

Leber hereditary optic neuropathy a disease overview case study sample

[Science](#), [Genetics](#)



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Leber hereditary optic neuropathy (LHON), also known as Leber optic atrophy, is a familial neuro-ophthalmologic disorder manifest by varying degrees of loss of ganglion cells from the optic nerve, with variable severity at onset, variable rate of deterioration, variable ultimate vision outcome and variable recovery of lost vision (Kelly).

Causes

LHON is caused by any of eighteen mutations of various mitochondrial genes coding for subunits of electron transport chain complexes, primarily complex I (NADH-dehydrogenase), which are responsible for converting energy derived from food into a form usable at the cellular level. Three of these mutations, those at base pairs 11778, 3460 and 11484, are responsible for at least 90 % of cases of LHON. There appears to be some correlation between mutation and disease severity, with the 11484 mutation being the mildest, with the greatest chance of vision recovery and the 11778 mutation

among the most severe, with one of the poorest ultimate vision outcomes and one of the poorest chances of recovery (Kelly).

Mitochondrial genes, located on the single mitochondrial chromosome, as opposed to the genes located on the 46 nuclear chromosomes, are transmitted solely maternally (since the relatively few mitochondria in the spermatozoa are lost or destroyed at fertilization). Thus, the mutation can be transmitted only through females, from generation to generation, affecting both males and females. However, this does not explain why over 80 % of affected individuals are males. This observation has led to the hypothesis that there may be some “susceptibility gene” located on the Y chromosome (possessed only by males). Also, penetrance varies, with some individuals in the same family mildly affected, while others are severely affected. This may be explained by heteroplasmy, meaning that not all the mitochondria in a given cell may carry the mutation. It is thought that the various mutations impede the transport of glutamate, leading to accumulation of oxygen radicals, causing early death of optic nerve ganglion cells (Kelly).

History

The onset is usually between the late twenties and early thirties, although onsets much earlier and later have been described. The initial complaint is usually an acute or subacute (more gradual) painless loss of central vision in one eye, with central scotomata (blind spots), followed approximately two months later by similar symptoms in the other eye. Simultaneous bilateral onset also occurs. Diminished color vision (dyschromatopsia) is also noted.

Physical Findings

Fundoscopy examination shows peripapillary telangiectasiae (dilation of capillaries near the optic nerve head), vascular tortuosity, microangiopathy and pseudoedema (the appearance of swelling of the optic disc without leakage on fluorescein angiography) (Howell et al. 939). The temporal portion of the optic disc appears pale, with relative sparing of the nasal portion. An imaging technique called optical coherence tomography (OCT) confirms this observation, showing early and severe loss of temporal nerve fibers, with the nasal fibers less severely affected (Barboni et al. 120).

The more severe mutations, including that at base pair 11778, may show many neurologic manifestations, including ataxia, tremor, peripheral neuropathy, seizures, rigidity and myopathy, as well as cardiac conduction abnormalities (Howell 939).

Treatment

No pharmacologic treatment for LHON has been proven effective. Early trials employing idebenone (a synthetic quinone, an analog of coenzyme Q10) (Klopstock 2677) and alpha-tocotrienol quinone (a Vitamin E metabolite) (Shrader 3693) have shown promise, especially if started at the onset of the disease. Substances that are toxic to the optic nerve, such as tobacco, ethanol and the antituberculous medication ethambutol, should be avoided (Kelly).

Outcome

The progression ranges from sudden and complete vision loss at the outset to progressive decline over two years. The ultimate vision outcome ranges from 20/50 to no light perception (Howell et al. 939). However, vision changes may not be monophasic. A pattern of initial vision loss, followed by a latent period, with a period of further deterioration or improvement has been described (Kerrison 1).

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Temporal Pallor with Nasal Sparing, Left Eye

[www. disorders. eyes. arizona. edu.](http://www.disorders.eyes.arizona.edu)

End Stage LHON

[www. content. lib. utah. edu.](http://www.content.lib.utah.edu)