GENOTYPIC DRIFT OF MITOCHONDRIAL DNA IN A PATIENT WITH LEBER'S HEREDITARY OPTIC NEUROPATHY

May-Yung Yen, Jorn-Hon Liu,
Yau-Huei Wei *

We report the drift of genotype from heteroplasmic to homoplasmic mutation at np 11778 of mitochondrial DNA (mtDNA) within 5 years in a 32-year-old patient with Leber's hereditary optic neuropathy (LHON). The patient underwent molecular test for the 11778 mtDNA mutation 5 years ago when his brother developed LHON and he was visually normal. At that time, the genotypic analysis revealed a heteroplasmic mutation at nuclotide position 11778 of the mtDNA. Five years later, the patient developed LHON. The molecular test for the 11778 mtDNA mutation was repeated. The mtDNA mutation converted to a homoplasmic state. Genotypic analysis demonstrated that rapid drift of mtDNA genotype in an individual can occur and the mutant mtDNA may reach the level that is required to cause the clinical features of LHON.

Key words: Leber's hereditary optic neuropathy, mitochondrial DNA mutation, homoplasmy, heteroplasmy

Leber's hereditary optic neuropathy (LHON) is a maternally inherited mitochondrial disease. It is characterized by acute, or subacute simultaneous or sequential visual loss, which affects predominantly young men with a peak age of onset at about 20 years. In 1988, Wallace et al.[1] first reported a point mutation at nucleotide position 11778 of mitochondrial DNA (mtDNA) from several patients affected by LHON. The mutation results in the substitution of histidine for the highly conserved arginine at amino acid position 340 of the ND4 subunit of Complex I of the mitochondrial respiratory chain. Since the report of the 11778 mtDNA mutation, 17 other point mutations of mtDNA have been identified in patients with LHON.[2] LHON has now been clearly linked to 3460, 11778 and 14484 mtDNA point mutations. These mutations are estimated to account for 15%, 50-70% and 10% of LHON patients, respectively.[3] The pathogenecity of 15 other secondary LHON mtDNA mutations is less clear.

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*Department of Ophthalmology, Taipei Veterans General Hospital, National Yang-Ming University, and *Department of Biochemistry and Center for Cellular and Molecular Biology, National Yang-Ming University, Taipei, Taiwan.*
Correspondence and reprint requests to: May-Yung, Yen, Department of Ophthalmology, Veterans General Hospital, Taipei 201, Sec. 2, Shih-Pai Rd., Taipei, Taiwan.