

Holoprosencephaly and Cyclopia Visualized by Two- and Three-Dimensional Prenatal Ultrasound

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We report on the ultrasound (US) detection of holoprosencephaly with cyclopia at a gestational age of 16 weeks. The sonographic diagnosis was based on the intracranial finding of fused thalami with no visible midline structures and facial abnormalities, including cyclopia and proboscis. We evaluated the fetal face by 3-dimensional (3D) transabdominal US and were able to identify the cyclopia below the proboscis. These findings are characteristic of alobar holoprosencephaly. With the informed consent of the patient, the pregnancy was terminated by prostaglandin induction after proper counseling. Chromosome study of the abortus revealed a normal karyotype (46, XY). Postmortem examination of the abortus confirmed the presence of cyclopia and a proboscis. The use of 3D prenatal US made additional diagnostic images possible. (*Chang Gung Med J* 2002;25:207-10)

Key words: holoprosencephaly, cyclopia, proboscis, 3-dimensional prenatal ultrasound.

Holoprosencephaly is a rare cerebral abnormality arising from failure of the prosencephalon to cleave, which is accompanied by incomplete midfacial development. Cyclopia associated with holoprosencephaly is a severe central nervous system anomaly. The prenatal diagnosis of holoprosencephaly by ultrasound (US) has been described.^(1,2) A transabdominal route allowed a prenatal diagnosis mainly after the second trimester, and a transvaginal approach made earlier diagnosis in the first trimester possible.^(3,4)

We describe a case of holoprosencephaly with proboscis and cyclopia identified at 16-weeks' gestation by 2- (2D) and 3-dimensional (3D) transabdominal US.

CASE REPORT

A 27-year-old, gravida 5 para 2, Taiwanese

woman was referred to our department for targeted US because of a previous obstetric history of fetal anomaly. The para 2 fetus was terminated at a gestational age of 25 weeks due to holoprosencephaly. At the first examination, the gestational age was 16 weeks according to her last menstrual period. The US data of biometric measurements were biparietal diameter of 35 mm, abdominal circumference of 107 mm, and femur length of 25 mm. Evaluation of the fetal anatomy showed abnormal development of the brain with an appendage protruding from the forehead being noted (Fig. 1). A fused thalami was seen, and no mid-line echo could be identified. We evaluated the fetal face by 3D US with a transabdominal transducer (Medison 530D, 5-MHz probe, Korea) and were able to identify cyclopia below the proboscis at 16th week of gestation (Fig. 2). These findings are characteristic of alobar holoprosencephaly.

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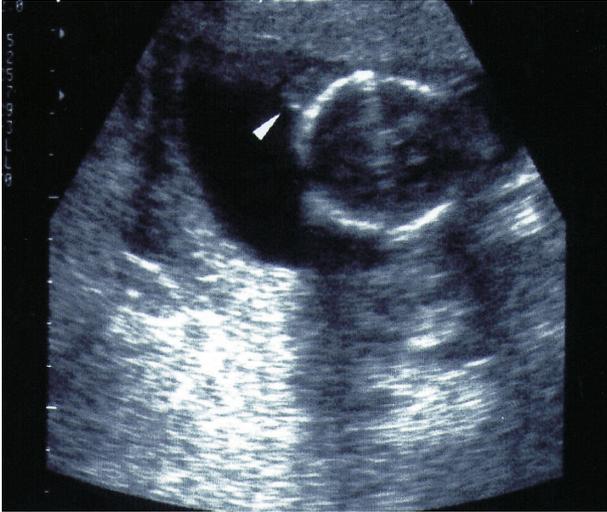


Fig. 1 Axial view of the fetal head showing the fused thalami with the absence of a midline echo, and a proboscis (arrowhead).



Fig. 2 Three-dimensional reconstruction of the fetal face revealing the cyclopia and a proboscis above it.

With the informed consent of the patient, the pregnancy was terminated by prostaglandin induction after proper counseling. A chromosome study of the abortus revealed a normal karyotype (46, XY). The TORCH (toxoplasmosis other rubella cytomegalovirus herpesvirus) serum tests revealed positive immunoglobulin G for cytomegalovirus. Postmortem examination of the abortus confirmed the presence of cyclopia and a proboscis (Fig. 3).



Fig. 3 Postmortem photograph of the fetus with cyclopia and proboscis.

DISCUSSION

Holoprosencephaly refers to a spectrum of malformations resulting from incomplete or a total lack of cleavage of the prosencephalon into cerebral hemispheres during embryogenesis. It is generally accepted that the disorder can be divided into 3 categories: alobar, semilobar, and lobar types.⁽⁵⁾ Alobar holoprosencephaly is the most severe form and is characterized by an absence of the interhemispheric fissure, a single primitive ventricle, neurohypophysis, and olfactory bulbs. The prosencephalon is responsible for normal development of the median facial structures. Failure of the process of induction between development of the brain and the face results in several facial deformities that accompany holoprosencephaly including cyclopia, ethmocephaly, cebocephaly, and a median cleft lip.

Chervenak et al.⁽¹⁾ proposed that both hypotelorism and the absence of the midline should be observed sonographically to diagnose holoprosencephaly with certainty. In our case, 2D transabdominal US demonstrated the fused thalami with the absence of a midline echo, while 3D transabdominal US showed cyclopia with a proboscis. These findings are typical of alobar holoprosencephaly.

The etiology of holoprosencephaly is still largely unknown. Most cases are sporadic. Heterogeneous factors have been implicated as possible

causes. Chromosomal abnormalities are found in 20%-67% of fetuses with holoprosencephaly, with trisomy 13 being the most common.^(6,7) Cyclopia has been associated with prenatal infection by cytomegalovirus.⁽⁸⁾ Hereditary patterns have been reported with an autosomal dominant inheritance with variable penetrance as well as autosomal and X-linked recessiveness.^(6,9)

Genetic counseling in couples who have had 1 child with holoprosencephaly is complex. The reported prevalence of holoprosencephaly has been estimated to be between 0.6 and 0.9 of 10,000 live births.^(10,11) Cyclopia has been reported to occur in 1 out of 40,000 births.⁽³⁾ The recurrence risk is estimated in chromosomally normal cases to be 6%; with an abnormal karyotype, the recurrence risk is about 1%.⁽¹¹⁾ Familial autosomal dominant or recessive inheritance has been reported to have a recurrence risk of 50% or 25%, respectively.^(9,11) Therefore, karyotyping should be offered in an effort to help with counseling on the recurrent risk. Early attempts at detection of this anomaly are justified in pregnancies with a positive familiar history.

Two-dimensional US imaging is the basis for the detection of holoprosencephaly. Three-dimensional US represents a diagnostic tool which may enhance the imaging of the anomaly with greater confidence.⁽¹²⁾ Our experience suggests that 3D US can play a role in a prenatal diagnosis and applies to identification of the surface anatomic structure by sonographers and parents as well. With advances in diagnostic imaging and the use of a transvaginal approach, a prenatal diagnosis is possible at an earlier gestational age than with transabdominal ultrasound.^(3,4)

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空前腦症合併獨眼畸形之二維及三維胎兒超音波影像

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空前腦症合併獨眼畸形為一極罕見之先天性中樞神經異常。本文報告一位27歲孕婦，因前一胎經產前診斷為空前腦症而接受引產之產科病史，於妊娠16週時轉診本院接受產前檢查，經二維及三維超音波診斷為空前腦症合併獨眼畸形及象鼻。三維超音波之影像，呈現空前腦症之眼鼻異常，有助於本例之產前診斷。(長庚醫誌 2002;25:207-10)

關鍵字：空前腦症，獨眼畸形，象鼻，三維超音波。