

Prenatal diagnosis of microcephaly assisted by vaginal sonography and power Doppler

G. Pilu, P. Falco, V. Milano, A. Perolo and L. Bovicelli

Department of Obstetrics and Gynecology, University of Bologna, Bologna, Italy

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ABSTRACT

In two mid-trimester fetuses with microcephaly, transvaginal sonography revealed aberrant findings, including large subarachnoid spaces and a rudimentary shape of the lateral ventricles. In one of these fetuses, power Doppler ultrasound demonstrated a discrepancy in the size of the signals generated by the intracranial arteries branching from the internal carotids and those branching from the vertebral arteries, and this was interpreted as the consequence of a reduced blood supply to the undersized cerebral hemispheres. We suggest that evaluation of intracranial anatomy by transvaginal sonography and power Doppler examination of the cerebral vessels may be of value in the diagnosis of fetal microcephaly.

INTRODUCTION

The term 'microcephaly' is used to indicate a heterogeneous group of conditions that share in common a small brain¹. Microcephaly can result from primary cerebral malformations or exposure to teratogens. It is a part of a wide variety of syndromes and it can also be transmitted via Mendelian inheritance, most frequently as an autosomal recessive trait¹.

Obstetric sonographers are not infrequently faced with the problem of diagnosing fetal microcephaly, usually in one of two situations: first, examining a patient at increased risk because of a genetic predisposition or exposure to teratogens, or, second, finding a small fetal head serendipitously during a routine examination.

The experience thus far indicates that the diagnostic value of antenatal sonography for the detection of microcephaly is limited, with high rates of both false positives and false negatives^{2–4}. However, the available reports focus mostly upon measurements of the fetal calvarium. We report two cases in which transvaginal multiplanar brain imaging and power Doppler produced intracranial findings that assisted the diagnosis of microcephaly.

CASE REPORTS

Case 1

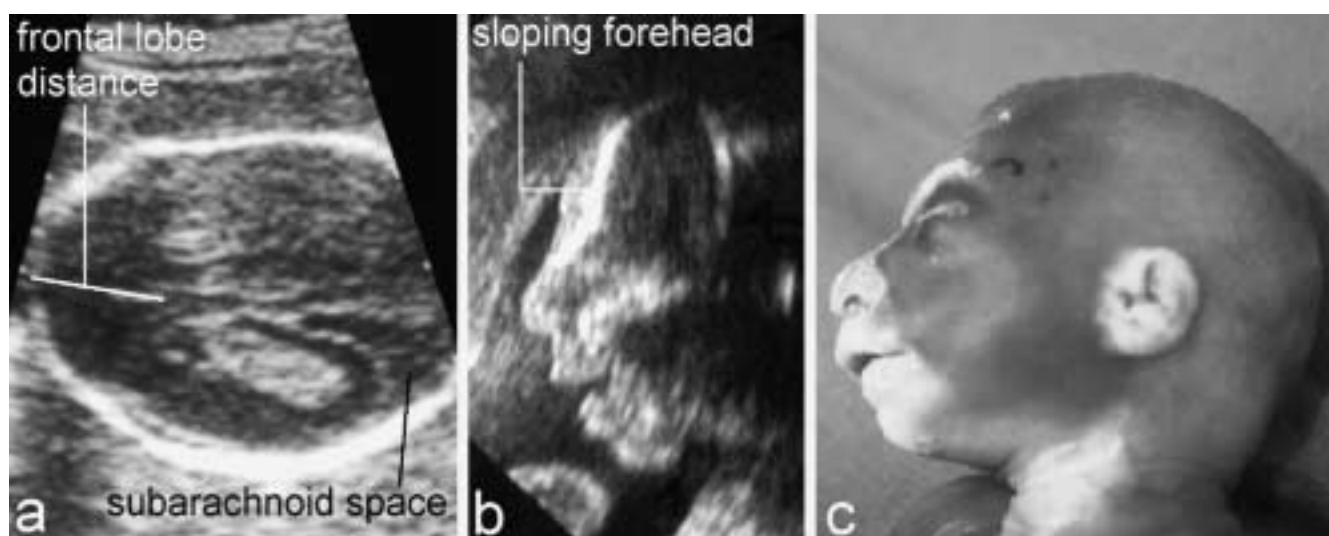
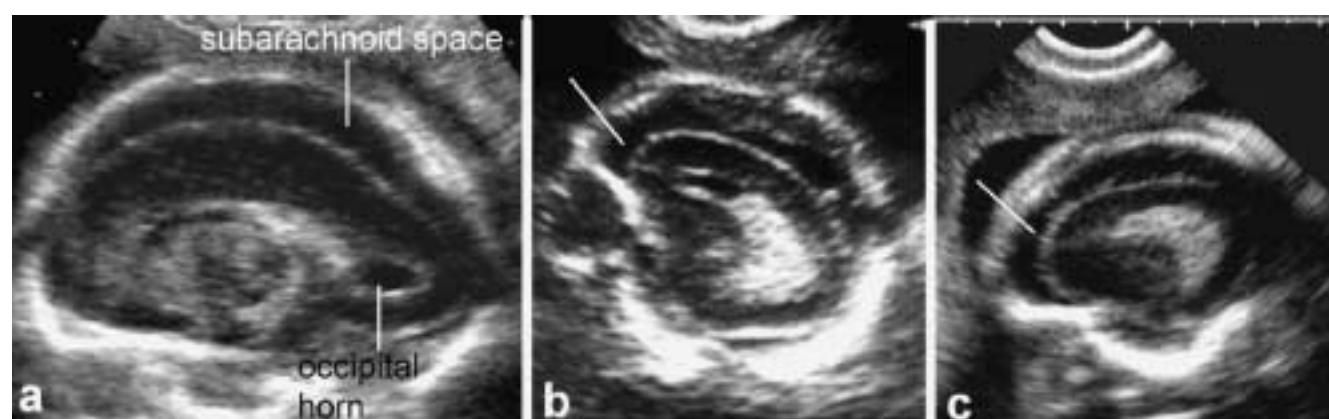
The patient, gravida 2, para 1, was referred for a targeted examination at 19 weeks' gestation (confirmed by a first-trimester scan) because of a small fetal head size detected during a routine examination performed elsewhere. An Ansaldo Au 570 ultrasound machine (Esaote, Genoa, Italy) was used. Fetal measurements were obtained (Table 1) and they confirmed borderline values of the head circumference⁵ and biparietal diameter⁵ relative to both gestational age and the other measurements. The frontal lobe distance⁶ was markedly diminished. A survey of the fetal anatomy was conducted by standard transabdominal sonography, and was unremarkable but for the impression of a sloping forehead (Figure 1) and of an enlargement of the subarachnoid space surrounding the hemispheres. The fetus was in a vertex presentation. Transvaginal sonography was then performed with a 6.5-MHz transducer. The fetal brain was visualized in multiple planes, as previously described⁷. The impression of a disproportionately large subarachnoid space, particularly overlying the frontal area, was confirmed. It was also noted that the lateral ventricles were abnormal in shape, because of a large atrium and the absence of the occipital horns, resembling the appearance that is normally noted at around 16 weeks' gestation^{8–10}. Although these findings could be documented in a variety of sections, the appearance of the oblique-1 plane⁷ was particularly striking (Figure 2).

Demonstration of abnormal brain morphology in association with a small head size prompted the diagnosis of microcephaly. The couple requested termination of pregnancy. Autopsy was performed and confirmed the presence of a small fetal head (Figure 1c) with an obvious discrepancy between the neurocranium and splanchnocranium, and a diminutive brain. The fetal karyotype was normal and a TORCH screen on the mother was negative.

Table 1 Sonographic measurements and Doppler indices in two fetuses with microcephaly

	Case 1: gestational age 19 weeks		Case 2: gestational age 21 weeks	
	Measurements	Standard deviations from mean	Measurements	Standard deviations from mean
Biparietal diameter (mm)	37	-2.66	43	-2.79
Head perimeter (mm)	129	-3.25	156	-2.96
Cerebellar diameter (mm)	17	-0.41	19	-0.83
Frontal lobe distance (mm)	13	-4.00	14	-3.00
Abdominal perimeter (mm)	130	-0.96	169	0.29
Femur length (mm)	27	-0.41	37	1.00
Head/abdominal perimeter ratio	0.99	-3.00	0.92	-3.56
Femur length/head perimeter ratio	0.21	-2.14	0.24	-3.85
Internal carotid artery PI	—	—	1.55	-0.37

PI, pulsatility index

**Figure 1** Case 1: (a) axial view of the fetal head, demonstrating a reduced frontal lobe distance and a large subarachnoid space; (b) profile view of the fetal face, demonstrating a sloping forehead; (c) similar view of the aborted specimen, confirming microcephaly**Figure 2** A composition of oblique-1 views obtained at a similar gestational age in a normal fetus (a), in Case 1 (b) and Case 2 (c). There is an obvious discrepancy in the size of the subarachnoid space relative to the brain mass, particularly overlying the frontal lobes, as well as in the shape of the lateral ventricles, with no demonstrable occipital horn in (b) and (c), compared to (a)

Case 2

The patient, primigravida, was referred for a standard sonogram at 21 weeks' gestation (confirmed by a first-trimester scan). An Esaote Au 4 Idea ultrasound machine (Esaote, Genoa, Italy), was used. Standard transabdominal and transvaginal sonography revealed quantitative (Table

1) and qualitative findings (Figure 2) similar to those described for Case 1. An evaluation of the cerebral vessels was performed by the use of color and power Doppler, revealing an unusual appearance of the circle of Willis. Despite the favorable conditions of visualization and the high sensitivity of the ultrasound equipment (minimal

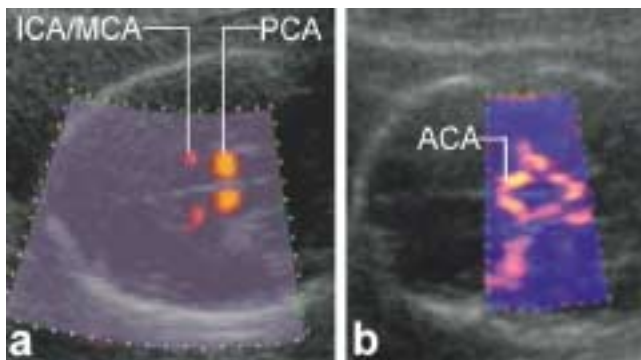


Figure 3 (a) Power Doppler demonstration of the circle of Willis in Case 2. There is a discrepancy in the size of the signals generated from the posterior cerebral arteries (PCA) compared to those derived from the complex formed by the anterior carotid and middle cerebral arteries (ICA/MCA). The anterior cerebral arteries could not be demonstrated. The minimal velocity detectable by the equipment during this examination is estimated to be about 1 cm/s; (b) the appearance of the circle of Willis in a normal fetus at a similar gestational age. ACA, anterior cerebral artery

detectable velocities in the range of 0.3–1.7 cm/s with the setting employed during the examination), it was impossible to demonstrate the anterior cerebral arteries either by the transabdominal or by the transvaginal route. Furthermore, signals originating from the branching of the internal carotids into the middle cerebral arteries appeared much smaller in size than those derived from the posterior cerebral arteries (Figure 3). Pulsed Doppler revealed normal waveforms from both the vessels presumed to represent the internal carotid arteries. When confronted with the diagnosis of fetal microcephaly, the patient requested termination of pregnancy. The antenatal diagnosis was confirmed by autopsy. Deterioration of the aborted specimen prevented a detailed evaluation of the cerebral vessels. The fetal karyotype was normal and a TORCH screen on the mother was negative.

DISCUSSION

Attempts to diagnose fetal microcephaly with ultrasound have been disappointing thus far. However, these attempts have focused mostly upon measurements of the calvarium^{2–4}, representing, at best, a rough estimate of cerebral development.

Postnatal studies have demonstrated that microcephalic infants have brains that are not only small, but dysmorphic as well. A wide spectrum of abnormalities has been described, from malformations such as holoprosencephaly, porencephaly and agenesis of the corpus callosum to more subtle degrees of maldevelopment, including undergrowth of selected areas and anomalous convolutions¹.

They have also shown that there is some form of anatomic derangement of the brain in about two-thirds of cases^{11,12}. An additional finding, demonstrated by postnatal imaging studies, is the frequent enlargement of the subarachnoid space, presumed to reflect cortical atrophy^{13,14}.

From these observations, it follows that a direct evaluation of the intracranial contents could be a useful adjunct

to the quantitative biometric evaluation of the fetal skull in predicting microcephaly. We have previously reported that measurement of the frontal lobes was helpful in two cases⁶. In another case, the demonstration of a small cerebellum was the first sign of microcephaly¹⁵.

More recently, the development of high-resolution high-frequency transvaginal probes has made possible the evaluation of very subtle details of the developing brain⁷. By applying this technique to our two cases, it was possible to document very similar findings which were strongly evocative of microcephaly. The large subarachnoid space overlying the cerebral convexities, particularly in the frontal area, suggested that the undergrowth of the cerebrum was of a greater extent than expected from the size of the calvarium. Furthermore, the shape of the lateral ventricles appeared more rudimentary than expected in mid-gestation. The absence of the occipital horns and the large size of the atrium resembled the appearance that is normally found prior to 16 weeks^{8–10}, suggesting a delay or an arrest in the qualitative development of the brain as well.

The deviation from normalcy was obvious in both cases. However, nomograms of the normal size of the cerebral mass and/or subarachnoid space of the fetus could be developed, as they have been recently for other parts of the intracranial anatomy depicted by multiplanar imaging¹⁶, and may prove useful for cases which are less conspicuous than the ones reported here.

The Doppler findings in Case 2 are worth noting. A diminished brain mass would require a smaller blood supply, and probably vessels of a smaller size. Cerebral vessels cannot be clearly demonstrated with current two-dimensional ultrasound imaging. However, blood flow is usually clearly visualized with both conventional color Doppler¹⁷ and power Doppler¹⁸ imaging. Neither technique allows precise quantification of the size of the vessels. However, it is a common experience that the signals generated by the anterior carotid/middle cerebral arteries are similar in size to those originated by the posterior cerebral arteries. In the case reported here, the anterior cerebral circulation was poorly visualized, and the vessels that were detected appeared smaller than the posterior ones. Unfortunately, deterioration of the specimen prevented a clear postnatal evaluation of the cerebral vasculature. We postulate that the prenatal findings reflected a reduction in the blood supply to the underdeveloped cerebral hemispheres, compared with a normal supply to the brain stem and cerebellum.

Sonographic evaluation of the fetal profile has been reported to be useful for the diagnosis of a variety of fetal anomalies¹⁹. Our experience suggests that a sloping forehead, although a rather subjective finding, may be of value in recognizing microcephaly.

The pathology and natural history of congenital microcephaly are heterogeneous. Previous reports suggest that an early antenatal diagnosis will not be possible in all cases^{3,4}. However, our experience indicates that evaluation of intracranial anatomy by transvaginal sonography and possibly power Doppler examination of cerebral vessels may be of value in doubtful cases, and allow the recognition of a

larger number of affected fetuses than by head biometry alone.

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