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A CASE REPORT ON – LEBER HEREDITARY OPTIC NEUROPATHY

Ophthalmology

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ABSTRACT

Leber hereditary optic neuropathy (LHON) is a maternally inherited disorder caused by mutations in mitochondrial DNA, affecting the optic nerve and leading to bilateral, painless vision loss 1. The condition typically manifests in young adulthood, predominantly in males. LHON is characterized by acute or subacute central vision loss, often starting in one eye and progressing to the other within weeks or months. Diagnosis is confirmed through genetic testing and clinical examination, ruling out other causes of optic neuropathy. While there is currently no cure for LHON, treatment options such as antioxidants and gene therapy are being explored to potentially improve vision outcomes. Early detection and genetic counselling are essential for individuals at risk of inheriting LHON to understand their prognosis and make informed decisions about their eye health. Our patient, a 15 years old male, who presented to our Out Patient Department with chronic central vision loss in both eyes.

KEYWORDS

Leber hereditary optic neuropathy, maternally inherited, M.11778G-

INTRODUCTION

Leber hereditary optic neuropathy (LHON) is a rare disorder, with an estimated incidence of about 1 in 30,000 to 1 in 50,000 individuals in the general population2. However, the prevalence can vary among different populations and regions. LHON primarily affects young adults, typically between the ages of 15 and 35, although cases outside of this age range have been reported. Males are more commonly affected than females, with a male-to-female ratio of around 4:1. The exact reasons for this gender difference are not fully understood but may be related to hormonal or environmental factors interacting with mitochondrial genetics. Due to its genetic nature, LHON can occur sporadically or be passed down maternally through generations. Understanding the incidence and inheritance patterns of LHON is crucial for accurate diagnosis, genetic counselling, and management of affected individuals and their families.

The majority of the patients have one of the three mitochondrial DNA point mutations M.14484T-C , M.3460G-A or M.11778G-A ,these mutation leads to disruption of the mitochondrial respiratory chain activate pro-apoptotic pathways3,6.For reasons unknown this insult tends to affect the regional ganglion cells more than any other cell in the body leading to diseased state. Additionally, some studies suggest that certain environmental factors, such as smoking and alcohol consumption, may influence the penetrance and expression of LHON mutations, potentially impacting its incidence in specific populations. However, further research is needed to fully understand the complex interplay of genetic and environmental factors contributing to the incidence of LHON across different regions and populations.

Case report

A 15 years old Indian male patient who is a student,presented to the outpatient department with painless diminution of vision in both eye for 5 to 6 years, which was gradually progressive.There is no history of trauma,the patient had no co morbidities and family history was insignificant.

Visual acuity in right eye was counting finger at 3meters and left eye was counting finger at 1meter, Anterior segment examination was normal, fundus examination revealed bilateral pale optic disc (Figure 3). optical coherence tomography (OCT) revealed thinning of the retinal nerve fiber layer (RNFL), RNFL thickness of 63µm in right eye(Figure 1) and 74µm in left eye(Figure 2).Genetic testing revealed a pathogenic mutation (m.11778G>A) in the MT-ND4 gene, confirming the diagnosis of LHON. Patient was started with antioxidants and referred to visual rehabilitation center. Genetic counselling was provided to the patient and his family regarding the inheritance pattern and risk of transmission to future generations.

DISCUSSION

Treatment for LHON can be broadly classified either mutation specific or mutation independent7.Mutation specific therapies aim to correct the underlying mutation through the use of gene editing platform or replace the faulty mitochondrial DNA encoded protein by delivering the wild type gene using a suitable vector.Mutation independent therapies can have various downstream targets, the aim to improve mitochondrial respiration,reduce mitochondrial stress, inhibit or delay retinal ganglion cell apoptosis and /or promote retinal ganglion cell survival.

CONCLUSION

Leber hereditary optic neuropathy (LHON) is a complex disorder that not only involves genetic factors but also environmental influences and mitochondrial function. The interplay of these factors contributes to the variability in clinical presentation, penetrance, and severity observed in affected individuals. Understanding LHON requires a multidisciplinary approach, involving genetics, ophthalmology, neurology, and molecular biology.

Most LHON patients develop permanent bilateral central vision loss. Pharmacologic and gene therapy treatment approaches have been shown to be safe and possibly effective in promoting some visual recovery. However even without treatment, at least partial spontaneous visual recovery is possible. Patient should be counselled to avoid environmental toxins and heavy alcohol and tobacco use. Patient often benefit from referral to vision rehabilitation clinics and affected patients should be offered formal genetic counselling.

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