We present a case with alobar holoprosencephaly (HPE) and proboscis diagnosed at 21 weeks of gestation during routine sonographic scanning. Chromosome analysis demonstrated an abnormal karyotype 46,XX,i(18)(q10). Isochromosome 18q is a rare cytogenetic abnormality. The phenotypical features of this chromosomal abnormality are variable and overlap with trisomy 18 and monosomy 18p. HPE is rarely described in trisomy 18, and occasionally in monosomy 18p. Actually, isochromosome 18q associated with alobar HPE was only described eight times before. We give a review of the literature and describe a case of alobar HPE, diagnosed by routine sonography in the second trimester, associated with an isochromosome 18q.

CASE REPORT
A 37-year-old, gravida 2, para 1 woman was seen for routine sonographic scanning at 20 weeks of gestation. Obstetric history revealed a spontaneous birth of a male fetus of 3080 g at 40 weeks of gestation. The parents were nonconsanguineous and without dysmorphic features or congenital anomalies. The family history of the mother mentioned a sister who died at the age of 17 because of an intracranial bleeding from an aneurysm. 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
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\textsuperscript{+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\textsuperscript{+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.
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.3

There have only been seven cases4–10 previously reported of isochromosome 18q in combination with HPE (Table 1). Of interest, Levy-Mozziconacci et al9 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 case11 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.1 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.

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