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CASE REPORT

A Rare Case of Early-diagnosed Trisomy 13 Syndrome with Typical Semilobar Holoprosencephaly, Cyclopia, and Proboscis: A Case Report

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Trisomy 13 syndrome is a lethal chromosomal disorder characterized by severe congenital anomalies. We report a case of trisomy 13 syndrome with semilobar holoprosencephaly, cyclopia, proboscis, omphalocele, and an absent nasal bone, prenatally diagnosed by first-trimester ultrasonography. The diagnosis was confirmed by chromosomal analysis. The pregnancy was eventually terminated at 14 weeks of gestation. The poor prognosis of trisomy 13 syndrome and holoprosencephaly prompts the demand for early prenatal diagnosis. We present this case to introduce some of the typical features of semilobar holoprosencephaly, including an anteriorly fused ventricle with partially fused thalami and absent falx, and to sensitize physicians to similar sonographic findings in the future.

Key words: Holoprosencephaly, trisomy 13 syndrome, chromosome disorders, neural tube defects

INTRODUCTION

Trisomy 13 syndrome, first described by Patau *et al*.[1] in 1960, is a lethal chromosomal disorder caused by an extra copy of chromosome 13. The prevalence of trisomy 13 syndrome in newborns is approximately 1 in 5000,[2] and early fetal death is commonly observed in prenatally diagnosed cases. Fetal sonographic findings can vary. Common anomalies include holoprosencephaly, cyclopia, proboscis, microcephaly, acrania, microphthalmia, and polydactyly.

We present a case of trisomy 13 syndrome with rare semilobar holoprosencephaly, cyclopia, and proboscis detected by early prenatal ultrasonography at 12 weeks of gestation, and chromosomal analysis confirmed the diagnosis.

CASE REPORT

A 42-year-old Asian woman (gravida 3, para 1, and abortus 1) was referred to our department for first-trimester fetal ultrasonography. Her personal and family histories were unremarkable. The patient's previous pregnancy ended at term, with the delivery of a healthy male weighing 4100 g.

The patient's first fetal ultrasonography was performed at 8 weeks of gestation, with normal findings and the fetal heartbeat detected. At 12 weeks of gestation, the patient underwent a second ultrasonography that revealed mild fetal tachycardia. Holoprosencephaly [Figure 1a], an absent nasal bone [Figure 1b], proboscis [Figure 2a], absent eye sockets and lens, and omphalocele [Figure 2b] were also noted sonographically, which are findings consistent with some congenital cytogenetic abnormalities, especially trisomy 13 syndrome. Typical anomalies of trisomy 13 syndrome include holoprosencephaly, microcephaly, acrania, microphthalmia, polydactyly, and early fetal death.[3] The patient underwent chorionic villus sampling for chromosomal analysis within the next few weeks, which confirmed the diagnosis of trisomy 13 syndrome. The pregnancy was successfully terminated at 14 weeks of gestation with the delivery of a dead fetus.

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External examination of the dead fetus [Figure 3] confirmed proboscis, cyclopia, and omphalocele, which were all consistent with the findings on fetal ultrasonography. The patient was ultimately discharged home 1 day later.

DISCUSSION

Holoprosencephaly is a spectrum of cerebral anomalies that develops from the failure of the prosencephalon to differentiate into two cerebral hemispheres and lateral ventricles in the first trimester. This failure is responsible for the partial-to-complete fusion of the cerebral hemispheres and lateral ventricles, which can be detected by early ultrasonography. The prevalence of holoprosencephaly is approximately 1 in 10,000–15,000 births. However, abnormalities have been detected in nearly 1 of 250 early abortion fetuses.[4]

"Face predicts the brain" is a concept introduced by DeMyer in 1971.[5] Various facial dysmorphisms are associated with holoprosencephaly. Some of the most severe facial dysmorphisms, including cyclopia and proboscis, may be observed in holoprosencephaly.[6] Our case involved two typical facial anomalies, including cyclopia, the absence of normal eyeballs and a medially placed eye, and proboscis, a noncanalized nose projecting from the medial forehead.

There are three main types of holoprosencephaly: alobar, semilobar, and lobar. Alobar holoprosencephaly is the most severe type, characterized by a complete failure of cleavage of the prosencephalon and resulting in fused cerebral hemispheres with a large monoventricle, completely fused thalami, and absence of the falx cerebri [Figure 4a].[7,8] Normally, the falx can be seen between the two echogenic choroid plexuses under coronal ultrasonography in normal brains. Semilobar holoprosencephaly is characterized by partial cleavage of the prosencephalon, which shows anteriorly fused cerebral hemispheres and lateral ventricles and a partially fused thalamus under ultrasound [Figure 1a]. Lobar holoprosencephaly, considered a mild type, is characterized by near-total cleavage of cerebral hemispheres in the presence of the falx [Figure 4b].[8] In our case, early sonography revealed some typical features of semilobar holoprosencephaly, including an anteriorly fused ventricle with partially fused thalami and an absent falx [Figure 1a]. Associated anomalies, including cyclopia and proboscis, were also noted and later proven using the gross

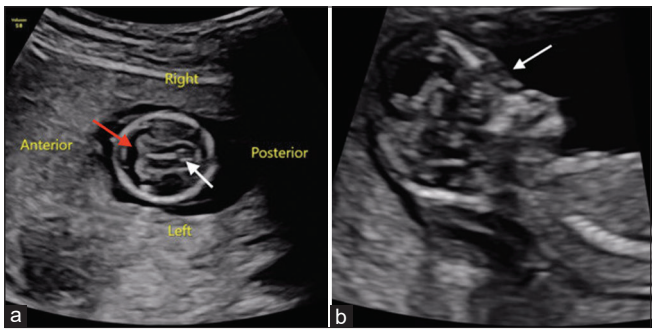

Figure 1: (a) Coronal ultrasonography at 12 weeks gestation revealing semilobar holoprosencephaly, including an anteriorly fused ventricle (red arrow) with partially fused thalami (white arrow) and an absent falx. (b) Sagittal ultrasonography showing an absent nasal bone (white arrow)

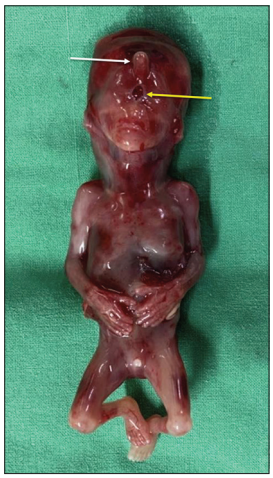

Figure 3: Frontal view of the dead fetus showing typical proboscis (white arrow) and cyclopia (yellow arrow)

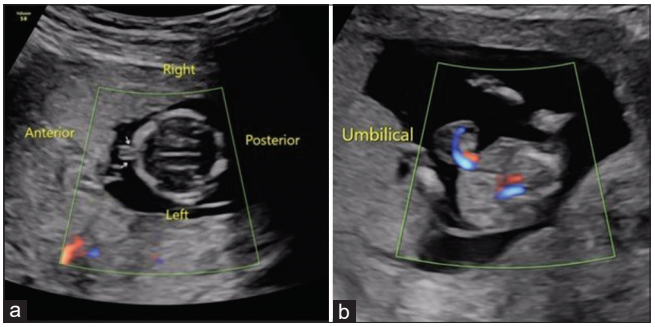

Figure 2: (a) Coronal ultrasonography showing proboscis (white arrows). (b) Doppler ultrasonography showing omphalocele

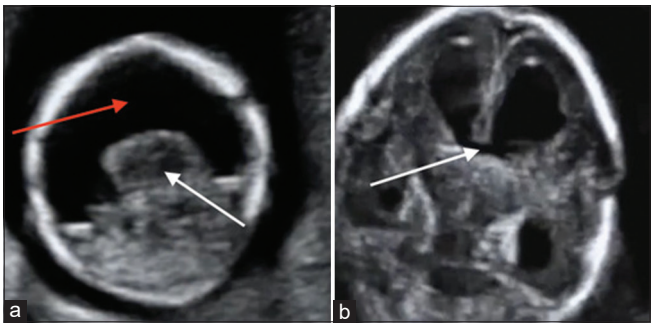

Figure 4: (a) Alobar holoprosencephaly revealing a large mono ventricle with fused lateral ventricles (red arrow), completely fused thalami (white arrow), and an absence of the falx cerebri under the ultrasound. (b) Lobar holoprosencephaly showing partial fusion of the lateral ventricles (white arrow)

specimen of the fetus. In general, physicians do not diagnose holoprosencephaly through sonography before the 10th week of gestation because the falx typically becomes sonographically obvious at 10 weeks of gestation.[9]

Holoprosencephaly is highly associated with trisomy 13 syndrome. According to previous studies, alobar holoprosencephaly accounts for 40%–75% of all holoprosencephaly cases, and 30%–40% have chromosomal abnormalities, particularly trisomy 13 syndrome.[10]

We searched relative articles in the recent 30 years and summarized the ultrasound finding during the second trimester with holoprosencephaly, cyclopia, and proboscis with trisomy 13 listed as shown in Table 1.

Thus, we inferred that it is also crucial that holoprosencephaly, cyclopia, and proboscis were significant in trisomy 13. When we found these characteristics during the prenatal ultrasound, we highly suspect it may be a trisomy 13.

The majority of fetuses with trisomy 13 display morphological abnormalities on ultrasound in the first and second trimesters with major structural abnormalities; however, it should be noted that a small number of fetuses with trisomy 13 can be missed on ultrasound. According to Danh Cuong Tran *et al.*,[11] the false-negative rate may be 15% that no anomaly with trisomy 13, and the false-positive rate may be 1% that anomaly in a normal fetus. It is so surprising that we may miss diagnosis with trisomy 13 if we detected it only by prenatal ultrasound. Besides, common malformations like craniofacial defects and cerebral malformations could also be seen in trisomy 18; hence, it is important to confirm the definite diagnosis by chorionic villi sampling or amniocentesis.

Diagnosis of Patau syndrome can be made prenatally with chorionic villi sampling, amniocentesis, or fetal-free DNA analysis. The differences are listed in Table 2.

Chorionic villi sampling and amniocentesis are both more invasive procedures and may cause miscarriage; a noninvasive prenatal test (cell-free DNA analysis) was less invasive; however, it is expensive. Accuracies of the three prenatal tests are all above 99%.

Overall, this is a typical case of trisomy 13 syndrome with semilobar holoprosencephaly with rare cyclopia and Proboscis. The purpose of presenting this case is to introduce some of the typical features of semilobar holoprosencephaly, cyclopia, and proboscis found in this case and to sensitize physicians to similar sonographic findings in the future.

Table 1: Summary of three articles of Trisomy 13 with finding of Holoprosencephaly, Cyclopia, Proboscis

Abnormalities Case	Holoprosencephaly	Cyclopia	Proboscis
C D Lehman 1995 (33 cases)	13	2	Not mentioned
T. Tongsong 2002 (15 cases)	7	6	4
Danh Cuong Tran 2023 (23 cases)	3	1	1
Our case	1	1	1
All (72 cases)	24	10	6*

*We only calculated T. Tongsong 2002. Danh Cuong Tran 2023 and our case

Table 2: Different method of diagnosis with Patau syndrome

	Chorionic villi sampling	Amniocentesis	Cell free DNA analysis
Times	10~13 weeks	15-20 weeks	10 weeks
Limitation	Invasive procedure		Non- Invasive procedure
Accuracy	>99%	>99%	>99%
Application	Changes in all chromosomes		Common aneuploid (Trisomy 13, 18, 21…)
Miscarriage risk	1/100-1/200	1/200-1/500	No risk

CONCLUSION

The poor prognosis of trisomy 13 syndrome with holoprosencephaly necessitates early prenatal diagnosis. We present a typical case of trisomy 13 syndrome with semilobar holoprosencephaly, cyclopia, and proboscis, introduce some of the typical features of semilobar holoprosencephaly, including an anteriorly fused ventricle with partially fused thalami and an absent falx, and sensitize physicians to similar sonographic findings in the future. With the help of the high sensitivity and accuracy of early prenatal ultrasound, we can detect fetuses with chromosomal disorders at an early stage to avoid the grief of bearing or delivering a deformed baby. However, there were some limitations that there were 15% of trisomy 13 fetuses without abnormal ultrasound finding; hence, we may miss the diagnosis. We can suggest the mother undertake a further prenatal examination like cell-free DNA analysis or amniocentesis. We also need to check the major structure in detail during the early second trimester. If we find abnormalities during the prenatal ultrasound, we need to confirm the definite diagnosis by chorionic villi sampling or amniocentesis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published, and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Data availability statement

The data that support the findings of this study are available from the corresponding author, Dr. Lin, upon reasonable request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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