Case Report

A Rare Case of Leber's Hereditary Optic Neuropathy

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Abstract

Leber hereditary optic neuropathy (LHON) is a mitochondrial genetic disorder characterized by acute or subacute loss of central vision, typically affecting young adult males. This case report presents a 25-year-old male with a history of gradual painless loss of vision for 4 months. The patient exhibited a significant family history of similar complaints with affected females in previous generations It is confirmed by a genetic sequencing CT 7044: Common mitochondrial mutation ND1: mt G3460A. Despite having mitochondrial point mutation, the patient had affected females in other generations. This case underscores the importance of heteroplasmy and the need for genetic counseling among females.

Keywords: Leber hereditary optic neuropathy, Mitochondrial mutation, Central vision

Introduction

Leber hereditary optic neuropathy (LHON) is a genetic disorder that causes optic neuropathy and a maternally inherited disease with one of the three primary mtDNA point mutations: G11778A, T14484C, or G3460A. It results in irreversible sequential or bilateral, painless, progressive visual loss with central (or ceco-central) scotomas in patients belonging to the age group of 15 to 35 years.[1]

It has incomplete penetrance and sex imbalance, thus indicating that there are factors beyond mtDNA mutations that affect disease phenotype. Approximately 50% of males and 10% of females who carry an LHON mutation manifest signs and symptoms.[2]

CASE REPORT

A 25-year-old male presented to our department with a recent history of vision loss. About four months back, he suffered a diminution of vision in his right eye. It was insidious in onset and gradually progressive in nature. The patient experienced a similar complaint in his left eye 1 month back. It was not associated with any history of pain, redness, discharge, photophobia, or difficulty in ocular movements. It was not associated with any other systemic symptoms, such as muscle weakness or wasting, respiratory insufficiency, or palpitation.

He was hemodynamically stable, with visual acuity of finger count close to face in both eyes. Color vision and visual field testing could not be done because of severely impaired vision. Intraocular pressure in both his eyes was within the normal range of 14 and 17 mmHg in both his right and left eye, respectively.

The patient has a significant family history of similar complaints. According to the patient, his maternal grandmother and her sister had identical complaints with the onset of symptoms around 14 years of age. Later, in the second generation, out of the five children his maternal grandmother had, two of them, one boy and one girl, were affected with the onset of symptoms around 13 and 14 years, respectively. The patient's mother was asymptomatic. Finally, in the third generation, one of the patient's male cousins, whose mother also had a similar complaint, had onset at 14 years of age (Figure 1).

On slit lamp examination, his conjunctiva and cornea were within normal limits. The anterior chamber is well formed, the iris has a normal color and normal pattern, the pupil has a regular shape a normal reaction, and the lens is normal.

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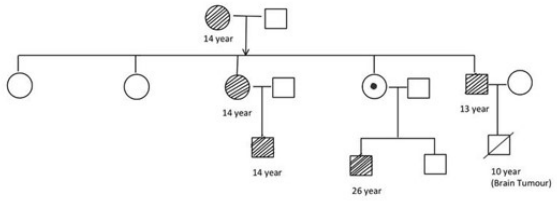

Figure 1: Pedigree of patient's 3 generation showing leber's hereditary optic neuropathy

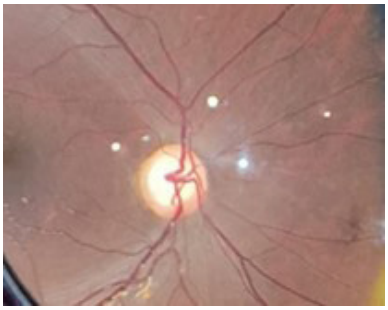

Figure 2: Right eye: Disc CDR

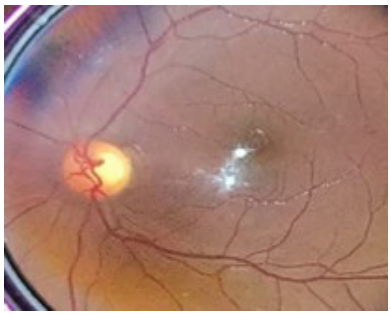

Figure 3: Left eye: Disc CDR

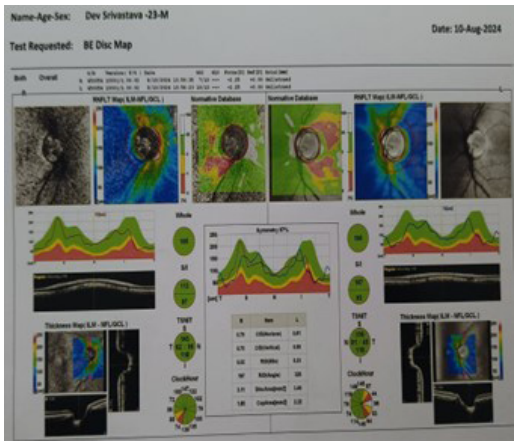

Figure 4: BE disc map

On Fundus Examination

Right eye

Disc CDR – 0.7–0.8 cupping rest within the normal limit (Figure 2),

Left eye

Disc CDR – 0.4–0.5 cupping rest within the normal limit (Figure 3)

To rule out any sort of inflammation, a blood profile of the patient was performed where his TLC, DLC, Platelet count, red cell indices, ESR and blood film morphology were within normal limits.

To rule out multi-organ involvement, a liver function test and Kidney function test of the patient were performed, which was within normal limits.

On performing OCT of the RNFL, there is thinning in RNFL left more than right, most severely in the temporal quadrant along the course of the papillomacular RNFL bundle (Figure 4). Thus signifying retinal ganglionic cell atrophy.[3]

Seeing the strong family history and pattern of vision loss, a differential of Leber's hereditary optic neuropathy was considered and a genetic sequencing CT 7044: Common mitochondrial mutation ND1: mt G3460A was detected in the sample tested. The result is consistent with the diagnosis of LHON.

Discussion

Leber hereditary optic neuropathy (LHON) is a mitochondrial disorder primarily affecting the optic nerve, leading to painless, bilateral visual loss.[1] It predominantly affects young adult males but can also be present in females, with variable penetrance and expressivity.[4] In the case presented, genetic testing revealed the mitochondrial mutation mt G3460A in the ND1 gene, which is known for its poor prognosis, as discussed by Mackey DA *et al.*[5] The presence of heteroplasmy in the patient aligns with the findings of Sundaramurthy S *et al.*,[6] which report heteroplasmy as a contributing factor to the variable clinical expression of LHON in the Indian population, especially in women.

The heteroplasmy observed in this case is particularly significant. It suggests that the degree of mutation load within mitochondria plays a key role in disease penetrance and clinical variability, consistent with findings from Sundaramurthy S *et al.*[6] Heteroplasmy, where both normal and mutated mitochondrial DNA coexist, complicates the clinical picture, making the prediction of disease onset and severity more challenging. This patient's family history also illustrates incomplete penetrance—a hallmark of LHON.[4] This case brings to light the unique risks posed to female carriers of LHON mutations. Unlike males, who rarely pass on mitochondrial disorders, women with LHON mutations are at high risk of transmitting the mutation to all of their offspring.[5] This maternal inheritance pattern necessitates thorough genetic counseling for affected females or female carriers, as they face not only the risk of developing the disease themselves but also the prospect of transmitting it to future generations.

The role of environmental factors[7,8] and lifestyle modifications can potentially delay or reduce the severity of vision loss, although the progression of the disease is typically irreversible once symptoms develop.

Conclusion

LHON, although more prevalent in young males, should not be overlooked in females. This case demonstrates the significance of heteroplasmy and the need for genetic counseling, particularly for women, as they carry the risk of transmitting the disease to their offspring. The incomplete penetrance and variable expressivity of LHON mutations suggest that environmental and genetic factors play a role in disease expression, emphasizing the need for personalized management and lifestyle modifications.

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