What You Should Know About Hereditary Optic Neuropathy

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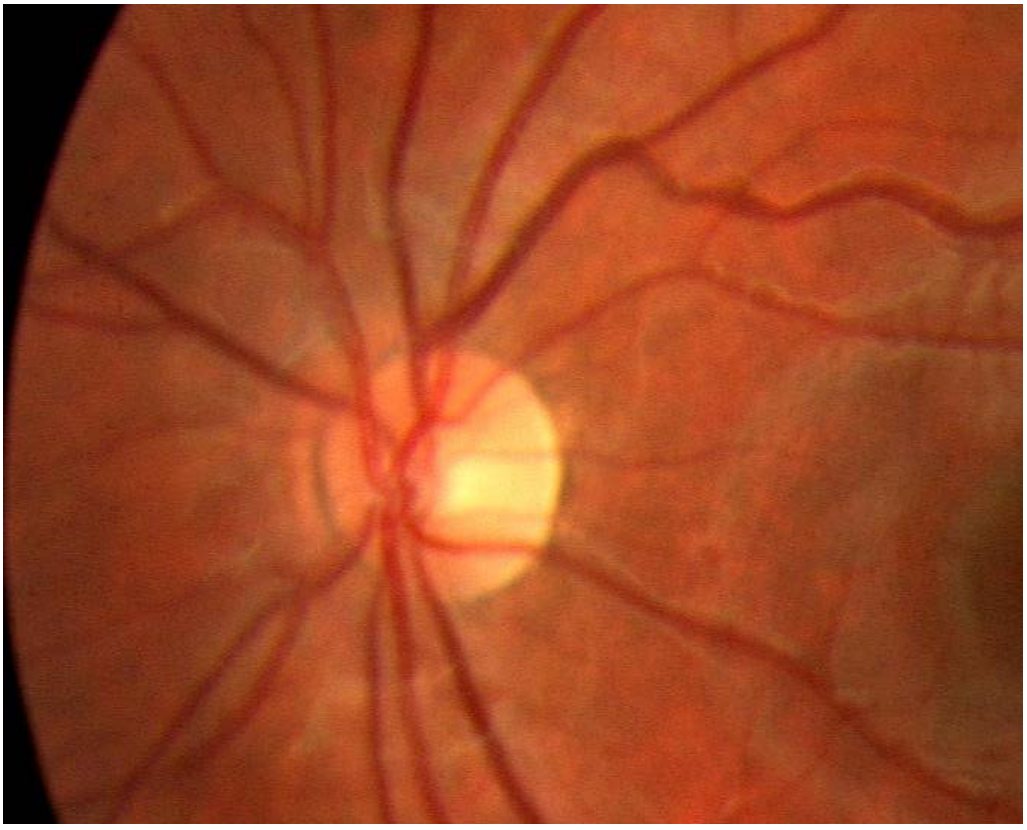
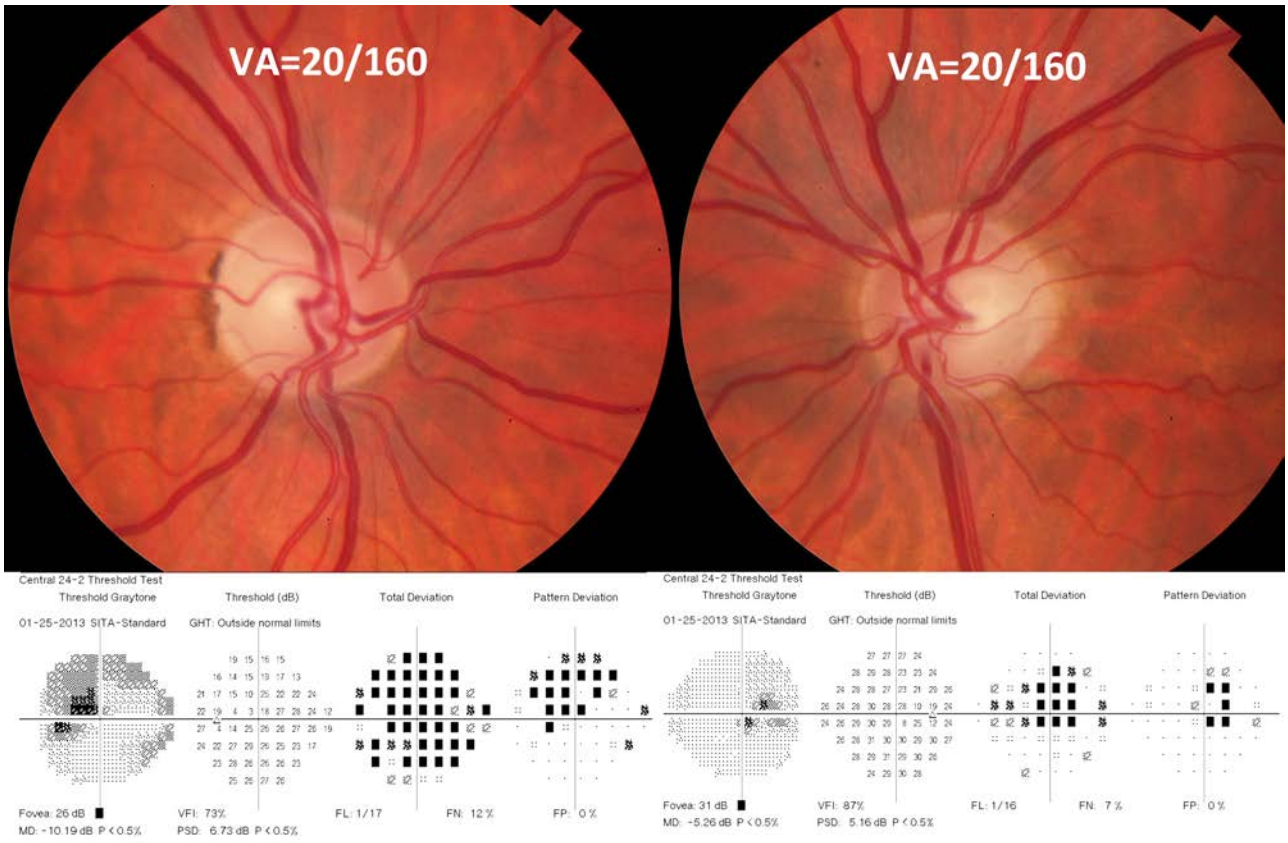
Hereditary optic neuropathies comprise a group of conditions in which neurons within the optic nerve die secondary to genetic mutations. The clinical picture is characterized by visual acuity loss, blue-yellow color blindness, central visual field loss, and temporal or global optic disc pallor and sometimes segmental optic disc excavation.[1] The appearance of a normal optic disc is shown in fig. 1. The appearance of the optic discs and the visual fields of a patient with hereditary optic atrophy is shown in fig. 2.

Fig. 1



Legend: Normal optic disc.

Fig. 2



Ishihara Plates 1/15 correct with each eye

Legend: Optic nerve appearance and visual fields in a patient with hereditary optic atrophy, suspected autosomal dominant type. There is temporal optic disc pallor. The visual fields show cecocentral scotomas bilaterally.

The most common form of hereditary optic neuropathy is autosomal dominant (Kjer type) with a prevalence of 1 in 50,000 persons. Much rarer is autosomal recessive optic neuropathy (Behr type). Mitochondrial inheritance is found in Leber's hereditary optic neuropathy.[2]

Autosomal Dominant (Kjer Type) Hereditary Optic Neuropathy

There are at least 7 different mutations of the optic atrophy 1 (OA1) gene on chromosome 3 that cause this condition. The affected gene codes for a GTPase protein important in mitochondrial function. It has variable penetrance (that is, manifestations in different ersons affected) according to the specific mutation and environmental influences. A completely separate disease caused by a mutation of the OA4 gene on chromosome 18 is also inherited in an autosomal dominant fashion.[1]

The visual acuity loss in autosomal dominant optic atrophy is variable. Forty percent of patients lose vision to the 20/20-20/60 range. Forty-five percent of patients lose vision to the 20/70-20/100 range. Fifteen percent of patients lose vision to the 20/200-20/600 range.

Many patients with autosomal dominant optic atrophy have only optic nerve involvement, but there are syndromes with other neural involvement, for example deafness. Therefore, all patients should be questioned regarding hearing loss and tested if the history suggests a problem.[3]

Leber's Hereditary Optic Neuropathy

Leber's hereditary optic neuropathy is maternally transmitted via one of several mutations in mitochondrial DNA. Such mutations are present in approximately 10 in 100,000 persons, but the optic neuropathy develops in only 3 in 100, 000 persons, an example of incomplete penetrance. Male carriers of the LHON gene mutation develop the disease more often than female carriers. Loss of vision occurs suddenly and painlessly in the age range 15-35 years with second eye involvement occurring within one year of first eye involvement in 97% of cases. There is a wide variation in visual acuity loss, and the loss of central visual field is typical. At presentation three signs are common:

- Telangiectatic capillaries around the optic disc
- No disc leakage when a fluorescein angiogram is performed
- Swelling of the peripapillary nerve fiber layer (pseudo-edema)

Different mitochondrial DNA mutations are associated with different penetrance. The 11778 mutation is associated with the highest penetrance and the 14484 mutation with the lowest. Occasionally there can be late recovery of vision for unknown reasons.[1]

Ancillary Testing

In the diagnostic evaluation of hereditary optic neuropathy, it is common to have testing performed to correctly diagnose the condition and to exclude other masquerade syndromes, such as tumors compressing the visual pathways or retinal disease. These tests would commonly include a visual field test, an MRI scan of the optic nerves and optic chiasm, a multifocal electroretinogram to test retinal function, a fluorescein angiogram (a set of pictures after the injection of a non X-ray dye in a vein), and an optic coherence tomography scan.[4]

Final Comments

There is currently no effective treatment for any hereditary optic neuropathy. Encounters with physicians are centered on making a correct diagnosis, providing education and genetic counseling, and helping with adaptation to the attendant visual handicap with various low vision aids. In the future, research may lead to an effective treatment, thus regular eye examinations are advisable to monitor the condition and provide updates on applicable research. If you have questions after reading this brochure, more in-depth research on your own is possible through the PubMed website of the National Library of Medicine, http://www.ncbi.nlm.nih.gov/entrez/query.fcgi. You can also submit a question online at the home page (click on Contact) of my website www.retinareference.com.

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