ID 4795: Utility of Olfactory Sulci as a marker of genetic disorders in fetuses with and without major congenital heart defect

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Aim

To assess the value of abnormal Olfactory Sulci (OS) as a marker of genetic disorder, in fetuses undergoing clinical exome sequencing according to the presence or absence of major congenital heart defects (CHD).

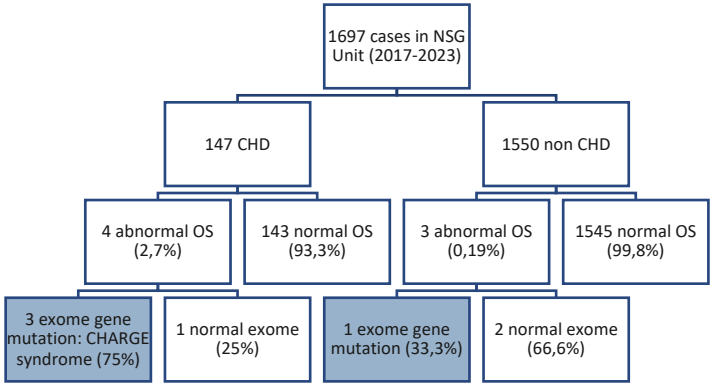
Methods

- Restrospective study including fetuses referred to our neurosonography (NSG) unit from 2017 to 2023. Cases were divided into 2 groups: those associated with CHD and those without.
- Systematic neurosonographic examination was performed in third trimester of gestation.
- OS assessment was carried out in the trans-frontal coronal plane and were considered as **abnormal** if they were underdeveloped (only primary smooth depressions) or **absent** (no depressions were observed).
- Abnormal OS were confirmed by MRI and genetic studies with microarray and clinical exome sequencing were performed to these patients.

Results

Among a total of 1697 cases studied, 147 fetuses had an associated CHD and 1550 had not. Abnormal OS was identified in 4 (2.7%) fetuses in the CHD group and 5 (0.17%) in the non-CHD group. In addition to abnormal OS in the CHD group the following ultrasound features were detected: (i)severe ventricular septal defect (VSD), aberrant right subclavian artery (ARSA), small stomach, short long limbs and small vermis; (ii) muscular and perimembranous VSD, abnormal left subclavian artery (ALSA), right aortic arch and hypoplastic cerebellum; (iii) perimembranous VSD, persistent left superior vena cava (PLSVC), aneurism of the fossa ovalis and a single umbilical artery, and (iv) small cerebellum, intrauterine growth restriction IUGR), VSD, PLSVC, and ARSA. Exome sequencing revealed a heterozygous de novo CHD7 gene mutation, confirming the suspicion of CHARGE syndrome in the first, second and fourth cases (75%).

Among the 5 cases of the other group, only 3 were confirmed by MRI (0,19%). The additional ultrasound findings in these 3 confirmed cases were the: (i) microcephaly and severe and early IUGR, (ii) ventriculomegaly and (iii) ventricle atrium in the upper limit. The 3 cases had normal microarray and only the first case (33%) had a heterozygous incidental variant in GHR gene, which explains growth disturbances.



Conclusions

In our study, the 75% of the CHD group with abnormal OS had a pathogenic variant at exome sequencing signaling CHARGE syndrome, whereas in the non-CHD group only 33% had a pathogenic variant. These results suggest that abnormal OS are a stronger marker of genetic disease when combined with CHD.