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What is This?
Prenatal Diagnosis of SLC26A4 Mutation and Delayed Onset of Hearing Loss

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deafness, hearing loss, pediatric, audiology, genetic

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The incidence of congenital hearing loss is approximately 0.1% to 0.2% in developed countries. More than half of these cases are genetic in origin, and most are nonsyndromic. Since passage of the Walsh Bill in 1999, universal newborn hearing screening has been widely adopted across the United States.1 Although universal hearing screening has been effective in identifying infants with congenital hearing loss, about 20% of children with permanent hearing loss have progressive or late-onset hearing loss. These children would be expected to pass hearing screening and thus remain at risk for delayed detection of hearing loss.2

Enlarged vestibular aqueduct (EVA) is the most common temporal bone abnormality seen in patients with childhood hearing loss and is associated with nonsyndromic (DFNB4) and syndromic (Pendred syndrome) deafness.3 Forty percent of whites with nonsyndromic sensorineural hearing loss and EVA have mutations in SLC26A4, accounting for 5% to 10% of congenital hearing loss.4

There have been reports of prenatal diagnosis of mutations in SLC26A4 in the Chinese literature.5 We report the postnatal audiological course in a patient with prenatal diagnosis of SLC26A4 mutations. In this case, the known genetic status of the newborn prompted frequent audiological testing. This led to documentation of normal hearing, prompt identification of progressive hearing loss, and appropriate intervention during a critical period for speech and language development. Institutional review board approval was obtained from Seattle Children’s Institutional Review Board (X-06-032).

Clinical Presentation
The parents of the patient presented at about 20 weeks’ gestation. Their older daughter had recently been diagnosed with SLC26A4 mutations, G316X and 918-2A to G, after she presented with probable progressive bilateral mixed hearing loss and EVA at 13 months of age. Upon learning the genetic diagnosis of their daughter, the parents requested genetic testing of amniotic fluid from the current pregnancy. The prenatal testing was positive for the same genotype as the older sibling.

As a newborn, the patient passed hearing screening using evoked otoacoustic emissions (EOAE) and brainstem auditory evoked response (BAER). Diagnostic EOAE and frequency-specific BAER showed normal values for both ears. Repeat BAER examinations were performed at 2-month intervals. He continued to have normal BAER bilaterally until age 10 months, when a mild to moderate hearing loss was identified in his right ear. At age 11 months, the right hearing loss was confirmed and reverse-slope hearing loss was identified in the left ear. These changes were again identified via diagnostic BAER and EOAE evaluations (see Figure 1). The patient was first fit with bilateral hearing aids at 12 months and enrolled in early intervention.

High-resolution temporal bone computed tomography (CT) scans at 12 months of age revealed bilateral enlarged vestibular aqueducts. Ultimately, his hearing loss progressed, and he received a right cochlear implant at 5 years of age.

Discussion
SLC26A4 is a gene located on the long arm of chromosome 7 and encodes the pendrin protein, a transmembrane ion exchanger of chloride, iodide, bicarbonate, and formate. It is expressed in many organs, and its roles in controlling the pH of the endolymphatic fluid of the inner ear and iodide transport in thyroid follicular cells are well studied.4 As an autosomal recessive trait, the recurrence risk is 25%.

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The role of prenatal testing extends beyond the scope of this case presentation. We choose to focus on the data that clearly demonstrate bilateral progressive hearing loss in this patient with mutations in \textit{SLC26A4}. If this child did not have a known deafness-causing genotype, he would likely have had delayed diagnosis of hearing loss.

Although this single case presentation does not allow us to make specific recommendations about frequency or type of audiological monitoring, it demonstrates the importance of continued vigilance in the audiological monitoring of children with a family history of hearing loss.

\textbf{Author Contributions}
Ayaka J. Iwata, analysis, presentation of research; Janet Dunnell, analysis, presentation of research; Susan J. Norton, analysis, presentation of research; Kathleen C. Y. Sie, conception, analysis, presentation of research.

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\textbf{References}