Introduction
Holoprosencephaly (HPE) is the commonest congenital brain malformation and indicates absent or incomplete midline cleavage of the developing brain during early gestation. Due to the common embryologic origin this abnormality is usually accompanied by abnormal craniofacial features. There are three types of the abnormality according the severity of features; alobar, semilobar and lobar HPE. Half of the cases will have genetic origin, mainly chromosomal, such as trisomy 13, 18 and triploidy. Four specific genes have been identified as responsible for HPE (SHH, ZIC2, SIX3 and TGIF), while other genes and chromosomal loci seem to play a role in rare cases. In the remaining cases an environmental factor, such as smoking, alcohol consumption, gestational diabetes, antiepileptic drugs or congenital infections, can be identified. Combination of mutations in major and/or minor HPE genes accounts for the variability of the disease and makes genetic counseling a challenge.

Case presentation
Our case was a 23-year-old female with no family or medical history referred for the first trimester combined screening. She reported a previous history of a daughter with severe intellectual disability without anatomical defects and a first-trimester termination of pregnancy for HPE. Unfortunately, our sonographic findings of absent cerebral hemispheres and fused thalami were compatible with the diagnosis of recurrent alobar HPE. Thus, chorionic villus sampling was performed and the sample was analyzed with conventional karyotyping and array-CGH, also including mutational analysis of the HPE genes. Interestingly, array-CGH analysis revealed an 8.9-Mb deficit at the chromosomal region 7q36.1q36.3 and a 4.9-Mb duplication at the chromosomal region 12q24.32q24.33. After genetic counseling, pregnancy was terminated and parental karyotyping was performed. The results showed that the father was a carrier of a translocation between chromosomes 7 and 12. It is assumed that when a 7q deletion is accompanied by partial trisomy of another chromosome, the result is a more severe cerebral phenotype, due to extra gene dosage. Furthermore, there are genes at the deleted region and one gene at the duplicated region, which may play a role in brain development.

Conclusion
Array-CGH has an incremental yield over conventional cytogenetics, which has been mostly highlighted in cases of fetuses with structural defects. HPE is a congenital disease with incomplete penetrance and variable expressivity; therefore, couples with history of HPE should be advised by specialized physicians and the use of array-CGH analysis is crucial to delineate the exact genotype of the fetus and to coordinate genetic counseling.