An effective integrated reproductive strategy for hearing loss

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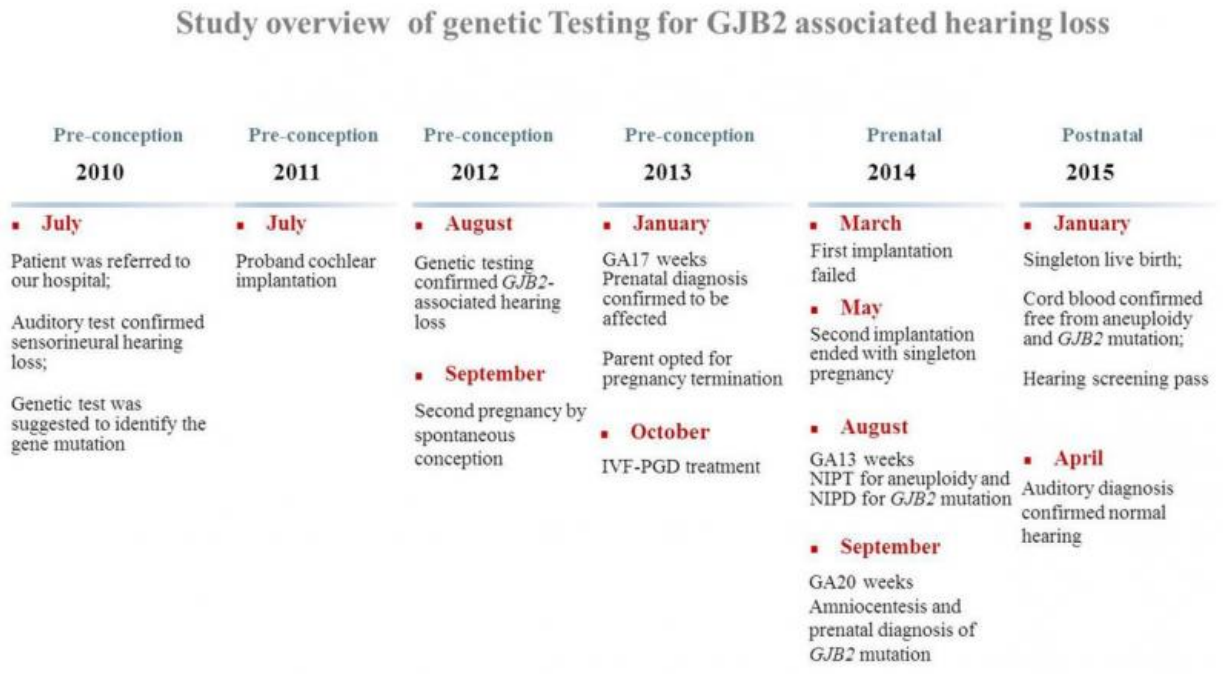

A timescale of the reproductive management of GJB2-associated hearing loss in a family desired to have a hearing normal child. GA, gestational age. Credit: ©Science China Press

Hearing impairment is a major public health problem in the world, affecting over 5% of the world's population - 360 million people, including 328 million adults and 32 million children. Professor WANG Qiuju and her group from Institute of Otolaryngology, Chinese PLA

General Hospital, cooperating with Professor CHEN Zi-Jiang from Center for Reproductive Medicine of Shandong University and, BGI, set out to tackle the transmission of hearing loss by preimplantation genetic diagnosis (PGD), noninvasive prenatal testing (NIPT), and noninvasive prenatal diagnosis (NIPD). They have successfully helped a family carrying mutations causing hearing loss to give birth a hearing normal baby. In addition, they developed an effective strategy in reproductive management of similar cases and potentially other monogenic disorders.

Their work, entitled "Reproductive management through integration of PGD and MPS-based noninvasive prenatal screening/diagnosis for a family with GJB2-associated hearing impairment", was published in *SCIENCE CHINA Life Sciences*. 2015, Vol 58(9).

In their study, a Chinese family with GJB2 associated non-syndromic hearing loss was recruited, consulting for reproduction solution to bear a hearing normal child. Professor Wang and her group developed a customized preconception-to-neonate care trajectory to fulfill this clinical demand by integrating PGD, NIPT/NIPD, invasive procedure and postnatal genetic/auditory diagnosis. After the treatment of in vitro fertilization (IVF), Preimplantation genetic diagnosis of GJB2 c.235delC/c.299-300delAT was carried out based on multiplex nested PCR and STR-based linkage analysis for the purpose of choosing an appropriate embryo for implantation. After counseling with the family, a carrier embryo was transferred to the woman's uterus, and resulted in a successful singleton pregnancy. At the 13th week of pregnancy, NIPT/NIPD, testing for fetal aneuploidy and GJB2-associated hearing loss, was done by genomic DNA (gDNA) from the trio family and cell-free DNA (cfDNA) from maternal plasma, showing the absence of chromosomal abnormality and GJB2-associated hearing loss in the fetus. Amniocentesis was performed at the 20th week, and prenatal diagnosis of fetal GJB2 gene by Sanger sequencing confirmed the safety of the fetus. Neonatal hearing screening by AABR and DPOAE at twenty four

hours after the delivery was performed, confirming the newborn with normal hearing.

Promotion of this integrated strategy could be good news for couples who suffer from deafness and want to have a hearing normal child. It may have a great contribution towards reducing hereditary hearing loss and public health burden. More importantly, this strategy of reproductive management can be also used for diagnosis of other genetic disorders potentially.

The strategy of reproductive management was a collaborative effort involving many scientists, medical physicians and clinicians from different institutes and hospitals. It is an important breakthrough in the reproductive medicine of hereditary hearing loss, which is the first successful PGD case in China of a child free of GJB2-associated hereditary hearing loss, and the first case in the world of integrating NGS-based NIPT/NIPD into the reproductive management of hereditary hearing loss. Though the benefit of the testing strategy presented in this study is obvious, the researchers suggested that the clinical utility needs to be further evaluated, tackling challenges of integrating new technologies into clinical practice. These efforts will have significant impact on the prevention of hereditary hearing loss globally.

More information: WenPing Xiong et al. Reproductive management through integration of PGD and MPS-based noninvasive prenatal screening/diagnosis for a family with GJB2-associated hearing impairment, *Science China Life Sciences* (2015). DOI: 10.1007/s11427-015-4936-y

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