Prenatal Sonographic Diagnosis of Holoprosencephaly

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Abstract

The purpose of this series was to describe the sonographic features of fetal holoprosencephaly prenatally. The study was undertaken at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University. A total of 12 fetuses with prenatal diagnosis of holoprosencephaly were sonographically evaluated and followed-up. The study revealed that all showed monoventricular cavity, fused thalami, no falx and cavum septum pellucidum. Eight of them were correctly diagnosed sonographically in the first two trimesters. Extrafacial anomalies were also identified in half of the fetuses and all of them had facial abnormalities. Twenty-five per cent (3 cases) had polyhydramnios and only one case had oligohydramnios. Chromosome study revealed that 70 per cent had normal chromosomes, 30 per cent were aneuploidy, trisomy 13; 2 cases and trisomy 18; 1 case. In conclusion, this series indicates that ultrasound has a high predictive value in the diagnosis of holoprosencephaly. The most valuable clue to the diagnosis is the demonstration of the single ventricle. Additionally, demonstration of facial abnormalities may add confidence to the diagnosis. Conversely, should any of these facial features be serendipitously encountered, a careful examination of the intracranial contents is recommended.

Holoprosencephaly is an anomaly of the forebrain that arises as an early embryonic failure of evolution of the anlage of the cortex and ventricles into bilateral structures. An incidence of 1 in 16,000 neonates is commonly quoted[1]. The etiology of the condition is unknown, although it does accompany certain chromosomal anomalies, notably trisomy 13, in which it is present in nearly two-thirds of cases[2]. It occurs sporadically and without a tendency to recur, although an autosomal dominant inheritance has been suggested in some families[3]. Holoprosencephaly is usually classified into three major varieties; the alobar, semilobar, and lobar types[1]. The alobar variety, the

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most severe one, is characterized by the complete absence of the intraventricular membrane, resulting in a common single lateral ventricle. This finding is pathognomonic of alobar holoprosencephaly. In the semilobar variety the two cerebral hemispheres are partially separated posteriorly but there is still a single ventricular cavity. In both forms, the roof of the ventricle, thela choroidea, normally enfolded within the brain, may balloon out between the cerebral convexity and the skull to form a cyst of variable size commonly refered to as the dorsal sac. With the lobar type the anatomic derangement is much more subtle. The brain is almost completely divided into two distinct hemispheres, the only exception being a variable degree of fusion and septum pellucidum is always absent.

Holoprosencephaly requires correct prenatal diagnosis for proper management which may be different from other types of intracranial malformations. Sonographic antenatal diagnosis of holoprosencephaly have been reported in a limited number, especially the semilobar type[4-7]. The objective of this study was to evaluate the role of prenatal sonography in identifying the characteristics of holoprosencephaly.

MATERIAL AND METHOD

Ultrasonographic examinations were performed by the authors from June 1989 to March 1997, using convex MHz transducers (Aloka Model 650 or 680). Indications for ultrasonographic examinations included abnormal growth, amniocentesis, fetal anomaly screening, etc. The most important sonographic findings were monoventricular cavity. The other associated anomalies were also carefully identified and documented.

When holoprosencephaly was diagnosed, previous obstetric history was carefully reviewed and counseling was given. The patient was followed-up until discharge from the hospital.

RESULTS

Twelve cases of holoprosencephaly (9; alobar, 3; semilobar) were diagnosed and followed by the authors. The demographic information and detailed ultrasound findings are presented in Tables 1 and 2, respectively. The majority of cases had no obstetric complications. Two patients, however, presented as large for date and finally proved to be polyhydramnios. One presented as small for date and the sonography showed oligohydramnios.

The mean maternal age was 28.0±6.3 years, ranging from 20-40 years. Fifty per cent of the patients were primigravid. Eight of them were unexpectedly found on the antenatal ultrasound during the first two trimesters. The mean gestational age at time of diagnosis was 25.0±6.3 weeks, range 14-35 weeks.

All showed monoventricular cavity, fused thalami, no falx and cavum septum pellucidum. Extrafacial anomalies were also identified in half of the fetuses and all of them had facial abnormalities. 25 per cent (3 cases) had polyhydramnios and only one case had oligohydramnios. Chromosome study was sucsessfully done in only 10 cases and it revealed that 70 per cent (7 cases) had nor-

Table 1. Baseline characteristics of the patients.

No.	Ages	Parity	Weeks of diagnosis	Indications for ultrasound examinataions
1	22	0-0-1-0	15	Rule out anomaly
2	28	0-0-0-0	31	Amniocentesis for genetic study
3	31	1-1-0-1	14	Rule out anomaly
4	28	1-0-2-1	18	Small-for-date
5	24	0-0-0-0	22	Antepartum hemorrhage
6	36	2-0-1-1	26	Amniocentesis for genetic study
7	35	3-0-1-3	35	Large-for-date
8	20	0-0-0-0	20	Gestational age determination
9	24	0-0-0-0	29	Large-for-date
10	40	2-0-0-2	30	Gestational age determination
11	23	1-1-0-1	24	Rule out anomaly
12	25	0-0-2-0	26	Rule out anomaly

Table 2. Ultrasound findings and chromosome studies.

	Number	%
Intracranial abnormalities	12	100
Single ventricle	12	100
Absent carvum septum pellucidum	12	100
Completely absent falx cerebri	10	83
Fused thalamus	9	75
Enlarge ventricle	8	67
Microcephaly	2	17
Dandy-Walker-Malformation	1	8
Macrocephaly	1	8
Extracranial abnormalities		
Proboscis	5	42
Hypotelorism	6	50
Cyclopia	2	17
Anophthalmia	1	8
Median cleft	3	25
Flat nose	6	50
Other congenital malformations (omphalocele, single umbilical artery hydronephrosis, clubfoot)	6	50
Intrauterine growth retardation	5	42
Amniotic fluid		
Polyhydramnios	3	25
Oligohydramnios	1	8
Normal amniotic fluid	8	67
Chromosome studies (10 cases)		
Normal	7	70
Trisomy 13	2	20
Trisomy 18	1	10

mal chromosomes, 30 per cent (3 cases) had chromosomal abnomalities, trisomy 13; 2 cases and trisomy 18; 1 case. All of them had extrafacial abnormalities as well. The case of trisomy 18 had small omphalocele. Of 2 cases with trisomy 13, one had omphalocele and hydronephrosis, whereas, the other had a single umbilical artery.

Elective termination was done in all cases after proper counseling. The diagnoses of all cases were postnatally confirmed by autopsy.

DISCUSSION

It is estimated that holoprosencephaly can be expected to represent 16 per cent or more of all cases of hydrocephalus detected prenatally[8]. It is important to differrentiate holoprosencephaly from simple hydrocephalus because they are different in aspects of both management and prognosis. Once alobar or semilobar holoprosencephaly is definitely diagnosed, therapeutic termination should be offered because of uniformly poor outcome.

This study indicates that the diagnosis of holoprosencephaly is based exclusively on sonographic features; there are no obstetric signs of the condition. As most anomalies, the diagnosis is made either in the course of routine ultrasound screening or as the result of a scan done for other indications.

Although, this conditon is rarely found at birth, it is probably associated with high intrauterine fatality rate and it is likely that the obstetric sonographers will encounter it more frequently than expected from epidemiological surveys at birth. This concept is supported by one study on voluntary terminations of pregnancies in the first and second trimesters, in which holoprosencephaly was found in 1 of 250 conceptuses[9].

By using high-frequency transvaginal transducers, diverticulation of the forebrain can be demonstrated as early as the seventh week of amenorrhea[10]. Indeed, by using this approach, a diagnosis of alobar variety can be easily made at the onset of the second trimester as in the third case of this report, and be possible as early as the 11th week[11].

From this study, we can summarize that the sonographic features of holoprosencephaly include fused thalami and monoventricular cavity and absent falx cerebri. Facial abnormalities are the most common extra-cranial anomalies including hypotelorism, cyclopia, proboscis, cleft lip or palate, flat nose. Facial anomalies have been identified in approximately half of them, which is consistent with another report[8]. When other extracranial anomalies are found, it is likely to have facial anomalies as well. The ultrasonographic hallmark of the diagnosis is the obliteration, either wholly or in part, of the membrane separating the lateral ventricles. For an uncommon form, semilobar type, we observed that all had a monoventricular cavity with increased cerebral tissue, especially in the occipital lobes, thus falx and separated ventricles are seen dorsally as shown in Fig. 1-C.

Although some authors have emphasized demonstration of intracranial findings together with characteristic facial anomalies for diagnosing holoprosencephaly[12,13], this series indicates that facial malformations are not always present and so are less sensitive than the intracranial findings alone. Nevertheless, demonstration of facial abnor-

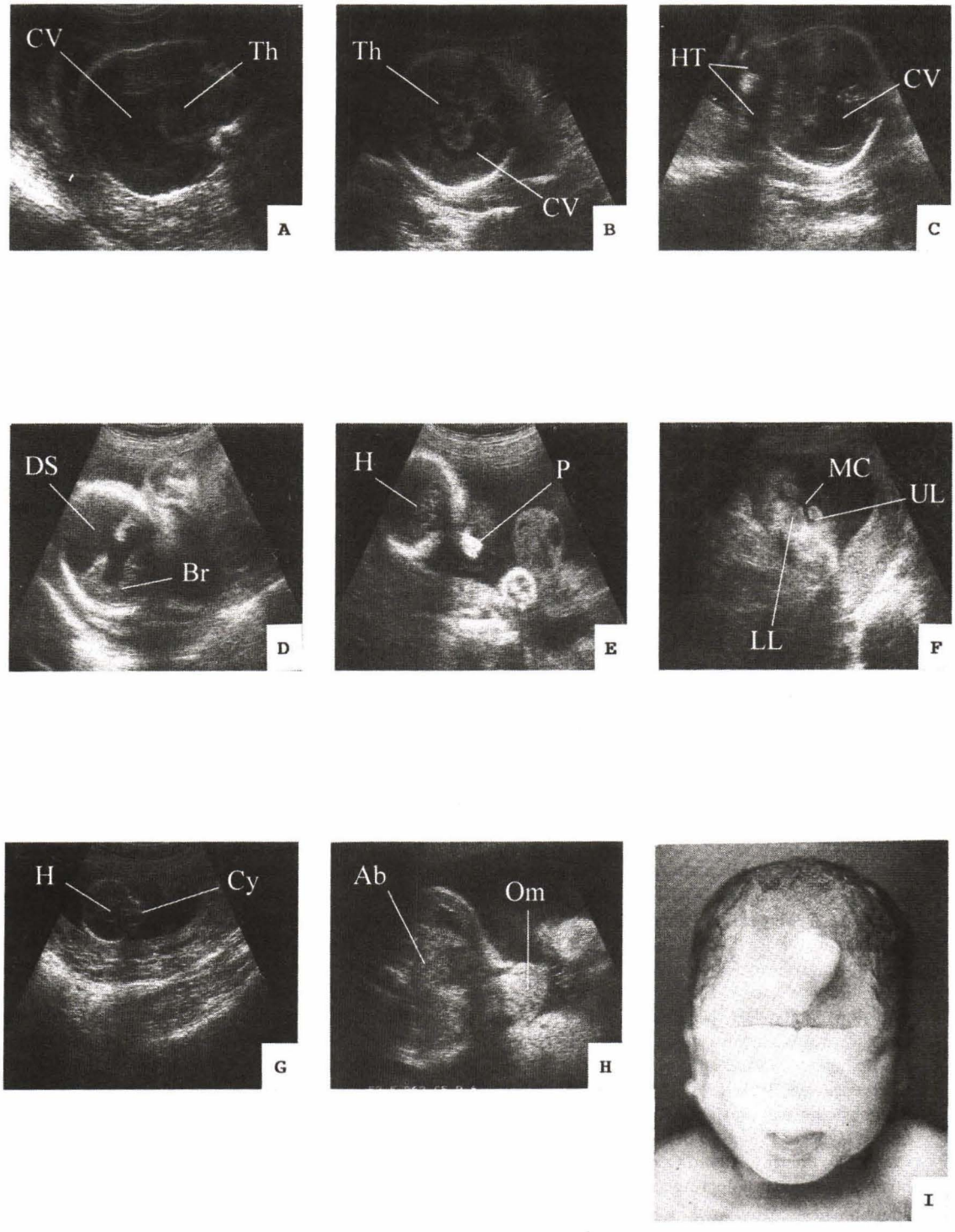

Fig. 1. Sonographic images show common ventricle; CV (A-C), dorsal sac; DS (D), fused thalamus; Th (A) in alobar type, non-fused thalamus; Th (B) in semilo bar type, hypotelorism; HT (C), proboscis; P (E), midline cleft; MC (F), cyclopia ; Cy (G), and small omphalocele; Om (H). Neonatal appearance of proboscis is shown in figure 1. (Br=brain, H=head, Ab=abdomen).

malities may add confidence to the diagnosis and help distinguish the pancake type of alobar HP from hydranencephaly. Knowledge of facial abnormalities may also be helpful for counseling and prognostic purposes.

Our experience shows that a diagnosis of alobar holoprosencephaly can be easily made at the onset of the second trimester, and may be possible as early as the 11th week[11] Evaluation of the karyotype should always be offered, as this information has a major impact on the formation of the recurrence risk for future pregnancies. It should be stressed that infants with any kind of holoprosencephaly may have a normal face.

Chromosomal abnormalities were found in only 30 per cent of cases in this series. This is somewhat lower than in other reports in which chromosomal abnormalities have been identified in approximately half of the fetuses[14-16]. However, our series is too small to make a definite conclusion. Trisomy 13 is the most common, followed by a variety of other karyotypes such as 13q-, trisomy 18, 18q-, and triploidy[15]. Interestingly, all cases of abnormal chromosomes in this study had associated extra-cranial anomalies other than facial defects. The findings suggest that prevalence of chromosomal anomaly be very low in cases of isolated holoprosencephaly or associated with facial abnormalities only. These findings are consistent with the report of Bery[17].

In conclusion, in our experience the most valuable clue to the diagnosis is the demonstration of the single primitive ventricle. When present, the dorsal sac can be recognized, as well as facial anomalies such as cyclopia, hypotelorism, anophathalmia, arhinia, proboscis, and median cleft lip. Demons tration of facial anomalies strengthens the diagnosis of holoprosencephaly based on central nervous system findings. Conversely, should any of these facial features be serendipitously encountered, a careful examination of the intracranial contents is recommended.

(Received for publication on September 8, 1997)

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การวินิจฉัย holoprosencephaly ก่อนคลอด ด้วยคลื่นเสียงความถี่สูง

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กระบวนรายงานผู้ป่วยของการศึกษาลักษณะทางคลื่นเสียงความถี่สูงในการวินิจฉัยก่อนคลอดของทารกที่เป็น holoprosencephaly ซึ่งได้ทำการศึกษาที่ภาควิชาสูติศาสตร์และนรีเวชวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่ โดยการรวบรวมภาวะ holoprosencephaly ซึ่งได้ทำการวินิจฉัยก่อนคลอดจำนวน 12 ราย และติดตามผลหลังคลอด (พยาธิวิทยา) ผลการศึกษาพบว่ามีความถูกต้องในการวินิจฉัยทุกราย โดย 8 รายวินิจฉัยได้ในสองไตรมาสแรกของการตั้งครรภ์ ลักษณะทางคลื่นเสียงพบว่าทุกรายมีการรวมกัน ของ lateral ventricle เป็นช่องเดียว ธาลามัสเชื่อมรวมกัน ไม่มี falx และ carvum septum pellucidum ครึ่งหนึ่งพบความผิดปกตินอกกระโหลกศีรษะร่วมด้วย ซึ่งทุกรายนั้นมีความผิดปกติที่ใบหน้า ร้อยละ 25 (3 ราย) มีภาวะครรภ์แฝดน้ำ และ 1 รายมีภาวะน้ำคร่ำน้อย ร้อยละ 30 มีความผิดปกติของโครโมโซมแบบ aneuploidy ซึ่งเป็น trisomy 13 และ 18 (2 และ 1 รายตามลำดับ)

สรุป คลื่นเสียงความถี่สูงมีความถูกต้องสูงมากในการวินิจฉัย holoprosencephaly ลักษณะที่จำเพาะที่สุดคือการตรวจพบการรวมกันของ lateral ventricles นอกจากนั้นการตรวจพบความผิดปกติของใบหน้าจะช่วยเพิ่มความมั่นใจในการวินิจฉัย และในทางกลับกัน การพบความผิดปกติที่หน้าโดยบังเอิญควรตรวจในกระโหลกศีรษะอย่างละเอียด

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