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Case Report

Right auditory dysfunction during acute Leber's hereditary optic neuropathy harboring the 14484 mtDNA mutation: a case report

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Abstract: Puspose: We report a case of a 17-year-old man who developed right auditory dysfunction, one month after the onset of visual loss caused by Leber's hereditary optic neuropathy (LHON). Methods: A full examination including a blood Mitochondrial DNA examination, auditory assessment and cranial magnetic resonance imaging were performed during the acute stage of the Leber's hereditary optic neuropathy. Results: A blood examination coexisted m.11969G>A, m.10398A>G and m.14484T>C mitochondrial DNA mutations. The right auditory assessment indicated auditory dysfunction. Cranial magnetic resonance imaging demonstrated abnormal signal in the bilateral prechiasmal optic nerve. Conclusions: The association between LHON and auditory dysfunction had been suggested more than case reports, however, to our knowledge, the unilateral auditory dysfunction has not been previously reported during the acute stage of visual loss in patients with LHON harboring T14484C.

Keywords: Leber's hereditary optic neuropathy, auditory dysfunction, magnetic resonance imaging

Introduction

Leber's hereditary optic neuropathy (LHON) is the most common mitochondrial (mt) genetic disease that is characterized by acute or subacute bilateral painless loss of vision. More than 90% of LHON cases have been linked to one of the three primary mt DNA point mutations: 11778G>A in the ND4 gene, 14484T>C in the ND6 gene and 3460G>A in the ND1 gene. Generally, visual impairment is the sole clinical manifestation of the disease. However, auditory impairment has been observed in some cases. For example, Funalot et al. [1, 2] reported brainstem involvement and abnormal ABR presentation in LHON patients harboring the T14484C mtDNA mutation. Paquay et al. [3] also reported a case of brainstem abnormality hypertension with LHON harboring 11778. Mondelli et al. [4] found auditory brain stem-evoked potential abnormalities in 7 of 11 patients. Yet these reports lacked a complete auditory assessment, and auditory dysfunction rarely occurs independently in unilateral. We report the case of right auditory dysfunction in a LHON patient harboring T14484C mutation, one month after visual loss.

Case presentation

A 17-year-old Chinese man experienced acute visual disturbance in his left eye (visual acuity: from 20/16 oculus sinister (OS) to 20/400). One week later, the same episode occurred in the other eye (visual acuity: from 20/16 oculus dexter (OD) to 20/50). In the initial stage, he was diagnosed with optic neuritis, and underwent intravenous methylprednisolone pulse therapy (1000 mg/day for three consecutive days), which did not improve his visual function. One month later, he was admitted to our hospital. A blood test suggested the homoplasmic 14484T>C mtDNA mutation along with the m.11969G>A and m.10398A>G mutations. His mother, older sister and a cousin were also found to have the same mutations but were

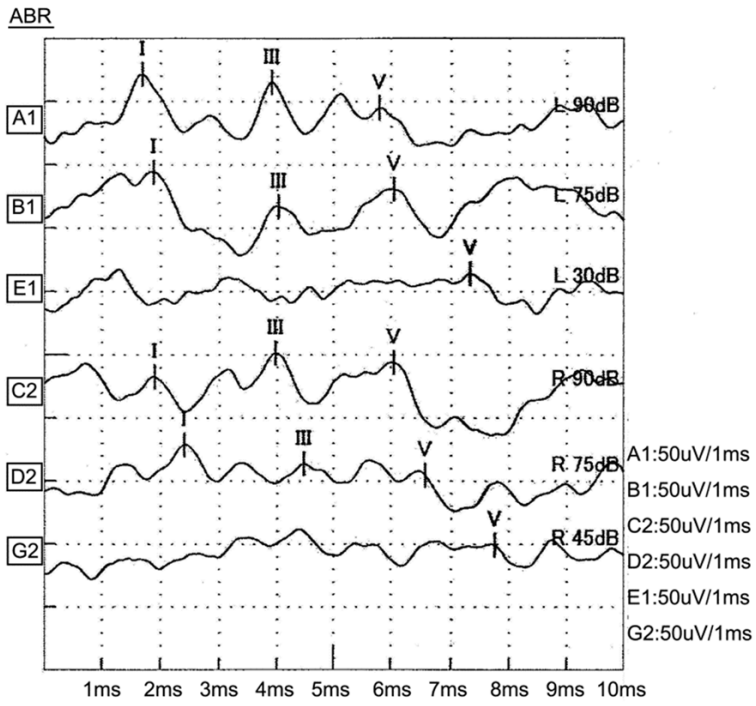

Figure 1. ABR records of acoustic clicks at 90 dB and 75 dB, indicating right prolonged latencies for wave I, wave III and wave V. The right high frequency auditory threshold was 45 dB.

asymptomatic. The family had no history of ophthalmological or auditory impairments.

Perimetry demonstrated large central scotomas in both eyes of the patient, which were more in the left eye than the right eye. The pattern visual evoked potentials (PVEP) revealed a P100 bilateral delayed response (left eye: 175 ms at 60', 151 ms at 15' and right eye: 147 ms at 60', 134 ms at 15').

Pure tone audiometry of the patient showed normal auditory threshold in both ears (20 dBHL for the left ear and 15 dBHL for the right), acoustic immittance audiometry and otoacoustic emission testing were normal. The brainstem auditory evoked potential (BAEP) showed right prolonged latencies for wave I, wave III and wave V, the neural conduction times for wave I-III, III-V and I-Vinterpeak latencies were normal, right high frequency auditory threshold was 45 dB (**Figure 1**). The patient did not report any exposure to specific medicines and environment that have a significant role in aminoglycoside-induced hearing impairment.

The cranial MRI revealed T2 hyperintensity signal in the bilateral prechiasmal optic nerve (**Figure 2**), with no enlargement.

Discussion

Recently, sporadic auditory dysfunction has been reported in LHON patients. However, prevalence of auditory dysfunction in LHON population is uncertain. Jansen et al. [5] reported a 53-year-old LHON patient whose brain stem auditory evoke potentials were normal on the right, but slightly delayed on the left. Ceranic et al. [6] reported two cases of LHON harboring the 11778 mitochondrial (mt) DNA mutation with AN. Rance et al. [7] studied 48 subjects carrying a LHON mutation and found that >25% of both symptomatic and asymptomatic patients showed electrophysiological evidence of AN with absent or severely delayed auditory brain stem potentials. Previous studies indicated that auditory impairment mainly occurred at the chronic stage of LHON, and which rarely occurs independently in unilateral. We present the first case of LHON haboring T14484C along with unilateral auditory dysfunction that occurred within one month of acute visual loss.

The G11778A alters the affinity of complex I for the ubiquinone substrate and induces resistance towards its potent inhibitor rotenone in mitochondria of LHON patients, which explains the pathological effect of this mutation [8]. The 14484 mutation leads to the substitution of valine with methionine in a poorly conserved region of the gene that code for the ND6 subunit, which causes reductions in complex I activity and ATP synthesis. However, the pathogenic basis of the relation between the T14484C mutation and auditory impairment remains unclear. Interestingly, in our patient, in addition to the T14484C mutation, we also found the coexistence of the A10398G and G11969A mutations. Accompanying mtDNA mutations can modify disease presentation through synergic interactions with the primary mutation. The coexistence of T14484C, and A1555G, A14693G, T4336C and T5655C mutations resulting in loss of vision and

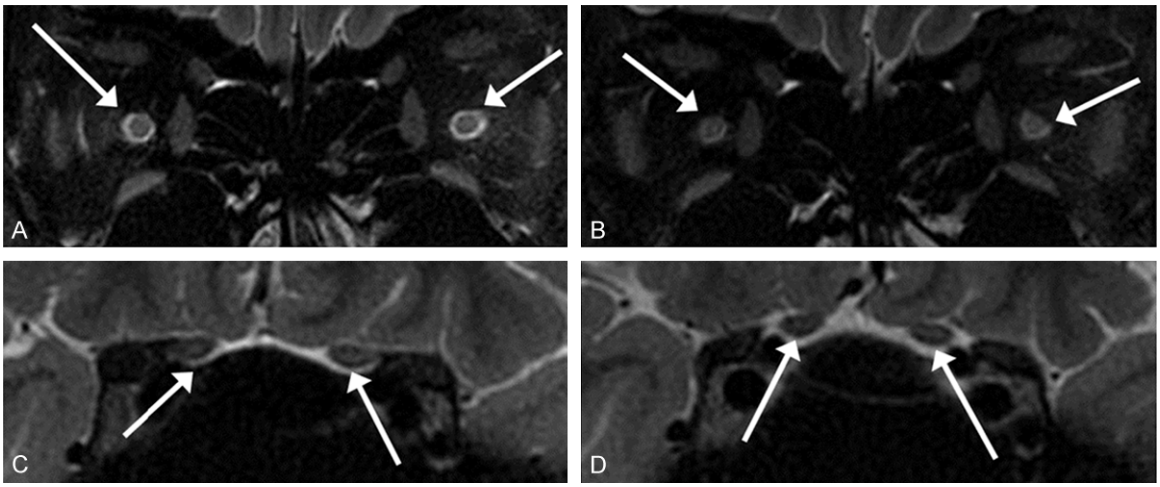

Figure 2. Coronal T2 MRI of retrobulbar (A, B) and prechiasmal (C, D) optic nerves. Arrows indicate increased signal in retrobulbar and prechiasmal without any enlargement.

hearing has been reported [9, 10]. However, the individual or synergistic effects of the A10398G and G11969A mutations in triggering visual and auditory impairments in LHON remain unclear and need further study.

We also found T2 hypertension abnormality along the bilateral prechiasmal optic nerve during the acute stage of LHON, which was consistent with previous reports [11-14]. However, we did not observe any enlargement of the optic nerve, which was in contrast to previous reports. Previous LHON reports showed T11778A mutation, but our case had T14484C mutation. Further study is needed to investigate whether theoptic nerve changes caused by mt gene mutations is related to the disease duration.

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Disclosure of conflict of interest

None.

Abbreviations

LHON, Leber's hereditary optic neuropathy; OD, oculus dexter; OS, oculus sinister; PVEP, pattern visual evoked potentials; BAEP, brainstem auditory evoked potential.

Authors' contribution

Wang L. and Ren Y.S. carried out the studies, participated in collecting data, and drafted the manuscript. Fan K. participated the design and ophthalmic testing.Zhang Y.Q. and Tian Q. Participated in optic MRI scans.Shi D.P. helped to draft the manuscript. All authors read and approved the final manuscript.

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