetuses. It is believed that the incidence rate of such cases varies between 0.2 and 1 per 1,000 live births. The predisposition is larger for fetuses of the male sex, and primigest women are more prone to this problem [3, 10, 11, 28, 31, 36].

The big difference between a hydrocephalic fetus and a hydrocephalic neonate is that, in the former case, it is the mother–fetus binomial that is involved. No matter what procedure should be performed, it is the mother that should be taken into consideration. From the simple natural childbirth to the most complex prenatal neurosurgical procedures, whenever hydrocephaly is to be treated during the fetal period, the mother will have to face some kind of risk involving ethical, religious, and socio-economical problems that normally do not exist for the newborn infant.

Another essential factor concerns prematurity: The decision to induce labor and treat the hydrocephalus cannot be complicated with prematurity problems. It is up to the neurosurgeon to choose the best moment for delivery, considering both the hydrocephalus degree and the risks of prematurity. The best overall results in fetal surgery have been those obtained in cases of acute obstructive hydrocephalus having developed no earlier than the third trimester of gestation and were not associated with any other malformation [9]. Knowledge about both diagnosis and treatment of this serious type of hydrocephalus can be still improved in health centers specialized in fetal medicine.

Materials and methods

In the period from January 1986, when our first fetal surgery was performed, to May 2011, 221 fetuses presenting with ventriculomegaly were attended to in the Pediatric Neurosurgery and Fetal Medicine Departments of the Federal University of São Paulo and Santa Joana/Promatre Paulista Complex. Fetuses with severe associated anomalies, such as holoprosencephaly, lissencephaly, and porencephalic cysts, have not been included in the present study. Thirty-nine fetuses had presented with a mild ventriculomegaly, and the follow-up during their first year of life showed that they did not need ventricular shunts. In 56 of those 221 fetuses, hydrocephaly was evaluated after 32 gestational weeks, and their birth was advanced to allow for postnatal treatment.

Forty-seven fetuses who had evolutive hydrocephalus associated with other malformations were not treated in utero*:* In 18 of them, the hydrocephalus was due to severe infection; 12 had a Galen's vein aneurysm (Fig. 1); and seven were twin gestations (Fig. 2). Seventy-nine had evolutive hydrocephalus and required some kind of antenatal treatment. Sixteen fetuses underwent either transabdominal cephalocentesis (14 cases) or transvaginal cephalocentesis (two cases) because they had not only ventriculomegaly but also macrocrania. These 16 cases,

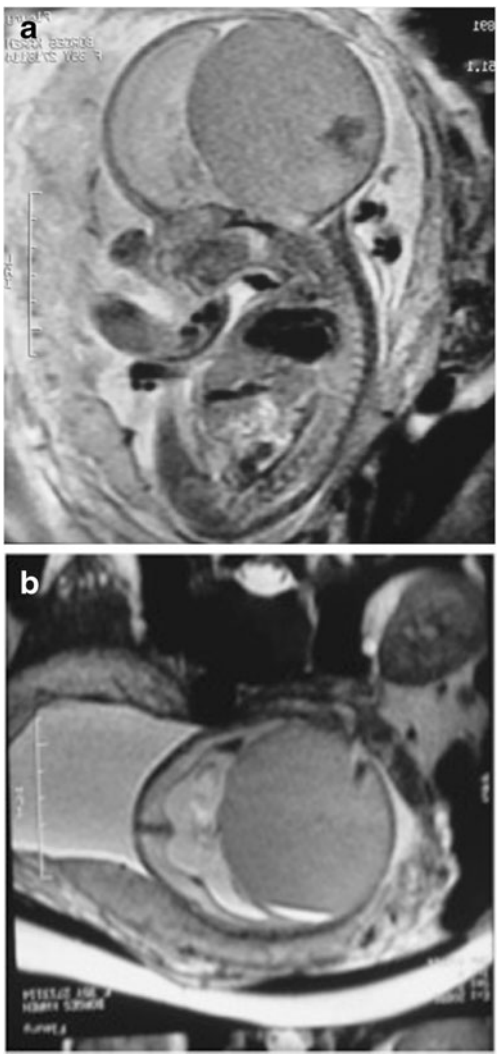

Fig. 1 **a** Fetal MRI at 26 gestational weeks showing a giant aneurysm of Galen's vein with cardiomegaly. **b** Axial MRI showing occupation of more than half the cranial cavity by the aneurysm

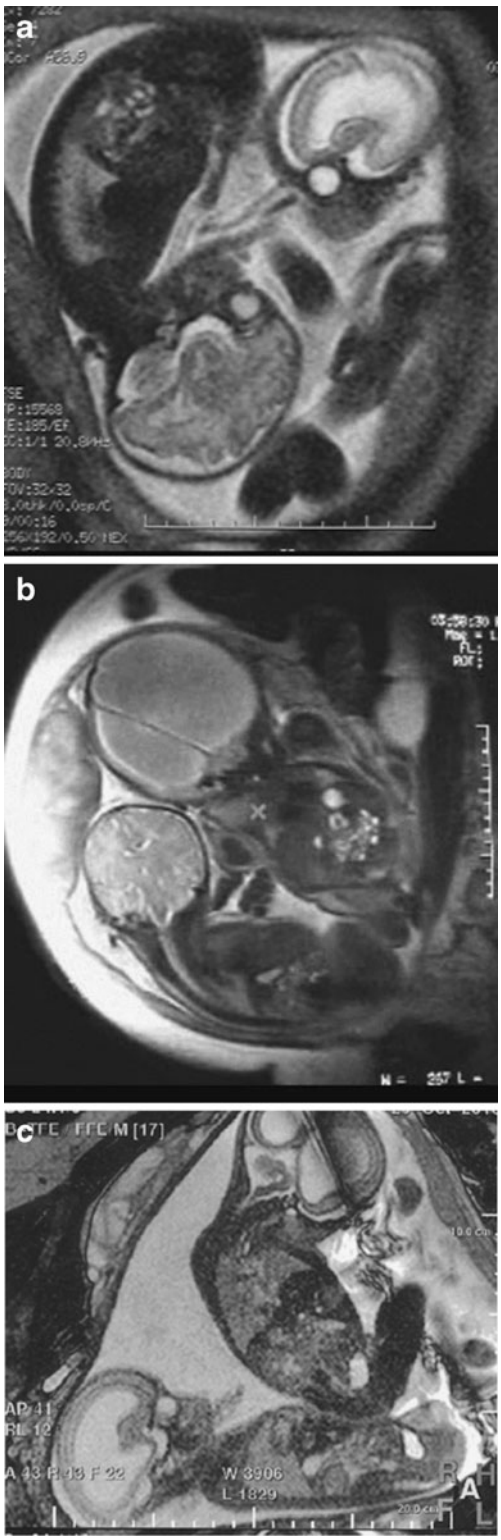

Fig. 2 **a** Fetal MRI evidencing a 27-week twin gestation. The hydrocephalic fetus's head is smaller than his brother's, an evidence that in this case the hydrocephalus is not hypertensive but destructive. **b** Twin gestation at 34 weeks . The hydrocephalic fetus presents with macrocrania—an evidence of obstructive hydrocephalus due to Chiari type II malformation. It was necessary to remove 300 ml of liquor at the moment of delivery (by cesarean section) in order to facilitate the extraction of the cephalic pole. **c** Twin pregnancy, both fetuses presenting with hydrocephalus and macrocrania due to stenosis of the Sylvian aqueduct due to ependymitis by coxsackievirus infection

however, were excluded from our study because the procedure had been performed only to facilitate the delivery. After that period, the chosen procedure was administration of corticoids to the mother, followed by preterm surgical delivery, and only fetuses having presented with evolutive hydrocephaly without any associated malformation were analysed and treated before the 32nd gestational week.

Six of the fetuses presented with hydrocephalus associated with brain tumors and underwent repeated cephalocenteses until they acquired lung maturity. These were also excluded from the global evolutive analysis since the evolution in those cases was associated with the tumor.

Fifty-seven fetuses with evolutive hydrocephaly, whose gestational ages were between 24 and 32 weeks, were analyzed and subjected to fetal neurosurgical procedures: 26 underwent repeated cephalocenteses; three underwent endoscopic third ventriculostomy (which was possible in only one of them—for the other two, the procedure had to be changed into ventriculo-amniotic shunting). Thirty fetuses received ventriculo-amniotic shunting; eight fetuses presenting with myelomeningocele were subjected to intrauterine treatment so that the myelomeningoceles could be corrected before 26 weeks of gestation—these cases were not included in the statistics either because surgery was then aimed at the reversal of Chiari II and prevention of hydrocephaly [2].

The repeated cephalocenteses were guided by ultrasound. The mother was sedated with opiates. The volume of liquor removed varied from 20 to 120 ml. The fetal heart beat was monitored throughout the procedure, and removal of liquor would be discontinued as soon as any deceleration should occur in the fetal heart rate.

Ventriculo-amniotic shunting was performed percutaneously, under ultrasound guidance, and a pigtail catheter (KCH-Rocket Medical PLC, New England) was inserted. One tip of the catheter was left in the fetal lateral ventricle and the other in the amniotic cavity (Fig. 3). Third ventriculostomy was performed under fetal anesthesia. With a thin needle, always under ultrasound guidance, the umbilical cord was punctured; the umbilical vein was catheterized, and a total dose of 5 μg/kg of fentanyl citrate and 0.1 mg/kg pancuronium bromide was injected. Five minutes after fetal anesthesia, a small incision was made in the mother's abdominal skin with an 11-blade scalpel, With a 2.5-mm-diameter needle, always under ultrasound guidance, the fetal skull was punctured on the brim of the bregmatic fontanelle, and the lateral ventricle could be

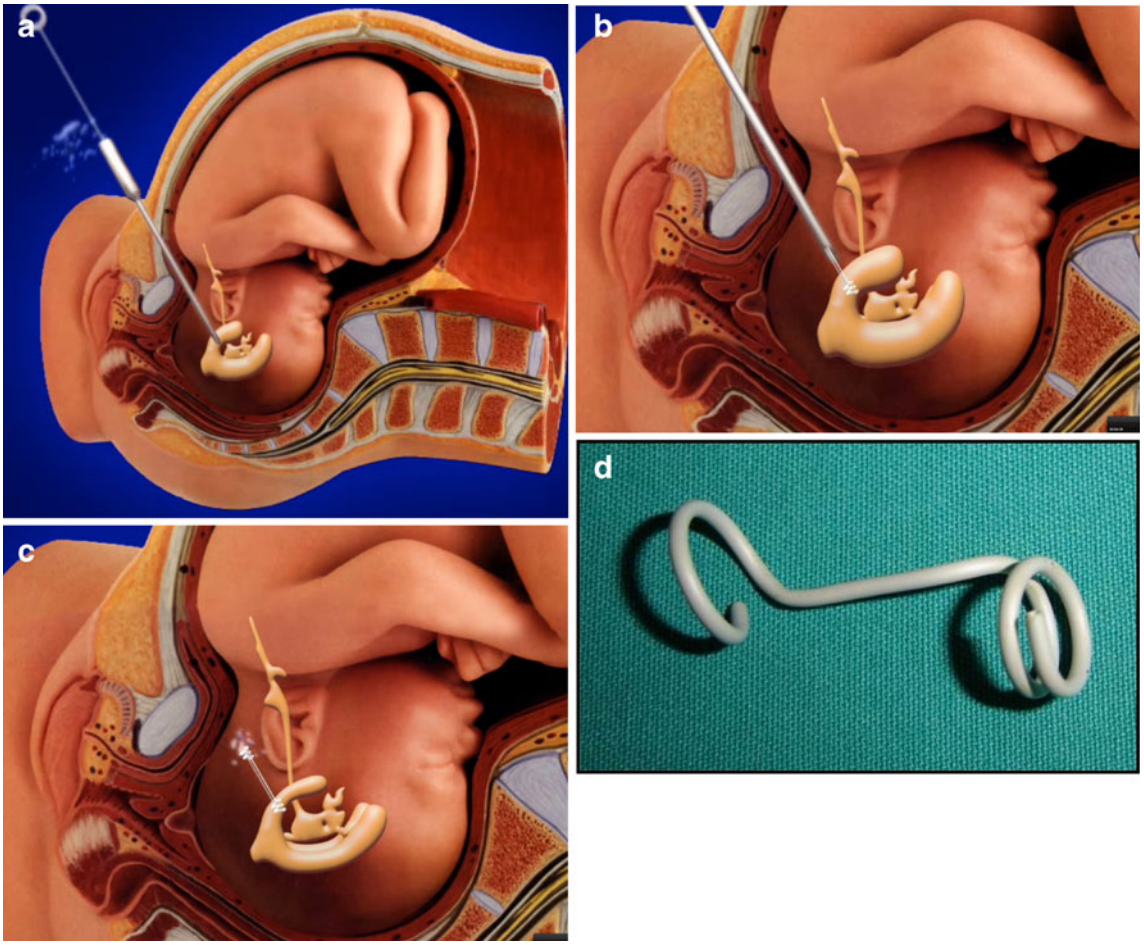

Fig. 3 Scheme of ventriculo-amniotic shunt placement. **a** Ultrasound-guided transabdominal puncture reaching the occipital horn of the lateral ventricle. **b** Catheter insertion and intraventricular portion released after partial removal of the trocar. **c** Complete removal of the trocar, so as to release the catheter in the amniotic cavity and decreased hidrocephaly. **d** View of the double pigtail catheter in good position—one tip in the ventricular cavity and the other in the amniotic cavity

accessed. As soon as the mandrel was withdrawn, liquor came out with increased pressure. A 2.3-mm-diameter neuroendoscope (Neuroview, flexible scope, 25C, Traatek, USA) was inserted through the needle, as well as a 1-mm working channel connected to a 300-W xenon lighting system. The Monro's foramen could be identified and the endoscope was inserted into the third ventricle—its floor was opened, and the fetal basilar artery could be visualized. The opening was sufficiently enlarged with a 2-Fr Fogarty catheter, and the endoscope was withdrawn along with the needle. A small occlusive dressing was applied to the mother's abdomen.

Results

Out of the 57 fetuses treated in utero, 26 underwent repeated cephalocenteses. Thirty fetuses were subjected to ventriculo-amniotic shunting (Fig. 4). Five fetuses underwent two procedures due to migration or obstruction of the shunting system. In ten cases, the shunt migrated to the uterine cavity, and in six cases, it migrated to the ventricular cavity. In the cases where the catheter had migrated to the ventricular cavity (Fig. 5), it was removed after birth by means of a neuroendoscopic procedure followed by third ventriculostomy. After birth, the ventriculo-amniotic shunts were removed, and the newborn infants underwent either ventriculo-peritoneal shunting or endoscopic third ventriculostomy.

No porencephalic cysts were observed in the patients subjected to repeated cephalocenteses. The number of punctures varied from two to five. The deliveries took place after lung maturity had been evidenced. Preterm labor occurred in four cases after cephalocentesis.

Endoscopic third ventriculostomy was attempted in three fetuses, but due to technical and anatomical problems, it could only be achieved in one of them.

Eight patients presenting with myelomeningocele were subjected to open surgery for intrauterine correction of this defect. Out of these eight operated cases, only two came to

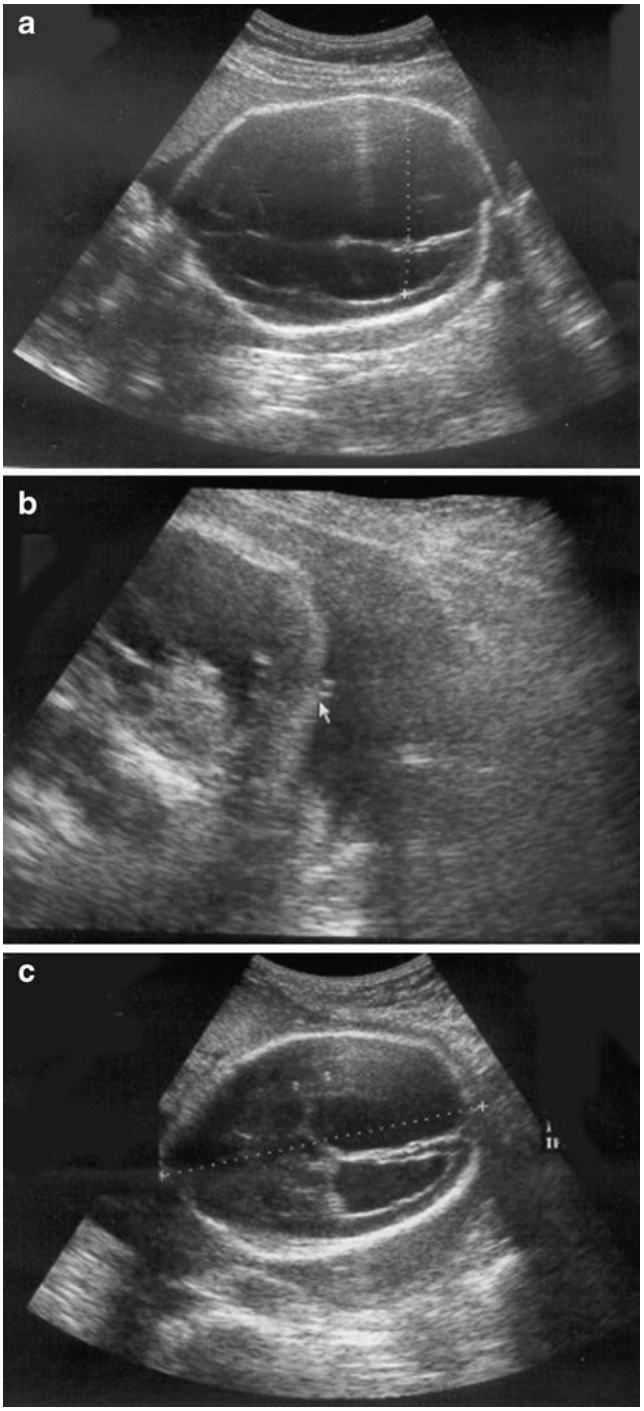

Fig. 4 **a** Twenty-six-week gestation, ultrasound imaging showing voluminous ventriculomegaly. **b** Ventriculo-amniotic shunt placement (*arrow*). **c** Second postoperative day, decreased ventricular cavity

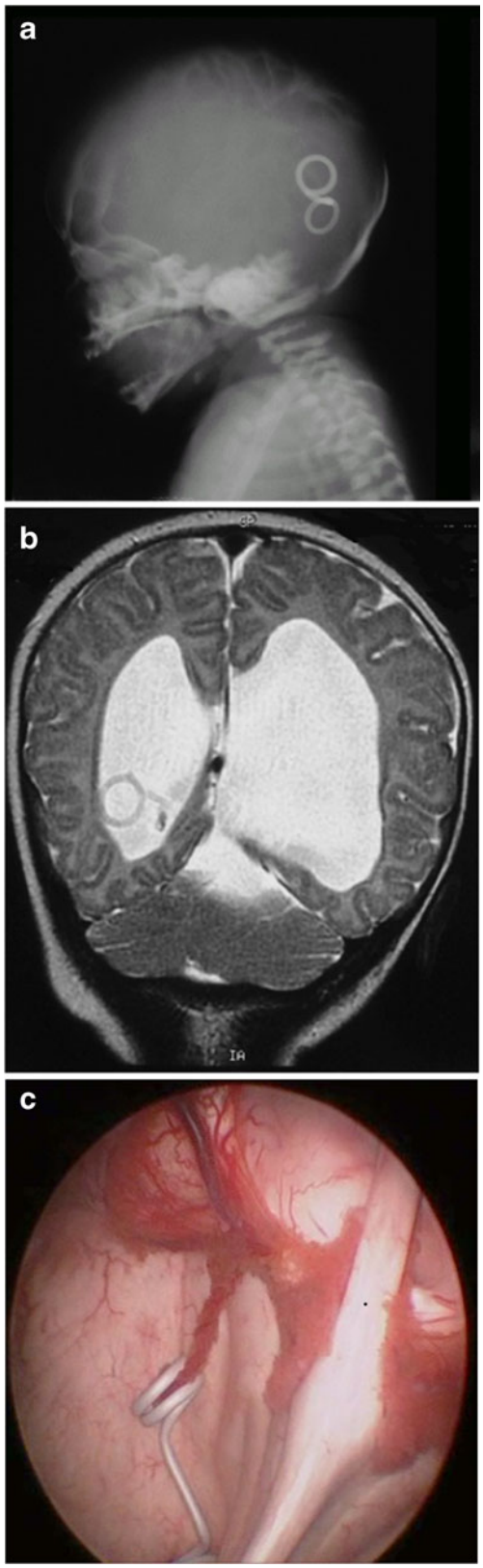

Fig. 5 **a** Skull X-ray showing presence of intracranial catheter. **b** MRI of a neonate showing the presence of an intraventricular catheter close to the choroid plexus. **c** Intraoperative endoscopic view of a catheter adhering to the choroid plexus

require ventriculo-peritoneal shunting in the postnatal period. In most of cases, reversal of Chiari II malformation and disappearance of the hydrocephalus were observed (Fig. 6).

The patient subjected to endoscopic third ventriculostomy did not require ventriculo-peritoneal shunting, but he was lost to follow-up 1 year later. The ventriculo-peritoneal system

inserted after birth in all the cases was a low-pressure-type Pudens (Codman's Accuo-Fluo) without the reservoir and the 4–5 cm right-angle ventricular catheter.

Eighteen patients were subjected to endoscopic third ventriculostomy after birth. In 11 of these cases, no shunting was required.

Thirty-nine patients were followed up for more than 3 years and had their intelligence coefficients assessed, with the following results: 26 were considered normal (IQ above 70); six had mild or moderate handicaps (IQ between 35 and 70); and seven were severely handicapped (IQ below 35). The best results were obtained in those cases where hydrocephaly had been diagnosed in a later period (third gestational trimester), upon acute installation after small intraventricular hemorrhages, which sometimes followed maternal trauma or acute infection by coxsackievirus. No porencephalic cysts were observed in the patients subjected to repeated cephalocenteses.

Among the cases of postnatal shunting, only one infection occurred, caused by Enterobacter, in the third month after insertion. No chemical (amniotic) ventriculites were observed in those patients who had undergone intrauterine procedures. No maternal morbidity was identified either during the puerperal period or in the long term.

Discussion

The term "fetal hydrocephalus" has been used in an overall manner in connection with any ventricular dilation diagnosed before birth.

When the ventricular atrium exceeds 10 mm at any gestational age, it is a case of ventriculomegaly. That is the standard measure adopted by most authors. In many instances of colpocephaly, however, there may be partial agenesia of the corpus callosum, and then, an increased

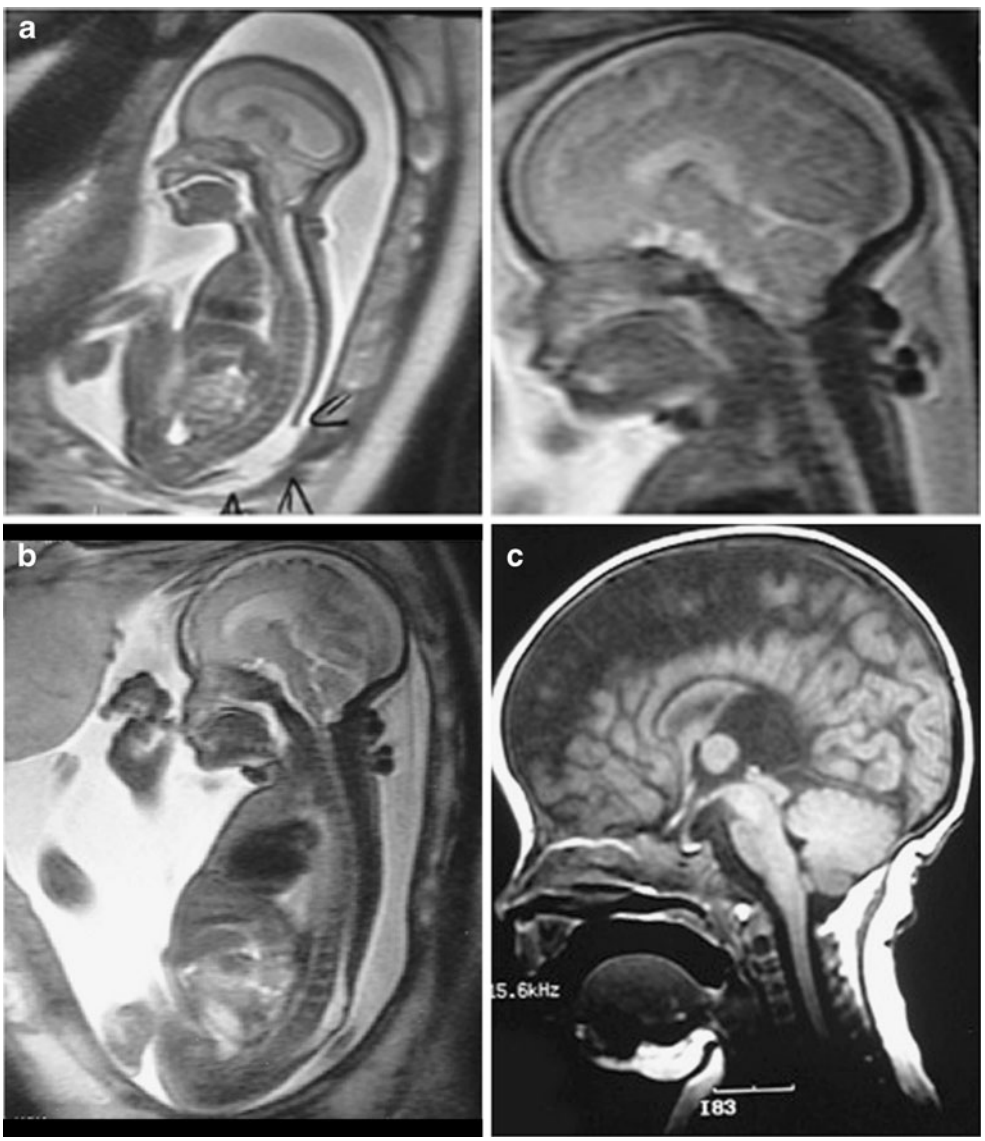

Fig. 6 **a** MRI at 25 weeks of gestation, showing a lumbar myelomeningocele, hydrocephalus and migration of cerebellar amygdalae into the cervical rachidian channel. **b** Fetal MRI 1 month postoperatively showing perfect closure of myelomeningocele—no more hydrocephalus and cerebellum in normal position. **c** MRI 2 months after delivery, showing partial agenesis of corpus callosum, interthalamic adhesion, and no more Chiari II

ventricular atrium will be encountered, though not in fact a hypertensive hydrocephalus. This type of alteration is often observed in cases of ventriculomegaly associated with myelomeningocele, ventricular dilations being then more prominent in the occipital horn of the lateral ventricle [30].

Due to this kind of terminology, the evolutive results under analysis are not in agreement with one another, and conclusions were different. That is why Garne et al. [21], in their analysis of 87 cases of fetal hydrocephalus over four European regions, have found a prevalence of 4.65 cases per 10,000 births. There were 41 live births (47%), four fetal deaths (5%), and 42 terminations of pregnancy because of fetal anomaly. In only 44% of the cases, there were no other anomalies associated. They have concluded that fetal hydrocephaly is a severe congenital malformation often associated with other congenital anomalies.

Futagi et al. [20], analyzing 38 cases of fetal hydrocephaly treated after birth, verified that only 21.1% of patients had an IQ above 84, and 65.7% had an IQ below 70. In that series, the analysis included 27 patients with holoprosencephaly, who should not have been classified under the generic term "hydrocephaly" because all holoprosencephalic subjects are known to have a lower IQ. The same occurs with regard to the cases of X-linked hydrocephalus, a disease that has retardation as a pathognomonic sign (Fig. 7) [5, 13, 16, 35, 37].

When such kinds of malformations are analyzed, both motor and intellectual developments are compromised, and it is to be concluded that no fetal procedures should be performed

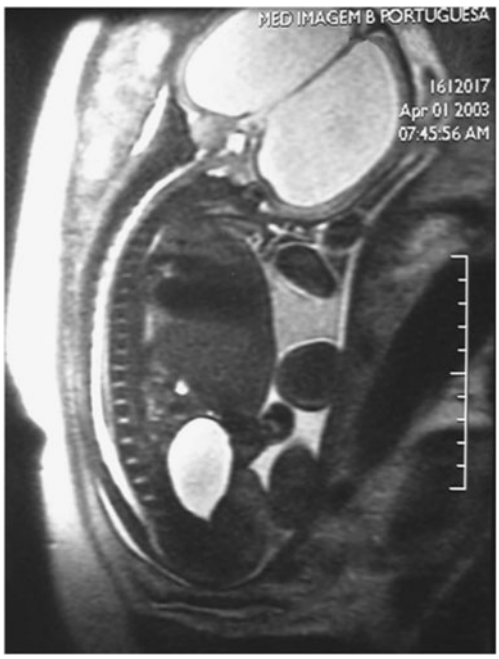

Fig. 7 Fetal MRI at 32 weeks of gestation showing huge hydrocephalus due to aqueduct stenosis by Adams Bricker syndrome (X-linked hydrocephalus—a family linkage)

for management of hydrocephaly in those cases. Concomitant use of ultrasound and fetal MRI has provided a better diagnostic accuracy concerning malformations of the central nervous system. Peruzzi et al. [34] have shown that 97% of all central nervous system malformations can be detected by MRI and US. As to a precise diagnosis, it is possible in 84% of cases, when MRI is used, and in 77% when only US is used. When cordocentesis followed by genetic and laboratorial testing of the fetal blood is used in addition to diagnostic imaging, the diagnosis accuracy is also improved.

From our series of 39 fetuses who had been treated in utero and whose IQ was later analyzed, 26 had an IQ above 70 (66.6%), but these were cases of evolutive ventriculomegaly; there had been acute installation, and in the best cases, intracranial hypertension had occurred. Cases with other associated anomalies were not treated. In fact, what is most difficult, really, is identifying the cases where evolutive fetal hydrocephalus is not associated with other malformations.

The efforts of a service specialized in fetal medicine should rely upon enough expertise to discern which are the cases that can benefit from intrauterine fetal procedures aiming at a better quality of life for the patient.

Cavalheiro et al. [9] have noticed a relationship between the results and the intracranial pressure measured at the moment of implantation of the valve: When intracranial pressure is higher, the results are then better than when the pressure is normal or lower than 20 mmHg. It is difficult, however, to quantify the normal intracranial pressure of a fetus.

Experimental studies inducing hydrocephaly into several animal species are unanimous in stating that precocious treatment of that disease is beneficial. Nonetheless, it is almost impossible to mimetize all the different associated malformations that may entail a worse prognosis.

Almeida (personal communication) observed that 100% of the fetuses whose mothers had small pox presented with hydrocephalus. Thus, the often devastating effect of viral infections was made clear: They may be responsible for fetal malformations and hydrocephalus. Infections by cytomegalovirus during the first gestational trimester usually cause destructive hydrocephalus and fetal malformation. Severe ependymitis can be observed and is usually associated with other symptoms of aqueduct stenosis, causing important ventriculomegalies. When infections do not cause aqueduct stenosis, ventriculomegaly occurs due to destruction of the encephalic parenchyma, and the measurements of the fetal intracranial pressure often result low. These are the cases we call destructive hydrocephalus, for the treatment of which intrauterine procedures are not indicated [23, 25].

The same features can be verified in the occurrence of other viral infections (rubella, chickenpox, and herpes simplex). Infections by the coxsackievirus have also frequently been detected, but in that event, hydrocephalus

has a more benign evolution, especially when viremia occurs in the third gestational trimester [33]. The most common clinical features are those of normal pregnancies, where possibly after several normal ultrasounds, one ultrasound exam reveals fetal hydrocephalus after the mother has felt some mild symptoms of a cold. These are cases of acute hydrocephalus, and no severe ependymitis is observed. The cause is a mild ependymitis sometimes associated with intraventricular hemorrhages, which provoke the hydrocephalus by blocking the Sylvian aqueduct. In these cases, earlier delivery and the performance of endoscopic thirdventriculostomy will permit an excellent evolution. If diagnosis is made before the 32nd gestational week, ventriculo-amniotic shunting is indicated, as it is a case of non-destructive hydrocephalus of acute installation.

Twin gestation

In face of a twin gestation in which both the fetuses present with hydrocephalus, the process is uniform, and both the fetuses can be treated within the same protocol. However, it is more common for only one of the twins to present with hydrocephalus. Termination is impracticable, and any fetal surgery procedure might mean a risk to the normal fetus.

Earlier delivery after confirmation of lung maturity becomes the choice procedure. When a twin gestation is carried to term and one of the fetuses presents with a voluminous macrocranium, cephalocentesis and removal of large quantities of liquor are indicated to ease the moment of childbirth. What is most remarkable in this picture is that sometimes only one of the fetuses is affected despite the infectious origin of the fetal hydrocephalus.

Fetal neurologic surgery

In 1981, Birnholz and Frigoletto [6, 19] described the performance of repeated cephalocenteses for the treatment of fetal hydrocephalus. Later, Clewel et al. [15] implemented the first ventriculo-amniotic shunting. Cavalheiro et al. [9]. described the first fetal third ventriculostomy in 2003. However, progress in the treatment of fetal hydrocephalus has been poor. The simple fact of reverting ventriculomegaly does not imply reversal of the devastating effects already caused by hydrocephalus and not even of those caused by the associated malformation.

Although diagnoses of fetal malformations have improved during the last few years, the same has not occurred with regard to surgical techniques for the treatment of hydrocephalus: There is nothing but cephalocenteses, which consist of multiple ventricular punctures for removal of liquor, and ventriculo-amniotic shunts, which provide a fast decrease of the ventricular cavity, but often migrate into either the ventricular or the uterine cavities.

There are not, as yet, drainage systems that can be placed percutaneously and fixed on the skin of the fetus that might be performed with open surgery. Fetal neuroendoscopy is feasible but technically very difficult because the fetus is seldom in a position that permits the surgeon to reach the Kocher's point and achieve the procedure. Neuroendoscopies in fetuses and newborns are most complicated because, at that age, the Lilequist membrane is too detached from the tuber cinerium, and for the procedure to be successful, it is necessary to open both membranes, which sometimes becomes very difficult in utero [8, 22].

Three times has that procedure been attempted, and in only one of them, it was effective. Authors are not unanimous either about neuroendoscopic procedures being as effective in newborns as they are when performed after the first year of life—which leaves a doubt about the convenience of performing fetal endoscopic third ventriculostomy.

The most developed surgical technique, not for treatment but for prevention of fetal hydrocephalus, is the in utero correction of myelomeningocele by open surgery. The randomized trial of prenatal versus postnatal repair of myelomeningocele has shown that when the myelomeningocele is repaired before the 26th gestational week, shunting after birth is only required in 40% of cases, while when myelomeningocele is treated only after birth, shunting has been required in 82% of cases. Furthermore, the cases treated in utero had considerable motor gains [1, 7]

In our series of eight patients treated in utero, only two cases required shunting, and there was no maternal morbidity. In two of those cases, the mothers have become pregnant again, and no complications have been verified concerning their gestations. In conclusion, a myelomeningocele repair in utero does not originate difficulties for future pregnancies and can be considered as just another Cesarean section.

Conclusion

Thirty years after the first in utero procedure for treatment of fetal hydrocephalus, little progress has been made as concerns neurosurgical techniques for management of that disease during the gestational period. Diagnostic techniques have evolved a lot, and today, we have better conditions to evaluate more precisely the cases of fetal hydrocephalus and associated malformations of the central nervous system. We believe that in utero fetal procedures should be performed in cases of acute installation of evolutive but not destructive hydrocephaly without any other associated malformation. Procedures for hydrocephalus prevention, such as closure of myelomeningocele in fetuses before the 26th gestational week, should be encouraged.

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