Possibilities of prenatal diagnosis in cases with brain anomalies and establishment of the risks for future pregnancy

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Introduction:

We present two cases of foetuses with midbrain malformations associated with chromosomal aberrations.

Case report:

Case 1: 24 years old primigravida with insignificant anamnesis and negative first trimestral screening. Ultrasound performed at 21st week of pregnancy revealed complete agenesis of corpus callosum (fig. 1).

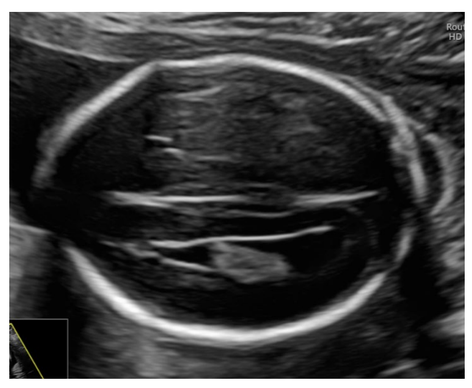

Fig. 1

Case 2: 36 years old primigravida with insignificant anamnesis, conception after IVF of one embryo with positive first trimestral screening and ultrasound finding in 13th week of pregnancy – holoprosencephaly (fig. 2), cheilognatopalatoschisis and absent nasal bone.

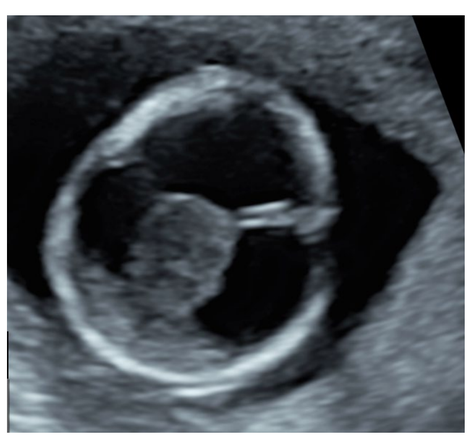

Fig. 2

Both pregnancies have been terminated because of discovered malformations, but previously we performed invasive prenatal array investigation because of determination of the risks for future pregnancy.

Results:

Case 1: array CGH investigation has found 12 kb large heterozygous 9q22.32 microdeletion (fig. 3) involving PTCH1 gene. MLPA analysis of PTCH1 gene has confirmed deletion of 2-3 exon of the gene. Neither of parents is carrier of PTCH1 deletion. We proved new microdeletion in the family with low risk of recurrence.

Case 2: SNP array investigation has found 8,1 Mb large heterozygous 7q36.1q36.3 microdeletion (fig. 4) involving 56 OMIM genes including SHH gene associated with holoprosencephaly. Further cytogenetic analysis proved structural imbalanced chromosomal aberration, 46, XX, del(7)(q36). Karyotype of both parents is normal. We proved new microdeletion in the family with low risk of recurrence.

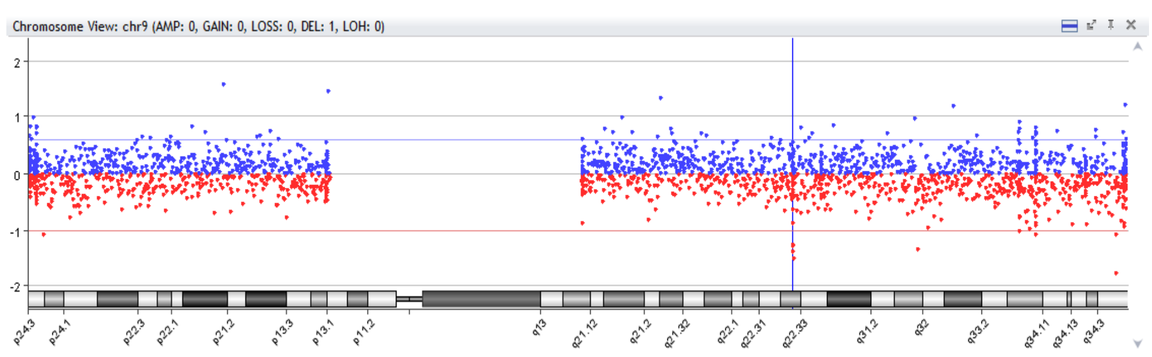

Fig. 3

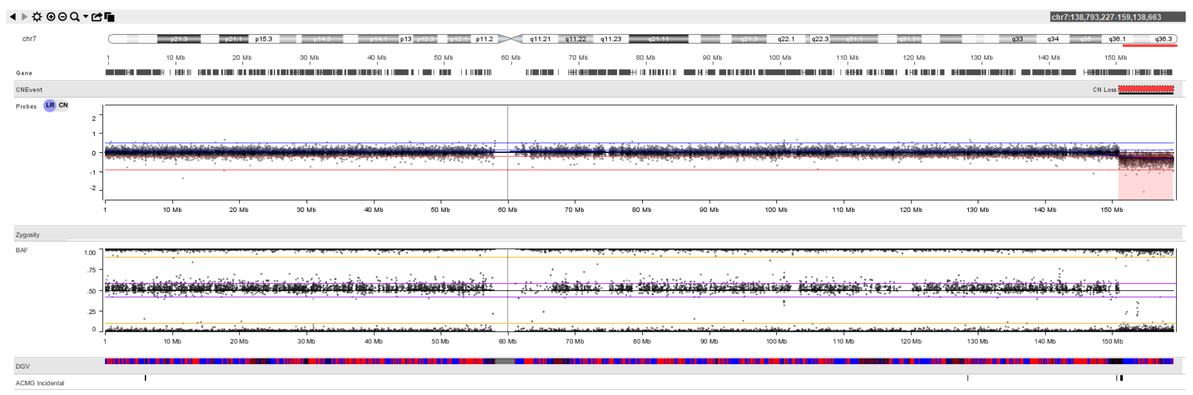

Fig. 4

Conclusions:

Differential diagnosis of agenesis of corpus callosum, holoprosencephaly and other congenital brain anomalies is wide, and may include chromosomal aberrations, single gene mutations, as well as multigene mutations with environmental factors. Identifying genetics cause of brain anomalies during limited time in pregnancy is challenging. Pathogenic mutations in SHH gene are linked to holoprosencephaly (OMIM *142945). Pathogenic mutations in PTCH1 gene are associated with Gorlin syndrome as well as holoprosencephaly (OMIM *610828) and have been repeatedly described in patients with agenesis of corpus callosum. In both cases array analysis allowed us to deliver quick genetic diagnosis during pregnancy and establishing the risk of recurrence for the parents in the future pregnancies.

References:

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