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Correlation of prenatal ultrasound diagnosis and pathologic findings in fetal brain abnormalities

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ABSTRACT

Objective *To determine the degree of agreement between prenatal ultrasound diagnosis of brain abnormalities and subsequent pathologic findings.*

Methods *Between August 1993 and August 1999 there were 62 cases where a fetus with a prenatal ultrasound diagnosis of a brain abnormality other than neural tube defects underwent autopsy at the Regional Department of Pediatric Pathology. The cerebral diagnosis at ultrasound was compared with the findings at autopsy in all cases.*

Results *In 47 of 61 (77%) cases the same defects were seen on ultrasound and at autopsy. The most common disparity was with the Dandy–Walker malformation or variant, where only six of the 14 (43%) cases prenatally diagnosed with this condition showed the same abnormality at autopsy. When fetuses with the Dandy–Walker malformation or variant were excluded, the scan findings correlated with autopsy in 41 of 47 (87%). In the main group with discordant findings, five of the seven cases where termination of pregnancy was undertaken had other fetal anomalies on ultrasound examination which were confirmed at autopsy. In the sixth case there was autolysis of brain tissue which affected detailed autopsy.*

Conclusions *A very high level of agreement between prenatal ultrasound and autopsy findings was found for all abnormalities of the fetal brain, except for the Dandy–Walker malformation or variant. Potential discrepancy in findings between ultrasound and autopsy should be explained to patients who are considering termination of pregnancy for the Dandy–Walker type of abnormality.*

INTRODUCTION

Prenatal diagnosis of a fetal brain abnormality is distressing for patients, not only because of the associated risks of handicap but also in some cases because of the uncertainty of the significance of particular lesions. Because patients may opt for termination of pregnancy it is important for the diagnosis to be as accurate as possible and for the accuracy and limitations of both prenatal ultrasound and autopsy to be understood. We noticed in our unit there are sometimes discrepancies between the findings at prenatal ultrasound and autopsy in the brain. Although there are reports on the correlation between prenatal ultrasound and autopsy in diagnosis, they include relatively small patient numbers and analyze data inclusive of neural tube defects, a prenatal diagnosis that is less prone to error than other central nervous system anomalies[1–4]. The aim of this study was to determine the correlation between abnormalities of the brain detected by prenatal ultrasound and autopsy exclusive of neural tube defects.

METHODS

Analysis of data collected by the Fetal Medicine Unit between August 1993 and August 1999 showed that there were 62 cases where fetuses with a prenatal ultrasound diagnosis of a brain abnormality other than neural tube defects underwent autopsy following parental consent. The median gestational age at ultrasound diagnosis was 20 weeks (range 15–35 weeks). The autopsies, carried out in our hospital in the Regional Department of Pediatric Pathology, were performed after intra-uterine death in six cases, neonatal death in two cases and termination of pregnancy in 54 cases. All fetuses underwent full autopsy that included photography, whole body X-ray, macroscopic examination, dissection and histology of all fetal organs. In appropriate cases of termination of pregnancy fetal intracardiac injection of potassium chloride was given according to published guidelines[5].

The cerebral diagnosis at ultrasound was compared with the findings at autopsy in all cases. The purpose of the study was the evaluation of brain defects only. Additional anomalies of other organ systems detected at ultrasound and autopsy were not analyzed. The *Dandy–Walker malformation* was defined as the sonographic demonstration of complete or partial agenesis of the cerebellar vermis

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Table 1 Number and types of fetal brain abnormalities where post-mortem findings agreed with prenatal ultrasound

Number	*Brain findings at ultrasound and autopsy*
31 cases	Ventriculomegaly
6 cases	Absent cerebellar vermis
6 cases	Holoprosencephaly
2 cases	Agenesis of corpus callosum, ventriculomegaly
1 case	Arachnoid cyst
1 case	Echogenic foci in cerebellum (ultrasound) Cytomegalovirus intranuclear inclusions in cerebellum (autopsy)

with a posterior fossa cyst. The *Dandy–Walker variant* was defined as only partial (inferior) absence of the cerebellar vermis[6,7].

The Fisher's exact test and odds ratio with corresponding 95% confidence intervals were used to compare the incidence of pretermination fetal potassium chloride administration in the group where the findings were the same at ultrasound with the group where the findings differed.

RESULTS

In 47 (77%) cases the post-mortem brain findings were the same as abnormalities seen on ultrasound (Table 1) and in 14 cases brain abnormalities which were detected by ultrasound were not seen at autopsy (Table 2). In one case where agenesis of the corpus callosum was diagnosed on ultrasound, autopsy of the brain was not possible because of complete autolysis. In two other cases additional significant brain abnormalities were reported at autopsy that had not been detected prenatally. These include one case of complete vermian agenesis diagnosed on ultrasound in which the additional finding of holoprosencephaly was diagnosed at autopsy. The second case was of apparent isolated ventriculomegaly diagnosed on ultrasound where autopsy demonstrated agenesis of the corpus callosum.

In nine cases no abnormality was detected at autopsy (Table 2). The ultrasound findings in five of these cases were of Dandy–Walker malformation or variant, in two cases of mild ventriculomegaly, in one of lobar holoprosencephaly and in another of absent cavum septum pellucidum. In the case with prenatally diagnosed lobar holoprosencephaly there was partial autolysis of brain tissue at autopsy. In five other cases abnormalities were found at autopsy which differed from those seen at ultrasound; in three of these (cases 10–12) ultrasound had demonstrated Dandy–Walker malformation or variant. In two (cases 13 and 14) porencephalic cysts were seen prenatally. When fetuses with the Dandy–Walker malformation or variant were excluded from the total number, the scan findings correlated with autopsy in 41 of 47 (87%) cases. In the main group with discordant findings (Table 2) five of the seven cases where termination of pregnancy was undertaken had other fetal anomalies on ultrasound examination which were confirmed at autopsy, and in another case there was autolysis of brain tissue which affected detailed autopsy.

Two cases of Dandy–Walker malformation were diagnosed before 20 weeks' gestation, one at 16 and the other at 19 weeks. Complete vermian agenesis was seen at autopsy in both. In one case in which partial agenesis of the cerebellar vermis was seen at 15 weeks, hydrops together with a trisomy 13 karyotype were found. The patient elected to have termination of pregnancy. Although hydrops was confirmed at autopsy, absence of the cerebellar vermis was not.

Fetal administration of potassium chloride for termination of pregnancy had been given in the case where autopsy of the brain was not possible because of autolysis. Potassium chloride was administered in five of the 14 cases (36%) where the post-mortem brain findings differed from those on prenatal ultrasound, including the case with partial autolysis (case 8), and also in nine of the 47 (19%) cases where there was agreement between prenatal ultrasound and post-mortem (Table 2). Although the incidence of potassium chloride administration was not shown to be significantly higher in the group with discordant findings at ultrasound and post-mortem compared with the group with corresponding findings ($P = 0.28$), the results demonstrated a trend for a higher risk of this with an odds ratio of 2.3 (95% confidence interval, 0.5–10.5).

Ventriculomegaly was seen at both prenatal ultrasound and autopsy in 31 cases. The median maximum prenatal width of the anterior or posterior horn of the lateral ventricle was 16 mm (range 10–39) in this group. In five of these cases, the maximum width was < 13 mm. In the two cases of prenatally diagnosed ventriculomegaly unconfirmed at autopsy, the anterior or posterior horn measurement on ultrasound was 12 mm.

DISCUSSION

These data demonstrate that there is good correlation between prenatal ultrasound diagnosis and pathologic findings in fetal brain abnormalities, with 47 of 61 (77%) cases showing the same defects. The most common disparity was with the Dandy–Walker malformation or variant, with only six of 14 (43%) prenatally diagnosed cases showing the same abnormality at autopsy. When fetuses with the Dandy–Walker malformation or variant were excluded, the scan findings correlated with autopsy in 41 of 47 (87%) of cases. Of the six remaining cases where prenatal ultrasound demonstrated an abnormality not seen at autopsy, two included mild ventriculomegaly, one lobar holoprosencephaly where there was partial autolysis of brain tissue, one absent cavum septum pellucidum and in two others porencephalic cysts. In one of these latter two

Table 2 Cases of fetal brain abnormalities where post-mortem findings differed from those at prenatal ultrasound including those with Dandy–Walker malformation (DWM) or variant (DWV). Details of gestational age at diagnosis in weeks (GAD) and other prenatal findings confirmed at autopsy with outcome for all cases including prenatal administration of potassium chloride (KCl) are given

Cases	*Ultrasound of brain*	*GAD weeks*	*DWM or DWV at ultrasound*	*Post-mortem of brain*	*Other prenatal findings*	*Outcome*	*KCl*
1	Partial absence of cerebellar vermis	19	DWV	NAD	Trisomy 13	TOP	No
2	Absent cerebellar vermis, posterior fossa cyst	23	DWM	NAD	IUGR	IUD	NA
3	Absent cerebellar vermis, posterior fossa cyst	15	DWM	NAD	Trisomy 13	TOP	No
4	Dilated fourth ventricle	25	DWV	NAD	Triploidy	NND	NA
5	Enlarged cisterna magna	27	DWV	NAD	AVSD, facial cleft	TOP	Yes
6	Ventriculomegaly (anterior horn 12 mm)	17	NA	NAD	Trisomy 21	TOP	No
7	Ventriculomegaly (posterior horn 12 mm)	17	NA	NAD	* Hydronephrosis (Abnormal post-mortem)	TOP	Yes
8	Lobar holoprosencephaly	25	NA	NAD (partial autolysis)	None	TOP	Yes
9	Absent cavum septum pellucidum	19	NA	NAD	None	TOP	No
10	Partial absence of cerebellar vermis, no posterior fossa cyst	20	DWV	Normal cerebellar vermis, posterior fossa cyst	None	TOP	Yes
11	Absent cerebellar vermis, posterior fossa cyst	34	DWM	Normal cerebellar vermis, Porencephalic cyst from occipital lobe	Duodenal atresia	TOP	No
12	Ventriculomegaly, posterior fossa cyst	20	DWM	Ventriculomegaly, no posterior fossa cyst	None	TOP	No
13	Porencephalic cyst	21	NA	Basal encephalocele to pharynx	None	TOP	No
14	Porencephalic cyst	30	NA	Extensive cerebral infarction	None	TOP	Yes

* Abnormal post-mortem findings included absent right kidney, unicornuate uterus. NA, not applicable; NAD, no abnormality detected; TOP, termination of pregnancy; IUGR, intra-uterine growth restriction; IUD, intra-uterine death; NND, neonatal death; AVSD, atrioventricular septal defect.

cases, although a cyst was not evident at autopsy, analysis showed cerebral infarction.

These findings compare favorably with data from other studies, particularly because neural tube defects were included in the analysis of others. As the sonographic features of neural tube defects are more obvious than other brain defects there will be a closer similarity in findings at ultrasound and autopsy. In a recent study from a total of 61 cases where nine with neural tube defects were included, there was agreement between ultrasound and post-mortem diagnosis of central nervous system defects in 40 cases (66%) and major differences in four (6%)[4]. In another study involving 140 patients where prenatal ultrasound was compared with autopsy and where 74 (53%) of the fetuses had neural tube defects, there was conformity with post-mortem in 132 (94%)[3]. In both studies, all cases of neural defects identified prenatally were confirmed at autopsy.

The finding in our study that vermian agenesis or a posterior fossa cyst may be seen at prenatal ultrasound without confirmation at autopsy or vice-versa (Figures 1 and 2) emphasizes the difficulties in prenatal interpretation and also post-mortem visualization of these lesions. Post-mortem autolysis and dissection difficulties such as with thin-walled posterior fossa cysts (Figure 2) may contribute to this discrepancy. The autopsy findings of the eight cases in our study where Dandy–Walker malformation or variant was diagnosed prenatally but not corroborated at autopsy included five with no abnormality, one with a posterior fossa cyst without partial vermian agenesis which was seen prenatally, and one with a porencephalic cyst in the occipital lobe without complete vermian agenesis being confirmed. In another case a posterior fossa cyst which was found on ultrasound was not identified at autopsy. The difficulty in post-mortem confirmation of the Dandy–Walker malformation has been highlighted in another report where pathological findings documented a normal posterior cranial fossa in three fetuses following an ultrasound diagnosis of partial vermian agenesis, and in one case where complete vermian agenesis was diagnosed prenatally[8]. Similarly, two other studies showed that three of eight fetuses with prenatally diagnosed Dandy–Walker malformation had discrepant post-mortem findings[3,4].

Additional radiological tests such as magnetic resonance imaging (MRI) to diagnose Dandy–Walker malformation or variant prior to autopsy could be helpful, and this is the subject of a future study. Indeed, one could argue that MRI should be performed prenatally in these cases and there are publications on MRI for visualization of the fetal brain[9,10] which suggest that it may be a useful prenatal tool as an adjunct to ultrasound in cases where there is diagnostic difficulty. In a previous study of 14 cases of agenesis of the corpus callosum it was shown that prenatal ultrasound achieved a definitive diagnosis in four cases compared with 13 cases diagnosed by MRI[11]. However, because of the high correlation of prenatal ultrasound findings with autopsy when the Dandy–Walker malformation or variant is excluded, our data suggest that the additional

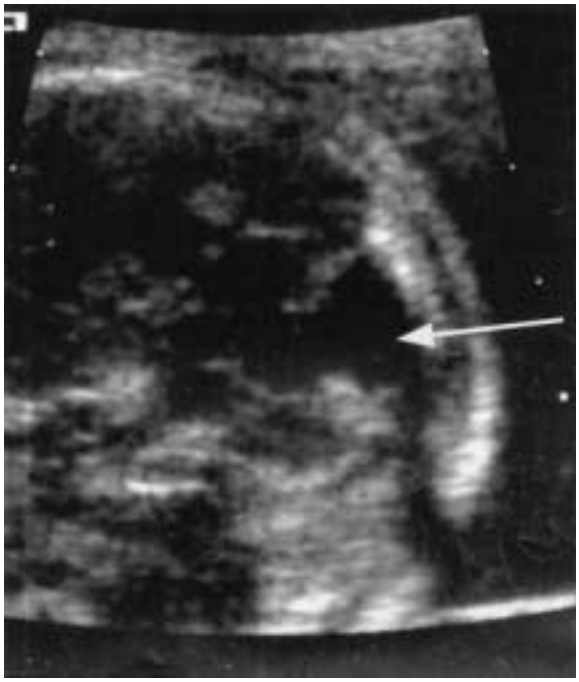

Figure 1 Ultrasound at 20 weeks of gestation demonstrating absence of the cerebellar vermis (arrow).

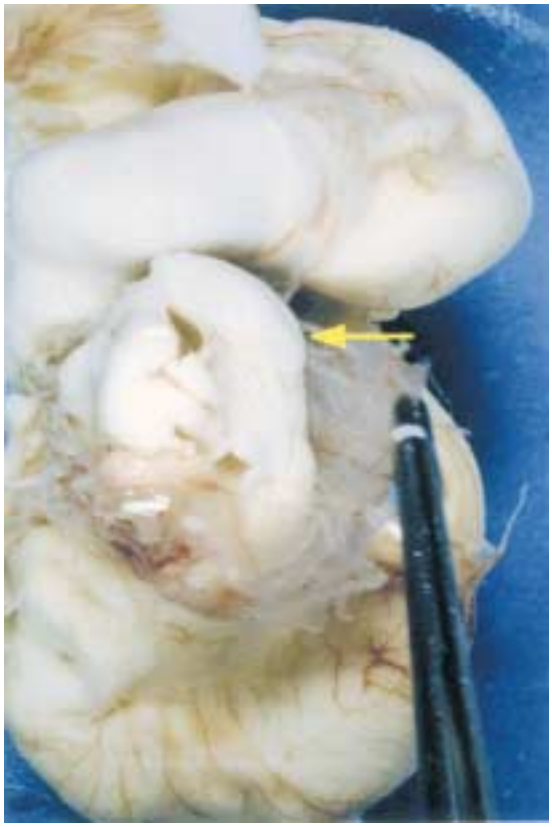

Figure 2 Autopsy of the same case as in Figure 1 at 21 weeks of gestation where the cerebellar vermis appears to be present (arrow points to cerebellar peduncle with vermis below). Note that a ruptured posterior fossa cyst which has a very thin-walled lining was seen at post-mortem (rod pointer).

utilization of prenatal MRI may not be necessary for the diagnosis of the majority of other brain defects.

In one case at 15 weeks, the absence of the cerebellar vermis was seen on scan with the additional finding of hydrops. It could be argued that it was inappropriate to label this as a defect of the cerebellar vermis because it has been shown that prenatal diagnosis of Dandy–Walker malformation should not be made before 18 weeks, due to incomplete development of the cerebellar vermis prior to this gestation. In a previous report on 116 cases with an open vermis at initial scanning, it was shown that 23% of fetuses have an open vermis at 15 weeks, decreasing to 4% at 17 weeks; only one of the cases had persistent opening of the cerebellar vermis beyond 18 weeks[7]. However, fetal karyotype following amniocentesis showed that this fetus had trisomy 13, which is known to be associated with the Dandy–Walker malformation.

Ventriculomegaly diagnosed by prenatal ultrasound was also seen at autopsy in 94% of cases. The two cases unconfirmed at autopsy had mild ventriculomegaly where the anterior or posterior horn measured 12 mm. Intracardiac potassium chloride was administered in one of these undergoing termination of pregnancy. Substantiating this diagnosis at fetal autopsy may be difficult because the ventricular spaces can be altered by autolysis, or deformed artifactually. Indeed previous publications have shown disparity between prenatal ultrasound and autopsy for this anomaly[4,12,13]. In support of this observation, a recent publication has suggested the incorporation of cerebral mantle thickness into post-mortem examinations for ventriculomegaly, as it was found that measurements at autopsy were 2 SD or more below the mean in half of the cases with an ultrasound diagnosis of ventriculomegaly[14].

Another suggestion from our study is a possible association between fetal potassium chloride administration and cerebral autolysis. Potassium chloride before delivery was given in 36% of cases where there was disparity between the ultrasound findings and autopsy compared with 19% in which the findings were the same. Although this difference was not shown to be statistically significant, it is possible that larger numbers would demonstrate that prenatal potassium chloride significantly reduces the quality of post-mortem information and this agrees with our clinical impression.

CONCLUSION

There was good correlation of prenatal ultrasound and autopsy in abnormalities of the fetal brain but less so for the Dandy–Walker malformation or variant. The possibility of discrepancy in findings between ultrasound and autopsy should be explained to parents who are considering termination of pregnancy especially for Dandy–Walker malformation or variant and ventriculomegaly. Our study also emphasizes the importance of a specialized fetal pathology service so that fetal medicine clinicians and pathologists can work jointly in the diagnosis of defects.

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