

A Case of Bilateral Hereditary Optic Neuropathy in a Patient of Progressive Atypical Multiple Sclerosis (Infantile / Behr's Optic Atrophy): A Rare Case Report with Literature Review

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Abstract: *We report a rare case of Bilateral infantile/Behr's hereditary optic atrophy in a young male patient who came with neurological complaints and blurring of vision. Examination and investigations revealed patient having progressive atypical Multiple sclerosis complicating with optic atrophy. Patient's neurological symptoms were treated and he was explained about the poor visual prognosis. Behr's optic atrophy presents with optic atrophy associated with multiple neurological conditions like ataxia, mental retardation, increased tonicity, urinary incontinence.*

Keywords: Behr's optic atrophy, Mendelian inheritance, Atypical Multiple sclerosis, poor visual prognosis

1. Introduction

Hereditary optic neuropathies constitute a significant cause of visual impairment in children and young adults. However, they comprise of a heterogeneous group of disorders whose primary manifestation is an optic nerve dysfunction or those in which optic neuropathy is part of the systemic disorder. Further, onset of the condition might be variable ranging from the infancy, young adulthood, and as late as late adult age. Inheritance of the condition may follow different pattern: Mendelian autosomal dominant and recessive (Behr's optic atrophy) even mitochondrial inheritance (Leber's Hereditary optic neuropathy).¹

1.2. Case report

A 30 year old male patient, with no previous comorbidities, complaint of blurring of vision in both eyes (Left > right) since 2 years, which started in left eye, insidious onset, painless and had diplopia and tremors. No complaints of headache, fever, nausea, vomiting, giddiness. On examination patient is conscious, and oriented to time, place and person and vitally stable. Patient was having pupil: 2mm, reacting to light with vision in RE = 3mfc and was having grade 3 RAPD pupil with vision in LE = Denies PL. Fundus evaluation shows both eye disc pallor present and right eye confrontation test showed generalized field restriction and no nystagmus was present. Tone-increased, with exaggerated reflexes (pyramidal tract dysfunction).

1.3. Family history

Patient had a positive family history of his older brother having similar condition diagnosed with B/L optic atrophy with Moderate Mental Retardation. No other family member had been diagnosed with similar condition. Family history of

consanguinity is present in patient's grandparents. (3rd generation pedigree).

MRI Brain with showed marked atrophy B/L occipital lobe, diffuse cerebral atrophy and subcortical white matter signal changes.

Repeat MRI Brain with contrast showed multiple confluent **T2** and **FLAIR hyperintensities** as in subcortical white matter in bilateral occipital region and calloseseptal interphase possibility of **DEMYLINATING DISEASE** likely.

MRI Screening of both optic nerves showed reduction in the optic nerve volume on either side predominantly on the left side suggestive of **B/L OPTIC ATROPHY**.

MRI Screening of whole spine was normal.

Pattern VEP findings in both eyes revealed mild delay in amplitude and latency of P100 wave. Suggestive of B/L Optic Atrophy. Fundus Fluorescein angiography suggestive of **B/L OPTIC ATROPHY**.

CSF analysis was done and it showed protein- 51.1; sugar- 61; and was **positive for the presence of the oligoclonal bands (bands >10) that suggested of the Intrathecal IgG Synthesis**. And was negative for NMO (Neuromyelitis optica) Aquaporin -4 antibodies Indirect Immunofluorescence was negative for presence of any antinuclear antibodies and serum ACE level was normal. LHON Gene study was negative for any mutations in mitochondrial DNA.

Patient was treated with Inj. Methylprednisolone 1gm for 5 days and with oral steroids. Some improvement was seen in neurological symptoms but no visual improvement was seen and then 2 doses of retrobulbar 0.75cc methylprednisolone was given in right eye but still no visual improvement seen. Poor visual prognosis was explained to the patient.

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2. Discussion

Most of the patients with hereditary optic neuropathy present with either insidious onset (ADOA, Recessive forms) or Sub acute vision loss (LHON). There might be significant family history, family history of consanguinity or pattern suggestive of maternal inheritance.

Genetic basis and molecular defects of all import pattern have been characterized and involve defect in high energy metabolism.

Autosomal dominant Optic Atrophy (Kjer's) involves mutation in the OPA1 gene that codes for the mitochondrial proteins and interrupts mitochondrial membrane folding, stress and activity.

Wolfram syndrome involves mutation in WFS gene that encodes for endoplasmic reticulum and induces excessive stress.

The LHON involves mutation in the mitochondrial gene (me 11778/ND4, mt14484/ND6, and mt3460/ND1) which are responsible for electron transport chain.

All of them have propensity to involve retinal ganglion cells and papillomacular bundle², while some of them may affect the other body systems.

Multiple therapeutic approaches are being tried including the substances that might alter the mitochondrial machinery (Idebenone and EPI-743) Or ER processing/stress (TUDCA and Dantrolene etc.) which have shown promise.¹

Gene therapy technology has shown significant advancement and promising results have been reported at least in LHON. This might be particularly beneficial in near future in ADOA and WFS.

3. Figures

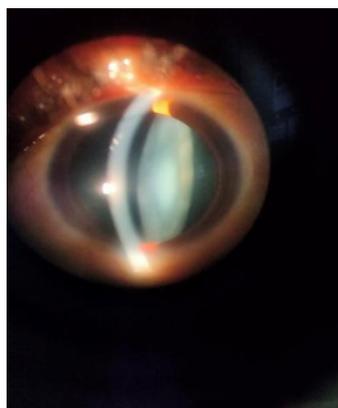


Figure 1: (original) shows **early onset cataract** on slit lamp examination.

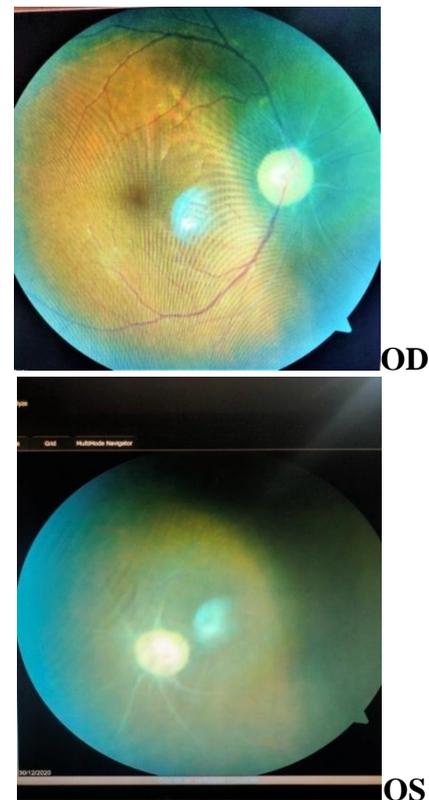


Figure 2 (original) shows Optical coherence tomography of both eyes; Right eye (OD) showed 0.7 CDR with pale disc and surrounding perivascular cuffing around vessels over the disc, while the Left eye (OS) showed Total pale disc with perivascular cuffing of vessels on and around the disc. The fundus and OCT finding suggestive of **B/L Secondary Post neuritic Optic Atrophy**.

4. Conclusion

Complicated Hereditary optic neuropathy was first described by Carl Behr.^{1,3} This condition presents as an optic atrophy that can be recognized in early childhood in association with ataxia, mental retardation, increased tonicity, urinary incontinence. This condition is characterized by marked optic atrophy with marked visual disability. Ophthalmoscopically there is presence of temporal disc pallor with associated dyschromatopsia.

Mutations in OPA3 gene have been described in patients with metabolic disturbances⁴ and OPA1 mutations in those patients without metabolic disturbances. Pyle et al. reported mutations in the C12 orf65 gene in four different patients matching the clinical description of classical Behr's syndrome.⁵

There is no definitive treatment for Behr's syndrome and largely is symptomatic.^{1,5}

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