A case report of optic neuropathy in Kjer's disease

Andrea Giuffrè OD¹, Viviana Randazzo OD¹.

¹ Orthoptists at Low Vision and Visual Rehabilitation Center (ARIS), Palermo ITALY.

Abstract

INTRODUCTION: We report a case of hereditary optic atrophy in female patient with diagnosis of autosomal dominant optic atrophy (ADOA), confirmed by molecular analysis.

CASE PRESENTATION: A 54-year-old, caucasian woman came to our attention with uncertain diagnosis of Leber hereditary optic neuropathy.

CONCLUSION: Molecular analysis allows diagnostic confirmation and can be used to support clinical diagnosis.

INTRODUCTION

Hereditary optic neuropathies lead to a decrease in visual acuity corresponding to a reduction of ganglion cell layer and nerve fiber layer. The most common neuropathies, Leber Hereditary Optic Neuropathy (LHON) and Autosomal Dominant Optic Atrophy (ADOA) are mitochondrial disorders. ADOA is characterized by bilateral and symmetric optic nerve pallor associated with insidious decrease in visual acuity with onset usually in early childhood. ADOA (estimated prevalence between 1/50,000 and 1/10,000) and LHON (prevalence between 1/15,000 and 1/50,000) are the most common forms of inherited optic neuropathies.

Even though evidence of dominant inherited optic neuropathy existed before 1900, only after the description of 19 families by the ophthalmologist Kjer ADOA (also called Kjer type optic atrophy) was recognized.

CASE PRESENTATION

A 54-year-old Caucasian female patient presented in 2013 at the Center for Low Vision and Visual Rehabilitation (ARIS) of Palermo, with a diagnosis of optic neuritis. The patient complains of low vision since childhood with worsening over years. She also refers worsening of vision bilaterally during pregnancy; she has no other health problems. She took for few years vitamin supplements, without benefit reported. She reported familiarity for low vision (a brother with optic atrophy in childhood died at age 27). She has no-consanguineous parents, apparently not suffering from eye diseases and a 56-year-old sister and a 28-year-old son both in good health, with no reported low vision. In 1999 the analysis of mitochondrial DNA mutations showed no mutations associated with common LHON mutations.

In 06/02/2013 her best-corrected visual acuity was 20/400 for the right eye and 20/1000 for the left eye.

In 9/01/1992 visual acuity was 20/200 for the right eye and 20/100 for the left eye.

The right end the left optic nerve appeared normally perfused, except for some temporal pallor.
In 1984 clinical and diagnostic history begins with a diagnosis of Leber's optic subatrophy. The VEPs showed a reduction in the amplitude and normal latency.

Goldmann visual fields made in the ‘90 showed progressive concentric reductions retinal sensitivity and central scotoma. The first computerized visual field made in 2010 showed in OD absolute cecocentral scotoma, in OS deep reduction of retinal sensitivity with absolute central scotoma.

Oct RNFL shows a marked reduction in the thickness of nerve fiber layer, with sparing of nasal area. Foveal profile is flattened with reduced neuroretinal thickness.
In 2010 VEPs recorded in both eyes a P100 wave with significant attenuation in amplitude (OS>OD) with increased latency.

ERG scotopic b-wave showed low amplitude in both eyes, while ERG photopic b-wave showed low amplitude in OD and normal amplitude in OS.
At the end of 2014, the patient was sent to a clinic for neurogenetic mitochondrial diseases. The analysis by direct sequencing of the 30 coding exons of the gene OPA showed the presence of heterozygous deletion exon 9 of the gene OPA I, which cause alteration of the reading phase of the protein and consequent introduction of premature stop codon. All the above mentioned results were compatible with autosomal dominant optic atrophy.

CONCLUSION

The diagnostic criteria for ADOA established in several studies during the past few decades include slowly progressive bilateral visual impairment, dyschromatopsia, loss of sensitivity in the central visual field, and temporal optic disc atrophy beginning before the age of 10 years. The precise age of onset is rarely established; most patients are diagnosed when they enter school or only incidentally following the examination of other affected family members. ADOA has been associated with more than 60 mutations in the gene OPA1, that map on 3q28, which encodes a homologue of the GTPase, dynamin associated in yeast, which is also expressed in retinal ganglion cells and optic nerve.

Leber's hereditary optic neuropathy (LHON) is a neurodegenerative mitochondrial optic nerve disease, which is often characterized by a sudden loss of vision in young adults, often between 18 and 30 years. It affects both eyes simultaneously or sequentially with vision loss in the second eye after several weeks or months. There may be other neurological symptoms. These abnormalities are known as Leber "plus" and may include movement disorders, dystonia, postural tremor and cerebellar ataxia.

LHON is caused by mutations in mitochondrial DNA (mtDNA). Over 90% of the mutations are located in the nucleotide positions 11778, 3460 or 14484. All mutations cause defects in the genes of the subunits of complex I of the respiratory chain in mtDNA: MT-ND1, ND4-MT and MT-ND6.

Molecular analysis allows diagnostic confirmation and can be used to support clinical diagnosis. There is currently no cure for optic atrophy. Aids for low vision represent the symptomatic treatment of choice. Several compounds have been effective for recovery of vision. Idebenone (which has obtained orphan drug designation for this disease in 2007), a synthetic analogue of coenzyme Q10, has improved the vision of patients after one year of therapy.

REFERENCES