ABSTRACT

We would like to present a rare case of alobar holoprosencephaly (HPE) in a fetus diagnosed by routine sonography in the second trimester. Structural sonography demonstrated multiple facial anomalies including absent nasal bone, flat facial profile, hypotelorism, fusion of the orbits and proboscis. After counseling, termination of pregnancy was performed by vaginally administered misoprostol. Karyotyping of amniotic fluid cells revealed an isochromosome 18q, resulting in a trisomy 18q and monosomy 18p. A stillborn female of 390 g with several congenital anomalies was born. Postmortem examination demonstrated several anomalies including the HPE, cyclopia, double fused eye, absence of the nose, and the presence of a proboscis. In the literature only a few cases have been published.

KEYWORDS: Alobar holoprosencephaly, cyclopia, proboscis, prenatal diagnosis, isochromosome 18q, sonography

CASE REPORT

A 37-year-old, gravida 2, para 1 woman was seen for routine sonographic scanning at 20†5 weeks of gestation. Obstetric history revealed a spontaneous birth of a male fetus of 3080 g at 40†3 weeks of gestation. The parents were nonconsanguineous and without dysmorphic features or congenital anomalies. There was no history of infection or drug abuse, and serological screening for HIV, hepatitis B, and syphilis was negative. Until then, the pregnancy had been uneventful. The patient had declined first-trimester aneuploidy screening. At routine sonography, an abnormal

1Department of Obstetrics and Gynecology, Amphia Hospital Breda, Breda; 2Department of Clinical Genetics, Erasmus MC, Rotterdam, The Netherlands.

Address for correspondence and reprint requests: Meike Bangma, Department of Obstetrics and Gynecology, Amphia Hospital Breda, Langendijk 75, 4819 EV, Breda, The Netherlands (e-mail: Mbangma@amphia.nl).
image of the fetal brain and facial structures was seen. The patient was referred to our hospital for detailed ultrasound examination. An alobar HPE with facial anomalies including absent nasal bone, flat facial profile, hypotelorism, fusion of the orbits and proboscis were noted. Other anomalies seen were a single umbilical artery, abnormal four-chamber view of the heart, especially abnormal shape of the right atrium, and cystic kidneys. Amniocentesis was performed at 21+1 weeks of gestation and an abnormal karyotype 46,XX,i(18)(q10) was diagnosed. The fetus therefore had a trisomy of the long arm and a monosomy of the short arm of chromosome 18. The parents decided to terminate the pregnancy on the basis of the ultrasound abnormalities. Eight hours after inducing labor with vaginally administered misoprostol, a stillborn female fetus was delivered at 21+3 weeks of gestation. Birth weight was 390 g (normal weight at 21 weeks: 360 g). Several congenital anomalies were confirmed at postmortem examination including a cyclopia with a double fused eye, the absence of the nose, and the presence of a proboscis (Fig. 1). Postmortem magnetic resonance imaging scan was performed. The coronal slides gave a definite view of the monoventricular cavity and the proboscis (Fig. 2). Autopsy demonstrated further the alobar HPE (Fig. 3), absence of the corpus callosum, perimembranous ventricular septum defect, bicuspid pulmonal artery valves, malrotation of the small bowel, bilateral hydronephrosis, right megaureter, and uterus bicornis.

Figure 1  Postnatal image of proboscis and cyclopia with a double fused eye.

Figure 2  Postmortem magnetic resonance imaging coronal slide demonstrating the monoventricle of the brain of the fetus.

Figure 3  Postmortem image at autopsy demonstrating the monoventricle of the brain.
DISCUSSION

In our case, the fetal karyotyping showed an isochromosome 18q, resulting in a monosomy 18p and trisomy 18q. This chromosome aberration occurred de novo because both parents had a normal karyotype. The HPE4 gene, *TGIF*, is located on the distal part of chromosome 18, namely 18p11.31. Hemizygosity of HPE4 does not automatically result in the phenotype of HPE, suggesting that multiple genetic and environmental factors are involved in the development of the HPE phenotypes. For the de novo case, the recurrence risk for siblings is not significantly increased above that of the general population.

There have only been seven cases previously reported of isochromosome 18q in combination with HPE (Table 1). Of interest, Levy-Mozziconacci et al described a case similar to ours, with a proboscis and a bicornuate uterus, related to i(18)(q10). The karyotype abnormality in that particular case, however, was a dic(18)(p11.3), which means the fetus had three copies of the q-arm and three copies of a small part of the p-arm, excluding the locus where HPE4 is located, therefore making their case different from ours.

Abnormalities in the forearms and hand positioning were described in another case with an isochromosome 18q without HPE, but not in ours. Although the mother in our case is 37 years old, reviewing the other reported cases, it is unlikely that there is an association between isochromosome 18q and increased maternal age. This case stresses the importance of standard sonography for all pregnant women between 18 and 21 weeks to detect any congenital anomalies of the fetus.

ACKNOWLEDGMENTS

The authors thank Dr. D. de Jong, Department of Radiology, for providing the magnetic resonance image.

REFERENCES

8. de Pater JM, Scheres JM, Brons J. Abnormal chromosome 18 in prenatal diagnosis with holoprosencephaly. Prenat Diagn 1997;17:887–888