SLC26A4 mutations in SNHL associated with EVA in a Chinese population

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Abstract

OBJECTIVE: Pendred syndrome and nonsyndromic recessive deafness DFNB4 are genetic disorders due to mutations in the SLC26A4 (PDS) gene. The aim of this study was to characterize the clinical features and spectrum of SLC26A4 mutations in a Chinese population with sensorineural hearing loss and enlarged vestibular aqueduct (EVA).

METHODS: From a Chinese population of patients suspected genetic hearing loss we identified 32 subjects (3 multiplex and 29 simplex families) with EVA using high resolution CT. Criteria for the diagnosis of EVA was a vestibular aqueduct diameter of >1.5 mm measured midway between the operculum and the common crus. All 21 exons and the intron-exon boundaries of the SLC26A4 gene were sequenced in each of the EVA subjects.

RESULTS: Nine novel mutations were identified 32 subjects. Of these, 21 had a prelingual onset of hearing loss with a mean age at onset of 1.02 years. None of the patients presented with goiter. All subjects were screened using DPHLC with sequencing confirmation in the control group.

CONCLUSION: Our data indicate that mutations in the SLC26A4 gene associated with a specific morphological appearance consistent with EVA, are a contributor to sensorineural deafness in Chinese population.

Introduction

SLC26A4 is the gene responsible for both Pendred syndrome (SNHL, EVA & goiter) and the DFNB4 form of nonsyndromic recessive deafness. Located on the long arm of chromosome 7, it is made up of twenty one exons. The encoded protein, pendrin, is expressed in nonsensory cells in scala media as well as thyroid, renal, uterine and placental tissue. Pendrin is thought to be involved in anion transport, although its remains unclear how this leads to cochlear dysfunction. Enlargement of the vestibular aqueduct is the most common anomaly associated with mutations of SLC26A4. Based on reports in Western populations, this is most commonly bilateral and may include other inner ear dysplasias. To date, most SLC26A4 mutations have been identified in Western populations. This study attempts to characterize the clinical features and spectrum of SLC26A4 mutations in a Chinese population with sensorineural hearing loss and enlarged vestibular aqueduct (EVA).

Materials and Methods

From a Chinese population of patients suspected genetic hearing loss we identified 32 subjects (3 multiplex and 29 simplex families) with EVA using high resolution CT. Criteria for the diagnosis of EVA was a vestibular aqueduct diameter of >1.5 mm measured midway between the operculum and the common crus. All 21 exons and the intron-exon boundaries of the SLC26A4 gene were sequenced in each of the EVA subjects.

A group of 100 normal hearing subject were also recruited from the same population to serve as controls. All 21 exons and the exon-intron boundaries were screened using DPHLC with sequencing confirmation in the control subjects.

Results

Hearing: All 32 subjects has moderate to bilateral SNHL. The onset was prelingual in 21 subjects. Nineteen subjects reported progressive or fluctuating hearing loss. Genetic Analysis: A total of thirteen different mutations were identified. The mutations were biallelic in 29 of the 32 subjects. Of these, 11 subjects has homozogotic mutations and 18 were compound heterozygotes. The most common mutation was a splice site mutation in intron 7 (IVS7-2A>G) found in 26 of 32 patients and 35 of 61 mutant alleles. A detailed listing of mutant alleles and clinical characteristics are provided in table 1.

Conclusions

This study characterizes the clinical features and spectrum of SLC26A4 mutations in a Chinese population with sensorineural hearing loss and enlarged vestibular aqueduct (EVA).

References

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