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Leber Hereditary Optic Neuropathy in 2 of 4 Siblings with 11778 mtDNA Mutation: Clinical Variability or Effect of Toxic Environmental Exposure?

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Key Words
Leber's hereditary optic neuropathy · Polycyclic aromatic hydrocarbons · Phenotypic variability

Abstract
Although mitochondrial (mt) DNA mutation at nucleotide position 11778 accounts for most cases of Leber's hereditary optic neuropathy (LHON), the phenotypic expression may vary greatly even in different members of the same family. The possible influence of exogenous toxicity on phenotypic expression is still debated in LHON. Here we describe 4 siblings carrying the 11778 mtDNA mutation with a different phenotype. The index case developed an atypical optic neuropathy at the age of 60 years after a long history of occupational exposure to polycyclic aromatic hydrocarbons (PAHs). This report underlines a number of unanswered questions about phenotypic variability of LHON including the possible influence of PAH toxicity.

Mitochondrial DNA (mtDNA) mutation at nucleotide position 11778 accounts for most cases of Leber hereditary optic neuropathy (LHON) [1]. This mutation affects complex I of the respiratory chain leading to mitochondrial dysfunction and selective damage to the papillomacular bundle of the optic nerve [2]. The possible influence of extra-mitochondrial factors, such as environmental or toxic agents that may precipitate an otherwise silent mtDNA mutation by increasing oxidative stress, is still debated in LHON [3].

Polycyclic aromatic hydrocarbons (PAHs) are a major source of toxicity for coke oven workers, although optic neuropathy has never been reported [4]. Here we report the case of 4 siblings (fig. 1), 3 males and 1 female, harboring a homoplasmic 11778 mtDNA mutation. The 2 with optic nerve damage differed greatly in age of onset, i.e. the index case had first symptoms at 60 years of age after a long history of occupational exposure to PAHs, whereas his younger brother experienced visual loss at the age of 17 years.

The proband (II-1) was a 60-year-old man referred to us for a second opinion regarding acute painless blurred vision in the right eye. Seven months previously, he had experienced acute permanent reduction of central vision

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