ATYPICAL PRESENTATION OF LEBER HEREDITARY OPTIC NEUROPATHY MIMICKING OPTIC NEURITIS: CHALLENGES IN THREE PATIENTS

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BACKGROUND AND OBJECTIVE

Leber's hereditary optic neuropathy (LHON) is a primary mitochondrial disorder that typically presents in young individuals with subacute, painless central vision loss, affecting both eyes sequentially over weeks to months. Although LHON often has distinctive clinical features, atypical presentations can complicate diagnosis. Notably, optic nerve lesions on MRI are uncommon in LHON and are more typically associated with inflammatory optic neuropathies, such as optic neuritis (ON), which increases the risk of misdiagnosis.

Here we describe three patients with genetically confirmed LHON who were initially misdiagnosed with ON due to atypical clinical and radiological features.

Tabella 1. Distinctive Features of LHON and ON

	LHON	ON
age and sex	young male (18-35 y)	young adults (20-45), mostly female
onset	subacute, bilateral (often sequential)	acute, usually unilateral
ocular pain	absent	common, with eye movements
visual loss	central scotoma, severe and persistent	variable, often reversible
fundus	optic disc edema, elevation, hyperemia, peripapillary telangiectasias	normal or optic disc swelling
MRI	usually normal	optic nerve T2 hyperintensity and Gd enhancement

Patient 1 ♂ 16 aa **Patient 2** ♀ 52 aa **Patient 3** ♂ 51 aa

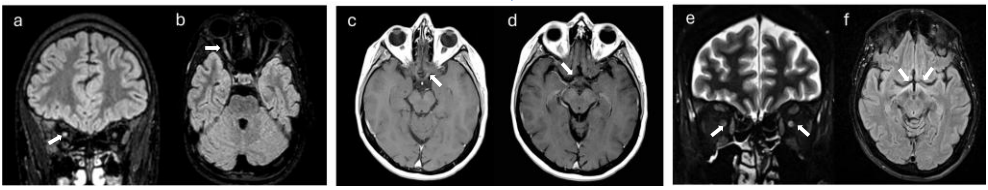

Fig 1. MRI abnormalities of the optic pathways in the three patients with LHON. (a, b) Patient 1: coronal and axial FLAIR images show hyperintensity of the right optic nerve. (c, d) Patient 2: post-contrast T1-weighted images show mild enhancement and enlargement of the intracranial segment of the left optic nerve (c) and of the right hemichiasm and optic tract (d); (e, f) Patient 3: coronal T2-weighted fat-suppressed image shows bilateral hyperintensity in the retrobulbar segments of the optic nerves (e), with additional bilateral involvement of the optic tracts on FLAIR sequences on follow-up MRI (f).

TYPICAL FINDINGS IN OUR CASES

- Bilateral, subacute vision loss (sequential in two cases);
- Consanguineous parents and an uncle with early-onset blindness in Case 1;
- Neurophysiological (VEP) and ophthalmological (OCT) findings consistent with LHON, showing bilateral pre-chiasmatic conduction delay and marked RNFL/GCL thinning;
- No response to steroids or plasma exchange.

ATYPICAL FINDINGS IN OUR CASES

- Late age at onset (>50 years) in Cases 3-4;
- Orbital pain and RAPD in Case 1;
- Lack of characteristic fundus findings in Cases 3-4;
- Comorbidities potentially affecting presentation: Fahr's syndrome (Case 3) and glaucoma (Case 4);
- MRI alterations: T2/FLAIR optic nerve hyperintensity with gadolinium enhancement in all cases; posterior extension to the optic chiasm/tracts on follow-up MRI (< 3 months) in two cases.

CONCLUSIONS

MRI optic pathway abnormalities do not exclude LHON, which should be considered in all patients presenting with bilateral subacute visual loss.