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Fetal cerebellar hemorrhage in a severely growth-restricted fetus: natural history and differential diagnosis from Dandy–Walker malformation

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KEYWORDS: cerebellar hemorrhage; Dandy–Walker malformation; intracranial hemorrhage; prenatal diagnosis; ultrasound

ABSTRACT

This is a report of an intracerebellar hemorrhage in a severely growth-restricted fetus with pathological Doppler findings of the fetal and uteroplacental circulations. The diagnosis was made sonographically at 22 weeks of gestation and the natural course of the hemorrhage was followed. Interestingly, the final sonographic appearance of the posterior fossa was quite similar to that of the classic form of Dandy–Walker malformation: absence of the vermis and an enlarged fourth ventricle. However, careful sonographic examination showed that the enlargement of the fourth ventricle was actually caused by a porencephalic cystic lesion of the left cerebellar lobe. Pathological examination revealed complete absence of the vermis and cerebellar hypoplasia. Copyright © 2003 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Most prenatally diagnosed intracranial hemorrhages are located in the supratentorial area[1]. Usually, bleeding occurs into the subarachnoid, subdural or intraventricular space, but it can also be confined to the brain parenchyma. Parer[2] estimated the actual prevalence of fetal intracranial hemorrhage to be approximately five in 10 000 pregnancies. So far only a few cases of isolated infratentorial hemorrhage diagnosed *in utero* have been described[1,3–7]. The bleeding was either located in the cerebellar parenchyma[1,3–5] or in the subdural space[6,7]. In one case severe early-onset pre-eclampsia and growth restriction may have led to intracerebellar bleeding[5]. Here we describe a similar case with pathological Doppler findings of the maternal and fetal circulations which indicated severe uteroplacental insufficiency. As serial ultrasound examinations were performed after diagnosis, it was also possible to examine the natural course of the intracerebellar hemorrhage.

CASE REPORT

A 31-year-old woman, gravida 1 para 0, was referred to our clinic following an abnormal result on second-trimester maternal serum biochemical screening. The maternal serum alpha-fetoprotein and total human chorionic gonadotropin concentrations were elevated, at 3.15 MoM and 2.62 MoM, respectively, whereas the unconjugated estriol concentration was low (0.55 MoM). Her history revealed no drug or substance abuse and there were no clinical signs of infection or any other complication during the pregnancy.

We performed a detailed sonographic examination at 22 weeks of gestation, which showed a structurally normal fetus in vertex presentation. As the fetal abdominal circumference, head circumference and femur length were all below the 5th centile, early-onset fetal growth restriction was diagnosed. Although no structural defects were detected during the scan, we noticed an irregular, hyperechogenic mass measuring 16 × 7.5 mm in diameter, confined to the superior vermis and medial part of the left cerebellar lobe (Figure 1). The amniotic fluid volume was within normal limits and the placenta was located anteriorly. Doppler analysis of the uterine arteries showed bilateral early diastolic notching and increased impedance to blood flow (bilaterally elevated systolic/diastolic ratios; 3.54 and 9.12). We observed a high pulsatility index (PI, 1.84) of the umbilical artery and a reduced pulsatility index (0.96) of the middle cerebral artery, which indicated an already well-established brain-sparing effect. The sonographic appearance of the cerebellar lesion raised

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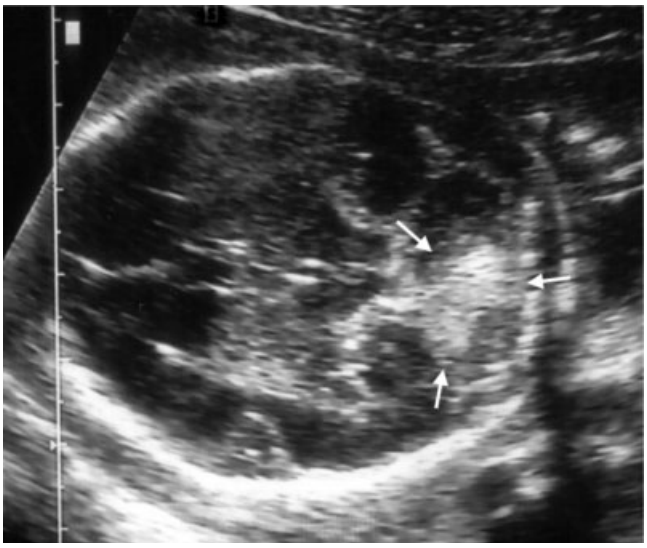

Figure 1 Ultrasound image of an axial transcerebellar scan of the fetal cranium at the level of the thalami and superior vermis. Sonographically the intracerebellar hemorrhage appeared as a bright echogenic area confined to the superior vermis and left cerebellar lobe (arrows).

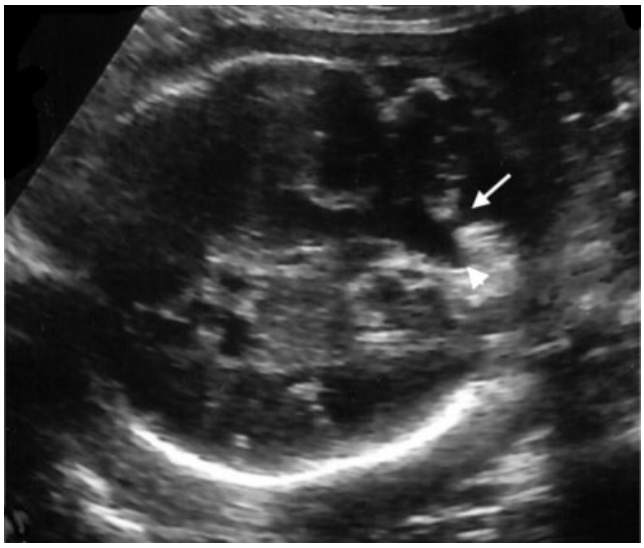

Figure 2 Ultrasound image showing sonographic appearance of the same lesion as in Figure 1 after 8 weeks. Note the large gap between the cerebellar hemispheres indicating complete absence of the vermis (arrow). There was also enlargement of the fourth ventricle due to destruction and hypoplasia of the left cerebellar hemisphere (arrowhead).

the suspicion of an intracranial hemorrhage. A follow-up examination 4 days later showed that the size of the still hyperechogenic cerebellar lesion had diminished (to 13 × 6 mm). Maternal serum screening ruled out seroconversion by rubella virus, cytomegalovirus or toxoplasma infection. An amniocentesis was performed to determine the fetal karyotype and amniotic fluid alpha-fetoprotein and acetylcholinesterase concentrations, which revealed a normal set of chromosomes (46,XY) and normal alpha-fetoprotein (< 2 MoM) and acetylcholinesterase ('negative' on polyacrylamide gel electrophoresis) levels. Maternal coagulation parameters were not investigated.

Although the next evaluation was scheduled 2 weeks later, the patient returned for a further prenatal follow-up at 30 weeks of gestation. At this time the left hemisphere of the fetal cerebellum appeared hypoplastic. Of particular note was the absence of the vermis and an enlarged fourth ventricle, which extended as a sonolucent area into the left cerebellar lobe. At this stage, the ultrasound findings of the posterior fossa were quite similar to those of a classic Dandy–Walker malformation (Figure 2). In addition, we noticed a mild intestinal dilatation and hyperechogenicity. Doppler examination of the umbilical artery showed reversed flow during diastole, whereas the impedance to blood flow in the middle cerebral artery was higher than before but still below the 5th centile (PI, 1.35). These Doppler findings were consistent with profound fetal hypoxemia and acidemia due to severe uteroplacental insufficiency. The estimated fetal weight was 660 ± 100 g. The couple was counseled that the presenting central nervous system malformation would further adversely affect the perinatal outcome of this extremely growth-restricted fetus suffering from severe uteroplacental insufficiency. As there exists no legitimate upper gestational age limit for pregnancy termination in Turkey, this alternative was accepted by the parents. Labor induction with vaginal misoprostol and intravenous oxytocin infusion resulted in a 750-g stillborn male fetus. Pertinent autopsy findings were limited to a porencephalic cystic lesion of the left cerebellar hemisphere accompanied by ipsilateral cerebellar hypoplasia. The vermis was completely absent. Macroscopically there was no visible coagulum beneath the cerebellum, nor was there any vascular malformation.

DISCUSSION

Intracranial bleeding in the newborn has several different causes. Most cases occur as a result of traumatic vaginal birth, with or without instrumental intervention. Prematurity, asphyxia and pre-existing coagulation disorders further predispose the fetus to such a complication[8]. In term infants the hemorrhage is frequently subdural in origin, whereas other forms of intracranial bleeding occur more commonly in preterm infants. Intracerebellar hemorrhage was found in 21% of preterm infants at autopsy[9], but this form of intracranial bleeding is extremely rare before birth and only four prenatally diagnosed cases have been reported so far[1,3–5].

The cause of fetal intracranial hemorrhage is not always clear. Although various etiological factors such as trauma, asphyxia, infection, congenital vascular defects, blood dyscrasia, ingestion of drugs that alter platelet function, maternal seizure, cocain abuse and alloimmune and isoimmune thrombocytopenia have been implicated, in most cases the cause remains obscure[10]. No predisposing factor could be identified in all but one[5] of the reported cases of fetal intracerebellar hemorrhage. Severe preeclampsia complicated by maternal HELLP syndrome (hemolysis, elevated liver enzymes and low platelet

count) and intrauterine growth restriction was the only abnormality found in the case reported by Ranzini *et al.*[5]. Early-onset severe growth restriction was also evident in our case but maternal blood pressure recordings were normal. However, it is not clear how these circumstances might actually cause intracranial hemorrhage. Sudden fluctuations in cerebral blood flow and arterial blood pressure can occur during hypoxia/asphyxia and may lead to fetal intracranial hemorrhage, as in cases of neonatal intracranial hemorrhage[11]. Although the fetal acid–base status is missing in our case, Doppler studies were clearly consistent with fetal hypoxemia. Dilatation of the cerebral vessels in response to hypoxemia (i.e. the brain-sparing effect) could further predispose premature infants to disruption of their peculiarly fragile cerebral circulation. The immature vessels of the periventricular germinal matrix or subependymal plate are especially vulnerable to such an insult, subsequently leading to intraventricular hemorrhage[1,8]. However, vascular connections between the germinal matrix and subependymal venous network, which are the actual bleeding points in these cases, are not present until 20 weeks of gestation, making this kind of intracerebral bleeding less likely early in pregnancy[1]. Supporting this concept, Vergani *et al.*[1] stated that none of their 20 cases of fetal intraventricular bleeding was detected prior to 23 weeks of gestation. Intrauterine growth restriction further protects the fetus against germinal matrix bleeding[12]. In view of these observations it does not seem surprising that in extremely preterm infants bleeding can occur in a somewhat unusual location. The bleeding site in our case seems to be somewhat atypical, but this shows that any point in the peculiarly fragile circulation of the fetus may be prone to rupture. The blood supply of the cerebellum is provided by the two inferior and one superior cerebellar arteries. The posterior inferior cerebellar artery supplies the inferior vermis, the medial border of the cerebellar lobes and the dentate nucleus (located within the cerebellar lobe). The porencephalic cyst which developed within a few weeks in our case, actually fits with these anatomical landmarks, making a hemorrhagic infarction secondary to rupture of the posterior inferior cerebellar artery the most likely reason for this malformation.

The other interesting aspect of our case was that the last scan showed sonographic features which were similar to those of the classic Dandy–Walker malformation. This has not been reported previously. Partial or complete absence of the vermis combined with an enlarged fourth ventricle and cerebellar hypoplasia are the sonographic hallmarks of classic Dandy–Walker malformation, which probably results from an abnormal formation of the roof of the fourth ventricle. Ultrasound allows its diagnosis from mid-gestation although it is recognizable as early as 14 weeks with transvaginal sonography. The identification of more minor variants such as Dandy–Walker variant (variable hypoplasia of the cerebellar vermis with or without enlargement of the cisterna magna) and enlarged cisterna magna (enlarged cisterna magna with integrity of both cerebellar vermis and fourth ventricle) is less straightforward. As the sonographic appearance of the cerebellum can be abnormal during the early second trimester, caution is needed when diagnosis is made before 18 weeks of gestation. Evaluation by magnetic resonance imaging has demonstrated that some degree of vermian dysgenesis is present even in cases with enlarged cisterna magna and that classic Dandy–Walker malformation and Dandy–Walker variant have so many similarities that clear-cut distinction is often impossible.

Genetic factors play a major role in the cause of Dandy–Walker malformation, although perinatal viral infections, maternal alcohol or coumarin consumption and diabetes mellitus have also been implicated[13]. Disruption of blood supply and the subsequent destructive process within the posterior fossa may have led to complete absence of the cerebellar vermis and dilatation of the fourth ventricle. At first glance these sonographic features were quite similar to those of Dandy–Walker malformation. However, careful sonographic examination and information gained from the previous scans showed that the enlargement of the fourth ventricle was actually caused by a porencephalic cystic lesion of the left cerebellar lobe. Folkerth *et al.*[7] stated that organizing posterior fossa hematomas can mimic a Dandy–Walker malformation. They reported three cases with prenatally detected cystic lesions of the posterior fossa. In one of them prenatal ultrasound showed a large cyst of the posterior fossa which precluded the identification of a normal cerebellum. Pathological examination revealed a large tentorial hematoma which had markedly compressed the cerebellum. On the other hand in the present case typical parenchymal features of the classic Dandy–Walker malformation (i.e. absence of the vermis and cerebellar hypoplasia) were evident rather than a cystic lesion in the posterior fossa.

In conclusion, although rare, the presence of hyperechogenic intraparenchymal lesions within the fetal brain, particularly in asphyxiated growth-restricted fetuses, should raise the suspicion of hemorrhage. If located in the posterior fossa, the sonographic appearance of these lesions changes over time and they may later resemble Dandy–Walker malformation, which can lead to a diagnostic dilemma.

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