Prenatal Diagnosis of Cerebral Neuroblastoma by Fetal Brain Biopsy

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Although several previous reports of the prenatal detection of intracranial tumors have been published, in each the final diagnosis of the histologic type of tumor was made only postnatally. Even postnatally, an exact diagnosis cannot be made without tissue sampling. We report here a case of ultrasonically detected fetal intracranial tumor, in which fetal brain biopsy was used to make an exact tissue diagnosis antenatally.

CASE REPORT

A 20 year old primigravida was referred from an outlying area for ultrasonography at 28 weeks' gestation as the fundal height exceeded that expected for dates. There was no history of consanguinity, and no other specific risk factors were identified. Sonography revealed a single live fetus lying transversely and the presence of polyhydramnios. The placenta was anterior. Although both femur length and abdominal circumference were appropriate for gestational age, both the biparietal diameter and head circumference (10.5 and 44.4 cm, respectively) were above the 95th percentile. A 7.0 × 6.0 cm solid, heterogeneous mass containing some areas of calcification was identified in the right cerebral hemisphere, shifting the midline to the left (Fig. 1A, B). The left hemicranium appeared largely to be composed of brain parenchyma, as indicated by the presence of sulci. A few cystic areas seen within the brain parenchyma were thought to be porencephalic cysts. A substantial subdural fluid collection also was noted, as shown in Figure 2. The lateral ventricles, choroid plexi, and thalami could not be identified. The calvarium and spine both appeared intact.

This lesion was considered to be a large intracranial tumor in the right cerebral hemisphere, the differential diagnosis of which included teratoma, glioblastoma, neuroblastoma, and craniopharyngioma. In view of the calcifications within the mass, a tentative diagnosis of teratoma was made. Despite the fact that the prognosis was likely to be poor, we were reluctant to recommend termination of the pregnancy in the absence of a more exact diagnosis. Furthermore, we were concerned that an exact tissue diagnosis might never be reached, either because the patient might be delivered in the remote rural area in which she lived, without access to the requisite laboratory facilities, or because the fetus might die in utero with the fetal brain then too autolyzed for histologic identification, or both.

Under local anesthesia a biopsy of the mass was done with a spring-loaded double needle biopsy device (Bioptycut biopsy needle and gun, Bard, Atlanta, GA), as shown in Figure 3, which has a 1.2 cm inner diameter. Two samples of tissue were obtained and sent for histopathologic examination. In addition, 20 ml of subdural fluid was aspirated and sent for cytologic examination. The procedure was uncomplicated, and no change was noted in the fetal heart rate or fetal movements. Cytologic examination of the smear preparation revealed a hypercellular aspirate composed of round cells with scanty cytoplasm arranged in sheets interspersed by numerous rosettes (Fig. 4). This

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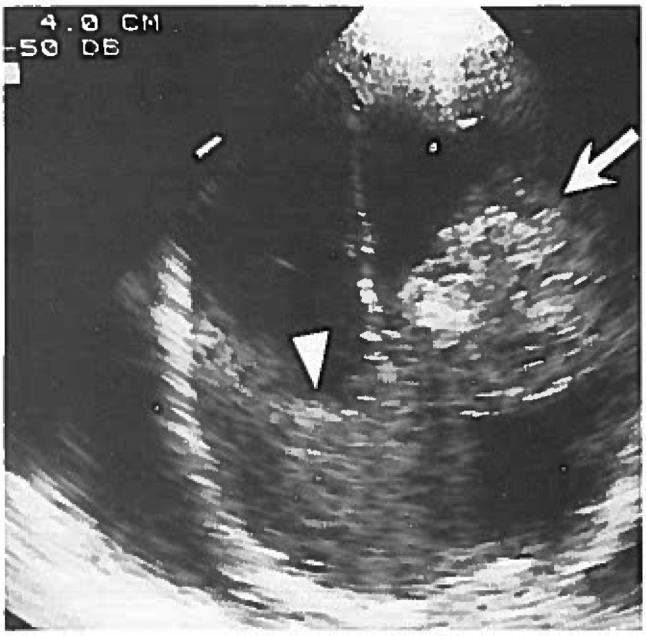
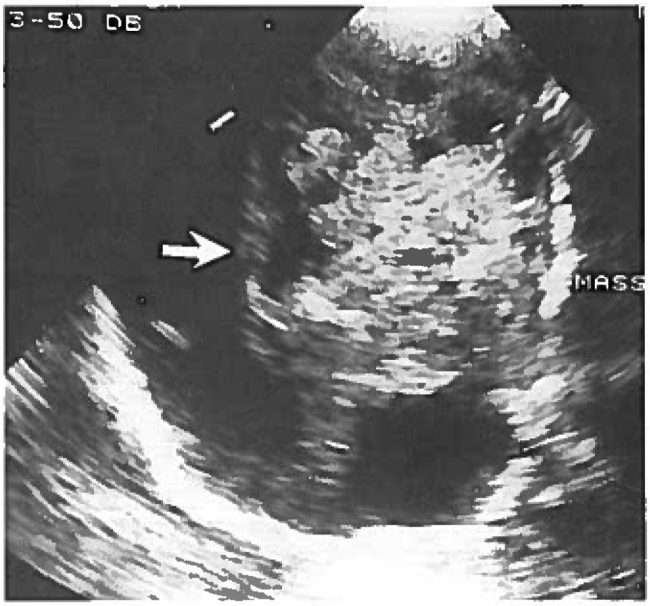


A



B

Figure 1 A, Coronal section of fetal head showing a solid mass with calcification (*arrow*) in the right cerebral hemisphere. A portion of the brain parenchyma (*arrowhead*) seen on the left side. B, The same mass producing marked shift of the midline falx (*arrow*) to the left.

appearance is considered highly suggestive of neuroblastoma, and this diagnosis was confirmed by histopathologic study of the biopsied tissue (Fig. 5).

In accordance with the patient's request, the pregnancy was terminated a week later by inducing labor with an oxytocin drip and performing cephalocentesis in the second

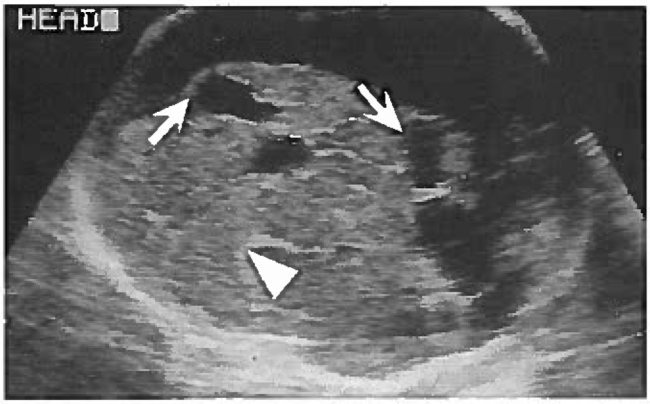


Figure 2 Left parasagittal section of fetal head showing brain parenchyma with few cystic areas (porencephalic cysts) (*arrows*). Note the sulci (*arrowhead*) indicating brain parenchyma.

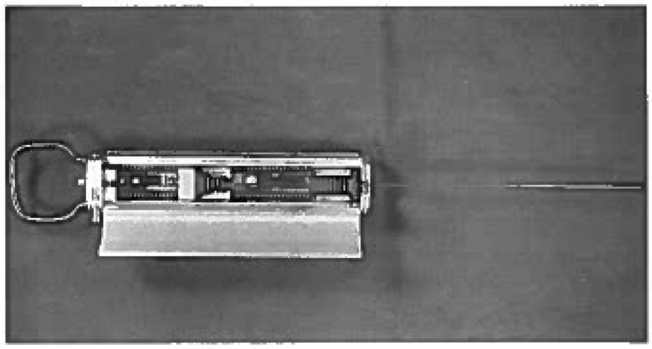
stage to facilitate vaginal delivery. Although the fetal heart rate had been present until the second stage, the 1.1 kg male infant was stillborn. Unfortunately, histopathologic results were not available.

DISCUSSION

Congenital tumors of the brain have been defined by Solitare and Krigman[1] as those that are present or produce symptoms at birth. Such congenital brain neoplasms constitute 0.5 to 1.5% of all childhood tumors.[2,3] The infants usually have an enlarged head and dystocia and often are stillborn. In childhood, the most common are neuroepithelial tumors (50%) and teratomas (36.5%), whereas in neonates ependymomas and medulloblastomas are also found.[4]

The most common prenatally detected intracranial neoplasm is teratoma.[5–7] A total of 10 cases have been reported, as reviewed by Lipman and coworkers.[8] Other prenatally detected intracranial tumors include

Figure 3 The Bard Biopty gun device and needle used for the biopsy.



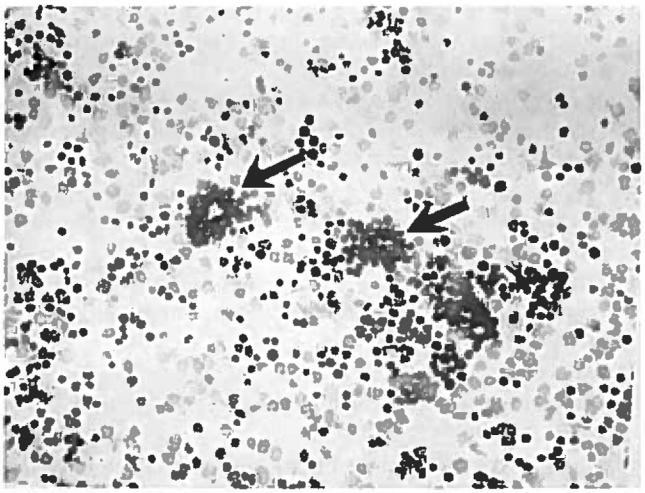
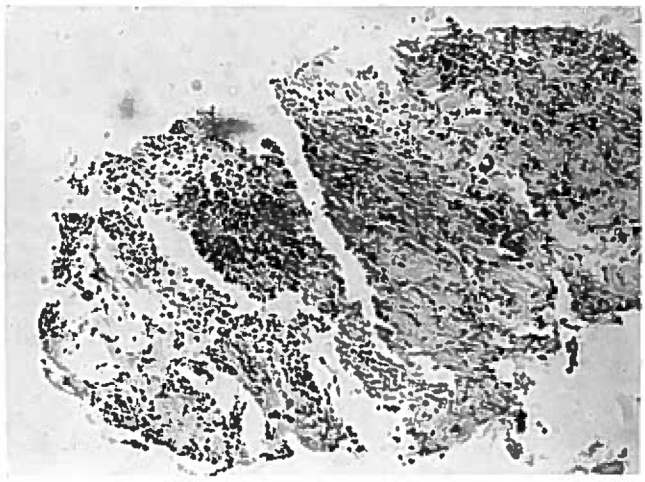


Figure 4 Cytologic examination revealed sheets of mononuclear cells with scanty cytoplasm arranged in a rosette-like pattern (*arrows*).

lipomas of the corpus callosum,[9,10] glioblastomas,[11] and craniopharyngiomas.[12] Rarely, an evolving fetal hydranencephaly can mimic an intracranial neoplasm,[13] such as that reported by Greene and colleagues,[14] wherein the main finding was echogenic material representing blood filling the supratentorial region.

Shizuo and coworkers[15] made an in utero diagnosis of intracranial teratoma on the basis of identification of calcification and multicystic components, which they considered to be diagnostic of teratoma. Our case does not support their contention, because although calcification and cystic changes were similarly present, the histologic diagnosis was not teratoma but neuroblastoma. This suggests that the antenatal ultrasonic features cannot be relied on to make the exact diagnosis, which requires histopathologic evaluation.

Figure 5 Hematoxylin and eosin stained section of needle core biopsy of the tumor, showing a pseudorosette.



Cerebral neuroblastomas are extremely rare nonepithelial tumors arising from primitive neuroblasts and resemble neuroblastomas of the adrenal medulla and sympathetic ganglia.[16] Some are associated with high urinary levels of catecholamines and their metabolic products.[17] In this case, however, there were no symptoms or signs of catecholamine excess in either mother or fetus that might have suggested this diagnosis. Macroscopically, cerebral neuroblastomas are sharply circumscribed, lobulated, firm lesions with necrosis and cyst formation. A classic histologic pattern composed of rosettes and densely cellular sections of small round cells is seen on microscopy. This pattern was seen histologically in our case in the fetal brain biopsy tissue. Although it was similarly seen on cytologic examination, cytologic appearances cannot be relied on as diagnostic, but the evaluation was peformed here as a complementary investigation.

The brain biopsy was of use in this patient in establishing the exact diagnosis of the intracranial lesion. Our reasons for performing it were largely related to the special problems that operate in India, where it is not always possible to ensure that women referred from poor rural communities are delivered in an environment in which the appropriate investigations can be obtained. It has recently been recommended that karyotyping of fetuses with anomalies be performed antenatally, because intrauterine death—the risk of which is increased in such pregnancies—prevents successful postabortal or postnatal cytogenetic studies.[18] Similarly, we performed fetal brain biopsy to avoid the problem of postmortem autolysis making subsequent histologic examination impossible.

It is difficult to envisage fetal brain biopsy having other applications. Possibilities might include the prenatal diagnosis of rare inborn errors of metabolism, in which the relevant biochemical defect is expressed only in cerebral tissue, or smaller intracranial neoplasms, in which early diagnosis might facilitate parental decision-making or optimal perinatal management. Any contemplation of these, however, would require consideration of the as yet unknown risks of fetal brain biopsy in continuing pregnancies. In our case, although biopsy was not associated with any obvious immediate complications, the needle went only into the tumor tissue and did not transgress otherwise normal cerebral tissue.

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