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Letter to the Editor Open Access

Leber's Hereditary Optic Neuropathy Associated with the m.10197G>A Mutation

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Letter to the Editor

Leber hereditary optic neuropathy (LHON) is an optic neuropathy caused by homoplasmic or heteroplasmic mtDNA mutations, which predominantly cause damage to the retinal ganglion cells (RGCs). The mtND3*10197A (m.10197G>A) mutation has been identified as the novel causative gene in Chinese patients with LHON and dystonia [1]. The m.10197G>A mutation also has been detected in patients with bilateral basal ganglia lesions and Leigh syndrome [2-4]. This mutation substitutes a threonine for an alanine at codon 47 of MTND3.

A 23-year-old Taiwanese man with a history of blunt ocular injury was referred to our clinic after sequential subacute onset of bilateral painless vision loss. The patient experienced blunt trauma to the left eye and was diagnosed with traumatic optic neuropathy four months prior to the onset of vision loss. At that time, his visual field examination showed cecocentral scotoma in the left eye and a normal visual field in the right eye. The Humphrey visual field (HVF) 30-2 showed a mean deviation (MD) of -10.70 dB in the left eye and -3.98 dB in the right eye (Figure 1A). He had no other neurological deficits at the time of injury. However, he noted painless visual deterioration of the right eye 2 months later. His visual acuity was 20/150 in the right eye, and 20/100 in the left eye. The patient failed to recognize any of the Ishihara color plates. The anterior segment of the eyes and extraocular movements were all unremarkable. The optic nerve heads were largely cupped with bilateral pallor over the temporal part of neural rim, and there was no prominent peripapillary telangiectasia in either eye. His HVF showed a progressive cecocentral scotoma in both eyes, which was worse in the non-traumatic eye. The MD had progressed to -14.83 dB in the left eye and -20.83 dB in the right eye (Figure 1B). His OCT showed a severe loss of the ganglion cell complex (GCC) and thinning of the left peripapillary retinal nerve fiber layer (RNFL) (Figure 2A). Magnetic resonance imaging (MRI) of the brain/orbits showed a normal optic nerve appearance bilaterally without enhancement and no periventricular white matter lesions. A review of the patient's medical history and family history was unremarkable. The patient had smoked for the past 10 years and denied current or past alcohol abuse. The patient underwent blood testing, which included biochemistry tests, a complete blood count (CBC), and tests for serum electrolytes, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), antinuclear antibodies (ANA), anti-double-stranded DNA antibodies (anti-dsDNA-Ab), protoplasmic/cytoplasmic antineutrophil cytoplasmic antibodies (p/c ANCA), angiotensin converting enzyme (ACE), antiphospholipid Ab, rheumatoid factor (RF), vitamin B12, and aquaporin-4 Ab. All tests were within the normal range or negative.

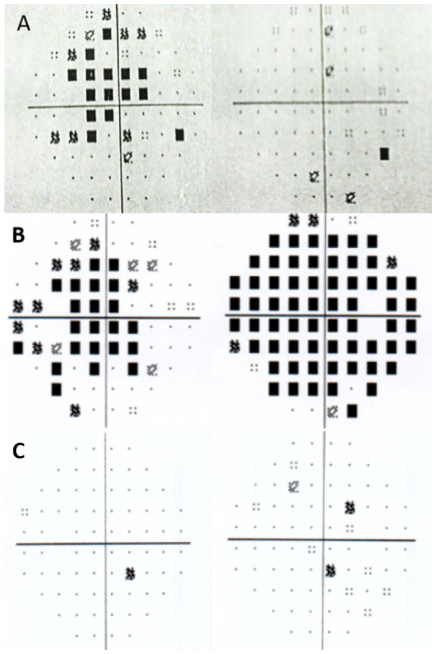

Figure 1: Pattern deviation in Perimetry. **(A)** The 30-2 Humphrey visual field (HVF) representing the left cecocentral scotoma after a blunt injury to the left eye. **(B)** Two months following the eye trauma, the HVF demonstrated a progressive bilateral cecocentral scotoma. **(C)** After taking idenbenone for 1 year, the HVF showed a decrease in the size of the central scotoma in both eyes; MD -5.92 dB in the left eye and MD -6.67 dB in the right eye.

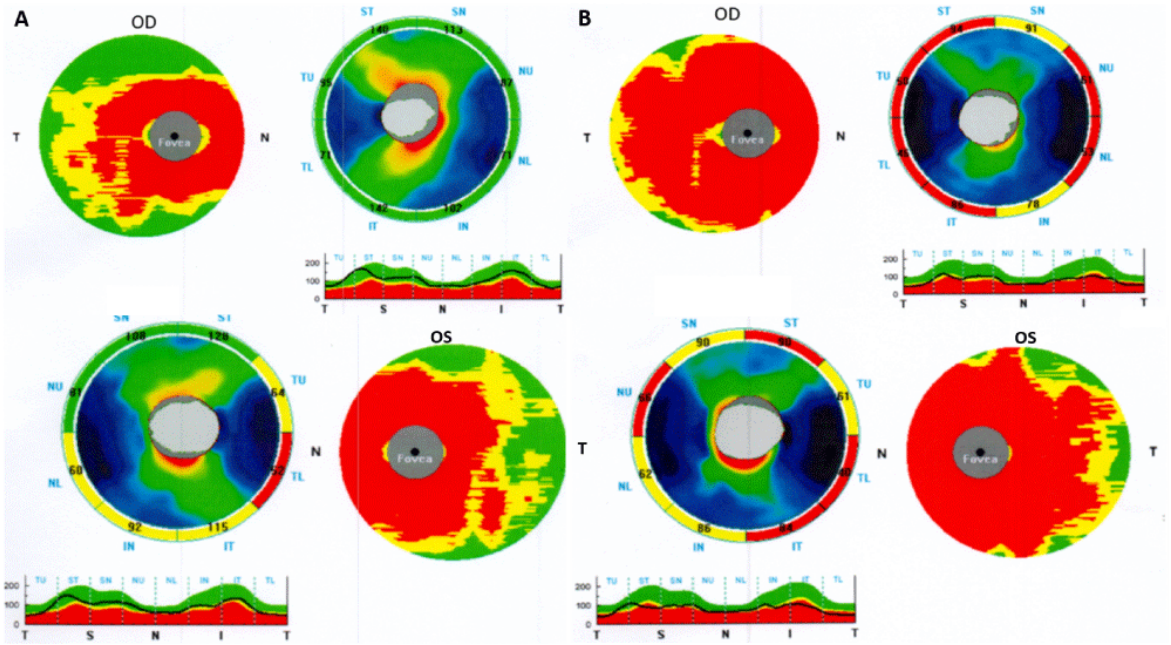

Figure 2: Optic coherence tomography (OCT). **(A)** OCT showed a severe loss of the retinal ganglion complex (GCC) in both eyes, and the left RNFL showed obvious thinning in the inferior sections of the optic nerve head. The right NFL was normal. **(B)** After six months, a severe loss of the GCC and RNFL was noted in both eyes, even after the patient continued taking idenbenone. The solid line represents the data of patient; the green zone=normal range of NFL; I=inferior; N=nasal; S=superior; T=temporal part of peri-papillary nerve fiber layer.

The patient underwent genetic testing for LHON at the Department of Research, Buddhist Tzu Chi General Hospital. The total DNA was isolated from the patient's blood. The mt DNA was amplified by PCR and subsequently confirmed by DNA sequencing to be free from the primary LHON associated –mt DNA mutation (11778A, 3460A, 14484C). However, the patient was found to have a heteroplasmic LDYT 10197A mutation affecting the NADH dehydrogenase 3 (ND3) gene. The mutation load in the leukocytes of the patient was 64.4%. We also tested blood samples from his mother, father, and younger sister. The 10197 G>A mutation was found only in the patient; his family members all tested negative for this point mutation. Three other mtDNA SNPs were found in this patient: m.3140 A>G(MT-RNR2), m. 10398 A>G (ND3, T114A) and m.10400 C>T (ND3).

After the patient was diagnosed LHON with mtND3*10197A (m. 10197G>A) sporadic mutation, he began taking idenbenone (150 mg) three times per day and vitamin C (500 mg) once daily. After one year of continued follow-up, the patient's visual acuity continued to improve and then stabilized at 20/20 (OD) and 16/20 (OS). In addition, his HVF showed improvement obviously (Figure 1C). On the other hand, his nerve structures showed a progressive thinning of the RNFL and a diffuse loss of the GCC in both retinas (Figure 2B). It is unknown whether the visual recovery of our patient was due to spontaneous recovery, idenbenone treatment, or prevention of exposure to smoke or alchocol in the acute stage. Major visual prognostic factors in LHON include the age of onset, type of pathogenic mutation, and optic disc structure. Interestingly, patients with a larger vertical diameter of the optic disc on OCT may be have a better visual prognosis, as well as a better visual outcome, compared to patients with a smaller optic disc [5]. The patient in this case had a large disc cup bilaterally, which may have contributed to his good visual prognosis.

We report the first instance of a rare LHON case with a sporadic mtND3*10197A (m.10197G>A) mutation in Taiwan. More cases need to be studied to draw conclusions regarding the pathogenesis and prognosis of this mutation.

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