Carbon Monoxide Poisoning as an Epigenetic Factor for Leber’s Hereditary Optic Neuropathy

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A 45-year-old Korean woman visited our hospital complaining of poor vision after carbon monoxide (CO) poisoning. We have confirmed the presence of a point mutation at position 11778 in the ND4 gene of mitochondrial DNA. This case suggests that CO poisoning may precipitate the clinical expression of Leber’s hereditary optic neuropathy (LHON). To our knowledge, this would be the first case report of clinical expression of LHON precipitated by CO poisoning.

Key words: carbon monoxide (CO) poisoning, Leber’s hereditary optic neuropathy (LHON)

INTRODUCTION

Leber’s hereditary optic neuropathy (LHON) is a maternally inherited disorder characterized by acute or subacute severe visual loss in both eyes.1 Since Wallace and colleagues identified a point mutation of LHON at nt 11778 in the gene for the fourth subunit (ND4) of complex I(NADH-ubiquinol oxidoreductase) of the electron-transport chain, many primary and secondary mutation sites have been identified.2-5 The presence of an mtDNA mutation is not the only determinant of the expression of the disease, and the interaction of genetic and epigenetic factors appears to be related with the pathogenesis of LHON.2-10 By clinically analysing patients with molecularly confirmed LHON, a number of epigenetic factors have been implicated as potential synergistic factors.3-10 This following case report addresses the possible relationship between the onset of optic neuropathy and metabolic dysfunction such as CO poisoning.

CASE REPORT

A 45-year-old woman visited our hospital complaining of the poor vision. Twenty-one years previously, she had noted painless blurred vision in the left eye and the same symptom in the right eye one and a half months later. One month prior to the first symptom, she had suffered carbon monoxide (CO) poisoning.

At the time of presentation, best corrected visual acuity was counting finger OD and light sense OS. She could not read any of the Ishihara plates including the control sheet with either eye. Visual field examination showed inferior small island OD, and OS was not possible. The pupils were reactive to light OD and sluggish to light OS and relative afferent pupillary defect was noted in the left eye. Both optic discs were pale and there were no microvascular signs. There was nerve fiber layer loss in both eyes. Orbital, lid and slit-lamp examination were unremarkable. The patient showed full ocular motility, and according to the result of the Hirschberg test was 15 prism diopter exotropic. She was a non-smoker and consumed little alcohol; her electrocardiogram was normal and
she was otherwise healthy. For her son, maternal family history was positive; he suffered from reduced vision. Subsequent genetic evaluation identified a point mutation at mtDNA 11778.

DISCUSSION

It has been postulated that the complex distribution of mutant and wild-type mtDNA in different cells, tissues, and individuals may explain the variable intra- or interfamilial expression of LHON. An individual with mtDNA mutation, present at a level below that required for clinical expression, will be vulnerable to a trigger effect; any metabolic or environmental condition which reduces the efficacy of the oxidative chain, or increases the rate of mtDNA mutation may impair the functional dominance of healthy mtDNA and induce the disease state. Such trigger effects have been observed most notably in LHON. The development of symptoms also seems to be influenced by environmental factors. It is widely held that metabolic poisons such as cigarette smoking can trigger or enhance symptoms. The combination of genetic and metabolic alteration of mitochondrial respiration at the onset of CO poisoning in our patient may have caused the onset of her neuropathy.

In this report, we have described a woman with the 11778 mtDNA mutation, the most common primary mtDNA mutation in LHON. She developed severe, permanent central visual loss at 25 years of age. This case provides an evidence that CO poisoning may play an important role in the clinical expression of visual loss in LHON.

REFERENCES