Prenatal ultrasound semiology of anencephaly: sonographic–pathological correlations

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ABSTRACT
A better understanding of the ultrasound findings in each of the different types of fetal anencephaly can help to reduce the number of false-negative diagnoses of this condition during the prenatal period.

Errors in the estimation of the remaining cerebral tissue (angiomatic stroma, area cerebrovasculara) can cause false-negative diagnoses or diagnostic confusion with cases of microcephaly or incomplete ossification of the cranial vault.

In a retrospective study, 30 fetuses with anencephaly (diagnosed at 13–38 weeks of gestation) were grouped, in terms of their ultrasound results, according to the Nanagas classification. The ultrasound diagnoses were then correlated with those found through autopsy, to identify any errors in the ultrasound classification.

INTRODUCTION
Anencephaly, multifactorial in etiology, is believed to result from the failure of closure of the anterior neuropore, which normally closes during the 6th menstrual week.

This abnormality was the earliest fetal malformation to be recognized by sonography1.

The cranial lesion of anencephaly is easily recognizable in utero with ultrasound. However, as stated by Stoll2, the false-negative prenatal diagnostic rate of anencephaly could be as high as 10–12%.

In spite of the fact that it is now possible to exclude anencephaly in the 9–10th week with transvaginal echography3, a more complete knowledge of the ultrasound characteristics corresponding to each of the anatomical defects in the anencephalic fetus should help to reduce the number of false-negative diagnoses and to improve the differential diagnosis with other cranial malformations.

Anencephaly, understood as the absence of the encephalon, is not a single entity. From ultrasound examination, it is possible to identify various pathological types of anencephaly; we describe here the ultrasound manifestations of the condition together with pathological correlations.

MATERIAL AND METHODS
Over the last 10 years, all cases of anencephaly in our hospital have been identified and analyzed for this study. There were 31 cases out of 34 271 babies born during this time, which represents an incidence of 0.9 per thousand, 30 of which were diagnosed prenatally by ultrasound diagnosis. One was first seen when the mother was admitted during labor, having had an uncomplicated pregnancy.

The ultrasound examinations were performed transabdominally with various models of commercial ultrasound equipment but always with a transducer frequency of 3.5 MHz.

The fetal age at diagnosis varied from 13 to 38 postmenstrual weeks (21 in the second trimester, nine in the third trimester).

In each case, the ultrasound findings were recorded graphically (photograph or video), and assigned to one of the types found in the Nanagas classification4, based on the morphology of the cranial region (Figure 1). Pathological follow-up was obtained in all cases and the detailed autopsy findings were also recorded and a sonographic–pathological correlation was made.

Neonatology was performed according to MacPherson and Valdes-Dapena5. The cephalic lesion was inspected with the aid of a dissecting microscope. No amniotic band syndrome was identified in these cases.
As shown in Figure 1, the characteristics which define each of the types of anencephaly are:

**Type I**: Anencephalic acrania (holoanencephaly, holoacrania) is the classic anencephaly, that is, the symmetric absence of calvaria above the orbits with almost no cerebrovascular matter.

**Type II**: Anencephalic craniorachischisis involves a more or less extensive deficit in the spine, always in continuity with the cranial defect.

**Type III**: Microcephalic acrania (merocrania) shows an appreciable exophytic stroma above the first cervical vertebra. There is no cervical lordosis.

**Type IV**: Microcephalic craniarachischisis (open inencephaly, exprophosomy) is characterized by a marked cervical lordosis with the cerebrovascular tissue covered with duramater.

**Type V**: Exencephalic acrania (acrania and exencephaly) involves extrusions of the brain tissues which are otherwise relatively well-formed.

Facial structures (albeit with bulging eyes, prominent ears and short neck) and the base of the calvarium are preserved.

In 12 cases (40%), polyhydramnios was present. In all cases the gestational age was greater than 27 weeks.

The prenatal ultrasound classification of the type of anencephaly and the pathological correlation are summarized in Table 1.

Type I (Figure 2) was the most common, with 16 cases according to the ultrasound charts. Autopsies confirmed 12 of these, while three were found to conform to Type II and one to Type III according to their anatomical characteristics. Sonographically, the brain is completely absent.

Type II appeared in three cases and all three were confirmed by the autopsies. Echographic characteristics are the presence of a defect involving the spine, and a vertebral lordosis is almost never observed (Figure 3).

Five cases of Type III were found according to the ultrasound assessment, but two were shown to be Type IV when the autopsy results were analyzed. The specific sonographic change is the extrusion of the brain tissues. The volume of this exophytic tissue is subjectively judged as moderate (Figure 4).

Two cases of Type IV were diagnosed ultrasonically, and in both cases the autopsy confirmed the diagnosis. The echographic appearance is bizarre (Figure 5), including malformed head retroflexion, cervical lordosis and rachischisis.

Ultrasound recorded two cases of Type V; one was confirmed by autopsy and the other shown to be microcephalic acrania (Type III). A large amount of brain tissue is the commonest echographic finding in this type, although normal ventricles and choroid plexus cannot be identified (Figure 6). This unusually large brain mass, in comparison with the other types of Nanagas’ classification, is often disorganized with pseudosulcations and cystic areas, sometimes pulsatile.

Finally, two cases were insufficiently documented to allow clear classification. The autopsies showed Type II in one case and Type III in the other.

### RESULTS

The symmetric absence of the bone skull vault is a constant finding in anencephalic fetuses in all types, and represents the first feature of the ultrasound diagnosis.

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<th>Table 1 Anatomical classification of anencephaly</th>
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<td>Ultrasound identification</td>
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Figure 2  Type I: anencephalic acrania. (a) Newborn; (b) sonogram at 31 weeks and (c) at 13 weeks

Figure 3  Type II: anencephalic craniorachischisis. (a) Newborn with more or (b) less extensive spinal lesion; (c) ultrasonogram of anencephalic fetus with spinal lesion (arrows)
Figure 4  Type III: microcephalic acrania. (a) Newborn and (b) echographic profile with obvious cerebrovascular zone (arrows)

Figure 5  Type IV: Microcephalic craniarachischisis. (a) Newborn; (b) ultrasound showed a cervical lordosis; (c) diagram of (b) illustrating the retroflexion (1); anterior wall of the thorax and abdomen (2); dorsolumbar spine (3), and the proximal part of a lower limb (4)
DISCUSSION

All five types of anencephaly are incompatible with life. Misclassification of a particular type of anencephaly is of academic interest but should not affect prenatal counselling and obstetric management.

The potential for a false-negative diagnosis increases before 14 menstrual weeks. The fetal cranium is not completely calcified before 10–11 menstrual weeks; therefore, findings other than absent calvarium should be sought.

Generally speaking, the sonographic appearance of anencephalic fetuses is representative of pathological correlates. The ultrasound errors in classification show that, 19 years after the first ultrasound diagnosis of anencephaly was made, there is still a definite problem with the ultrasonic diagnosis, which leads to false-negative diagnosis of an anencephalic fetus in 10% of cases.

Of course, errors such as misjudging the spinal defect (anencephalic craniorachischisis) or underestimating the deflection of the cephalic pole in the fetus (microcephalic craniorachischisis) are minor errors, because this is a lethal condition and there is no difference in the recurrence rate between the various types. Recently Bronshtein and Ornoy published one familial case report which supports the possibility of a secondary degeneration of a closed neural tube, and they discussed its recessive autosomic transmission.

However, in our opinion, errors in the estimation of the remaining cerebral tissue (angiomatic stroma, area cerebrovasculosa) are those that could cause false-negative results or confusions in the cases of microcephaly or incomplete ossification of the cranium (osteogenesis imperfecta, hypophosphatasia) with deformation of the cranial vault through contact with the uterine walls. Also from ultrasound findings, exencephalic acrania may resemble other cranial malformations, such as massive encephalocele.

The earlier the diagnosis is made, the more probable it is that there will be a greater number of exencephalies, or anencephalics with more cerebral tissue remaining that has not degenerated as a result of prolonged exposure of the developing encephalon to amniotic fluid and trauma in utero. We agree with Ganchrow and Ornoy that exencephaly precedes some cases of anencephaly. Indeed Types I, III and V may reflect differing degrees of secondary degenerative change after formation of the neural tube. As such, descriptions of cases of acrania and exencephaly have been more frequent over the last few years. Both conditions are defined as abnormalities in which flat bones of the cranial vault are absent and a substantial amount of brain tissue is present (this finding differentiates the condition from anencephaly).

We believe that a better knowledge of the types of acrania will facilitate prenatal and differential diagnosis. Although the prognosis is fatal in these situations, in terms of advice to the mother, the doctor must know whether the problem is a genetic one and whether the risk of recurrence should be considered. For example,
Anencephaly, osteogenesis imperfecta and amniotic band syndrome all have different recurrence rates.

In the next few years, higher resolution ultrasonic equipment, more frequent examinations earlier in the pregnancy and a better understanding of the pathology of anencephaly among sonographers will provide greater diagnostic success and a more precise classification of this condition.

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REFERENCES