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COMPLEX AUDITORY DISORDERS

The effectiveness of cochlear implantation in mild hearing loss caused by auditory neuropathy spectrum disorder associated with OTOF mutations

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Abstract

Genetics plays a significant role in the etiology of auditory neuropathy spectrum disorders (ANSD). According to previous studies, the most common genetic cause are mutations in the *OTOF* gene, which encode the protein otoferlin. These mutations lead to impaired synaptic transmission in the inner ear and result in auditory synaptopathy [1]. Over 100 mutations in the OTOF gene have been identified, most of them are inactivating mutations that lead to the absence of otoferlin and severe hearing loss. The effectiveness of cochlear implantation (CI) has been demonstrated in patients with this condition and profound hearing loss. However, there are isolated cases of mild to moderate hearing loss, as well as temperature-sensitive hearing loss, in patients with inactivating mutations in the *OTOF* gene [2]. Notably, these cases showed a marked reduction in speech intelligibility despite nearly intact hearing thresholds.

This clinical case describes two sisters with ANSD caused by mutations in the *OTOF* gene. Hearing impairment was identified at ages 5 and 2 years, respectively, for the older and younger sister. Their clinical and audiological data were similar: both had ANSD with mild hearing loss and severe impairment in speech intelligibility. Amplification proved ineffective. Genetic testing revealed two mutations in the *OTOF* gene, confirming the necessity for CI.

Unilateral CIs were performed at ages 9 and 5 years for the older and younger sister, respectively. One year after CI, both sisters demonstrated significant improvements in speech perception and language development.

Objectives

The aim of this study is to describe the clinical picture and management strategies for patients with ANSD caused by mutations in the *OTOF* gene, presenting with mild hearing loss and significant speech intelligibility impairment.

Patients and Methods

- **Patients**: two sisters with *OTOF*-related ANSD with mild hearing loss
- **Methods**: standard audiological assessment including impedancemetry, otoacoustic emissions, auditory brainstem responses (ABR), pure tone audiometry, speech audiometry; Genetic testing (clinical exome sequencing, then whole genome sequencing); eABRs after cochlear implantation.

Results

- ✓ The older sister was referred for audiological assessment at the age of 5 years due to speech and language delays, revealing ANSD with pure tone thresholds of 15-30 dB HL (fig.1). She had an uncomplicated medical history. CT, MRI of the temporal bones, examination by a neurologist and ophthalmologist did not reveal any pathology.
- ✓ The ongoing intensive intervention program (hearing aids and speech therapy) had no effectiveness.
- ✓ The clinical and audiological data of the younger sister were similar. Genetic testing revealed two mutations in the *OTOF* gene (splice site - c.3289-1G>C, and in the intron - c.897+1870A>G).
- ✓ Unilateral CIs were performed at the ages of 9 and 5 years respectively in the older and younger sister. Electrically evoked auditory nerve compound action potentials were recorded intraoperatively from each electrode. Electrically evoked ABRs were recorded (fig.2).
- ✓ Both sisters received intensive auditory rehabilitation. One year after CI they demonstrate significant improvement in speech perception and language development confirmed by speech audiometry data (fig.3-4, younger sister's data).

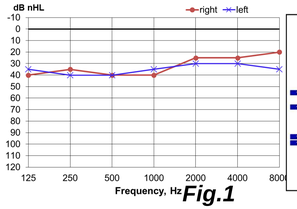

Fig.1

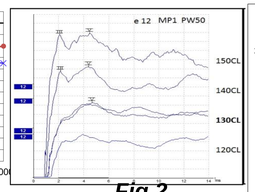

Fig.2

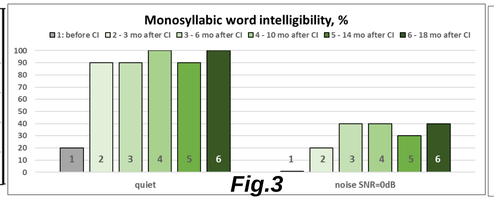

Fig.3

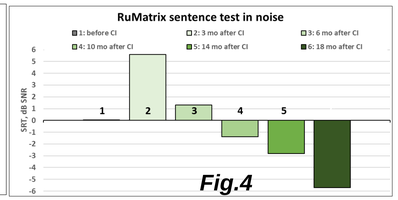

Fig.4

Conclusion

1. ***OTOF*-related ANSD** can be characterized by hearing thresholds ranging from **normal to profound** with severe speech perception impairment.
2. **Early identification** of this hearing impairment through timely referral to an audiologist is **crucial** even in cases where reactions to sound appear normal.
3. **CI** is an **effective rehabilitation** method for synaptopathy type of ANSD caused by mutations in the *OTOF* gene, including mild hearing loss.

References

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2. Santarelli R, Scimemi P, Costantini M, Domínguez-Ruiz M, Rodríguez-Ballesteros M, Del Castillo I. Cochlear Synaptopathy due to Mutations in OTOF Gene May Result in Stable Mild Hearing Loss and Severe Impairment of Speech Perception. Ear Hear. 2021;42(6):1627-1639.

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