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Original Research Paper

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LEBER'S HEREDITARY OPTIC NEUROPATHY IN AN OLD MAN: A CASE REPORT

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ABSTRACT Leber's hereditary optic neuropathy (LHON) is a rare mitochondrial disorder characterized by bilateral optic nerve atrophy leading to acute or subacute painless central vision loss. This case report describes a rare occurrence of LHON in a 71-year-old man, highlighting the clinical and genetic heterogeneity of the disease. The patient initially experienced visual loss in the left eye, which progressed rapidly, followed by deterioration of vision in the right eye six weeks later. Genetic testing revealed the pathologic mtDNA 14,484 point mutation, which is responsible for a significant proportion of LHON cases. Environmental factors such as alcohol and smoking, along with genetic mutations, contribute to the optic nerve degeneration seen in LHON. The diagnosis of LHON can be challenging due to its variable presentation, but early recognition and appropriate management are crucial. Although no specific treatment for LHON currently exists, supportive care is provided, and alternative therapies like idebenone/vitamin B/vitamin C combination therapy show some promise. Increased awareness and understanding of LHON will lead to improved outcomes and potential developments in effective treatments for this devastating condition.

KEYWORDS : Leber's hereditary optic neuropathy (LHON), Late-onset, Bilateral vision loss, mtDNA 14,484 point mutation

INTRODUCTION:

Leber's hereditary optic neuropathy (LHON) is an inherited mitochondrial disorder caused by mutations in mitochondrial genes encoding the NADH dehydrogenase and that leads to an acute or subacute painless loss of central vision resulting from bilateral optic nerve atrophy[1]. This disorder affects young males in the second through their fourth decade with both eyes affected simultaneously or in a few months one after the other[2]. Three mutations at positions 11,778, 3460, and 14,484 are responsible for more than 90 percent of all cases of LHON. These mutations lead to decreased ATP production[3].

Case Report:

A 71 year old man was referred to our department for acute visual loss in the left eye for 2 weeks. He had a sudden onset of blurred vision in the left eye 2 weeks back and it has been increasing progressively since then. He did not experience any visual discomfort before the recent onset of unilateral vision loss. The patient had been smoking about 30 cigarettes/day for the past thirty years and drinking heavily every day for the past one year, but had to quit these habits when the visual symptoms started to deteriorate. The patient had no significant past medical, surgical, trauma and family history.

A review of systems revealed no other complaints and his vitals are stable. Ophthalmological Examination Revealed a visual acuity in the right eye of 6/6 and 6/60 in the left. The Ishihara colour test score was 12/14 in the right eye and 0/14 in the left eye. The ocular surface and anterior segment, including the conjunctiva, cornea, anterior chamber, iris, and lens, all appeared to be normal under slit lamp examination. Intraocular pressure was also within normal limits. Fundus was normal too. However, a relative afferent pupillary defect was noted in his left eye. A central scotoma was noted in the left eye and the visual field was full in the right eye. The extra ocular movements were normal. The patient's medical records revealed no congenital or systemic illness, no drug or substance abuse, and no family history of poor vision.

The patient consequently underwent laboratory examination, fluorescein angiography, visual-evoked potential (VEP) examination, and magnetic resonance imaging (MRI), routine haematological and biochemistry studies, erythrocyte sedimentation rate (ESR), clotting studies and heavy metal screening were all within normal limits. Cerebrospinal fluid examination at lumbar puncture revealed an opening pressure of 180mm water with cerebrospinal fluid white count less than 1 million, protein 0.2g/l, with no oligoclonal bands. He was given 1 g of intravenous methylprednisolone daily for three days. His visual acuity continued to stay at 6/60 even after 2 weeks of the steroid pulse treatment.

Six weeks later, the patient subjectively felt a deterioration of vision in his right eye. Visual acuity decreased to 6/30 in the right eye. He showed a central scotoma in both the eyes now, while visual acuity in the left eye is at 6/60. On fundus examination, there was no optic disc swelling in the right eye. Nothing significant macular or vascular change was observed. MRI showed no enhancement in either optic nerves. The patient was given 1g of intravenous methylprednisolone daily for three days again, but his visual acuity did not improve. Genetic testing for LHON was per- formed and revealed the pathologic mtDNA 14,484 point mutation.

Six months later after the onset of bilateral visual loss, this patient's final visual acuity was registered as 6/120 in the right eye and 6/60 in the left eye.

DISCUSSION:

Leber's hereditary optic neuropathy (LHON) is a rare mitochondrial disorder characterized by acute or subacute painless loss of central vision resulting from bilateral optic nerve atrophy[5]. It primarily affects young males in their second through fourth decades, but this case report describes a rare occurrence of LHON in a 71-year-old man. The advanced age of onset in this patient adds to the growing body of evidence supporting the clinical and genetic heterogeneity of LHON[6].

One of the key features of LHON is the rapid progression of vision loss, which typically occurs sequentially in one eye followed by the other[6]. However, simultaneous loss can also occur in some cases. The patient in this report initially experienced visual loss in the left eye, which progressed over two weeks. Six weeks later, he subjectively felt a deterioration of vision in the right eye. This bilateral involvement is consistent with the characteristic pattern seen in LHON.

The etiology of LHON is attributed to mutations in mitochondrial genes encoding NADH dehydrogenase, specifically at positions 11,778, 3460, and 14,484[5]. These mutations lead to decreased ATP production, resulting in retinal ganglion-cell apoptosis and optic nerve degeneration. Genetic testing in this case revealed the pathologic mtDNA 14,484 point mutation, which is responsible for a significant proportion of LHON cases.

The triggers for visual loss in LHON patients are not fully understood. However, certain environmental factors have been implicated, including alcohol and smoking, which were notable in this patient's history. It is believed that these triggers, along with other factors such as lack of estrogens, trauma, antiretroviral therapy, HIV, anemia, cyanide and carbon monoxide intoxication, contribute to an imbalance in redox homeostasis and increased oxidative stress, leading to optic nerve degeneration.

Diagnosis of LHON can be challenging due to its low prevalence and variable clinical presentation. However, considering LHON in the differential diagnosis of painless, bilateral, and central vision loss in young or older adults is crucial for early recognition and appropriate management. Genetic testing plays a vital role in confirming the diagnosis and identifying the specific mutations responsible.

Currently, there is no specific treatment for LHON. Supportive care is the primary approach, and patients often receive initial diagnoses of optic neuritis, leading to steroid therapy. However, as inflammation is not the driving factor in LHON, high-dose steroid therapy does not result in improvement. Alternative treatments have been explored, including the use of idebenone/vitamin B/vitamin C combination therapy, which has shown some promising results in selected cases. Unfortunately, in this report, the patient did not respond to steroid pulse therapy or show improvement with idebenone [7].

Prognosis for vision recovery in LHON varies depending on the specific mutation. Patients with the 14484 mutation tend to have a better prognosis, with up to 50% experiencing gradual improvement. In contrast, only 4% of patients with the 11778 mutation, as observed in this case, show gradual improvement. It is important to provide appropriate counseling to patients and their families regarding the variable prognosis and potential challenges associated with LHON[7].

This case report emphasizes the importance of considering LHON in the differential diagnosis of painless, bilateral, and central vision loss, even in older adults. It highlights the need for further research into the pathophysiology of LHON to identify novel therapeutic targets. Additionally, the report underscores the importance of genetic testing for accurate diagnosis and genetic counseling. Increasing awareness and understanding of LHON will contribute to improved outcomes and potentially lead to the development of effective treatments for this devastating condition.

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