KLEEFSTRA SYNDROME - delayed diagnosis in prenatal case with heart malformations

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Introduction:
Kleefstra syndrome is a rare genetic disorder, characterized by intellectual disability, hypotonia, epilepsy, distinctive facial appearance, speech delay and congenital heart malformations (up to 50%). The syndrome is most often caused by a microdeletion of 9q34.3 or rarely by a mutation of EHMT1 gene, which is localized in the critical region.

Most cases occur de novo. Treatment requires a multidisciplinary approach and the prognosis is variable.

Case report:
2010
• 29 years old woman, first pregnancy
• 13+1 g.w.: NT 2,6mm (95th percentile), risk of Down syndrome 1:138
• CVS: karyotype 46, XX
• 22+3 g.w: US multiple heart malformations (AA, DORV, VSD, PS, PI) and a left sided club foot
• FISH (CVS): ish 22q11.2(D22S1627x2) excluded syndrome DiGeorge
• the patient decided to terminate the pregnancy

2016
• MLPA (CVS, kits P036 – E2, P070 – B3 subtelomeric deletions and duplications – MRC, Holland): rsa EHMT1(P036, P070, P250)x 1, (P311)x2
• the investigation revealed a deletion of the EHMT1 gene
• a diagnosis of Kleefstra syndrome in the fetus was determined
• as no duplication was found in the fetus, it is likely that the microdeletion occurred de novo and not as a result of balanced translocation in one of the parents. The recurrence risk in subsequent pregnancies is very low.

Conclusion:
Congenital heart abnormalities occur sporadically or as a part of chromosomal or monogenic disorder. The knowledge of etiology allows to determine recurrence risk.
New methods of molecular genetic testing enable us to establish the diagnosis in cases where it was previously not possible. This is of importance to patients and their families.
A close co-operation between specialties is necessary.

Bibliography: www.rarechromo.org (Kleefstra syndrome), www.kleefstrasyndrome.org