Highlighting optic radiations in Leber's hereditary optic neuropathy and multiple sclerosis.

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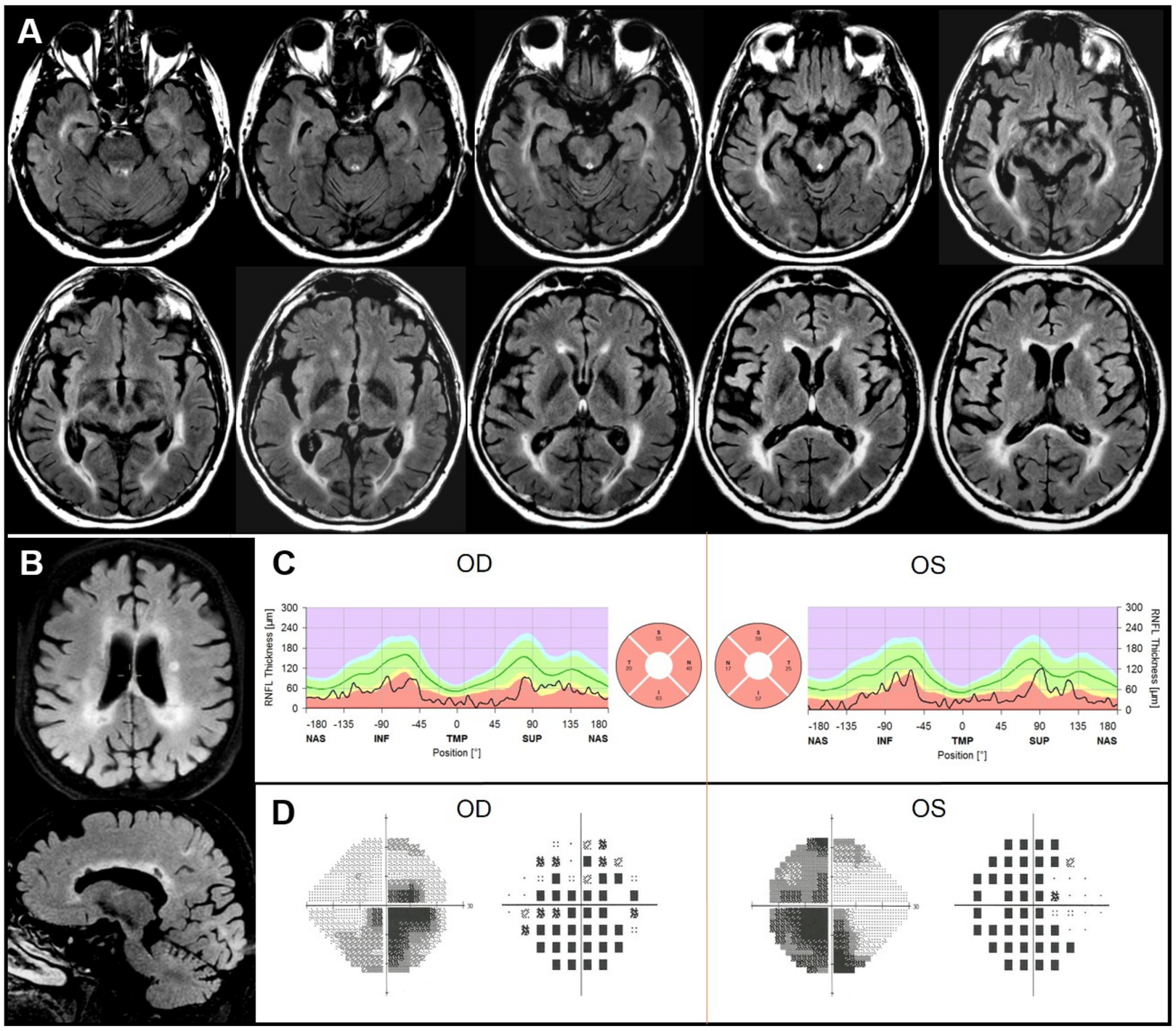
Introduction

Leber's hereditary optic neuropathy (LHON) and multiple sclerosis (MS)-like syndrome, also known as "*Harding's disease*", is a highly debated clinical entity.

It has been recently proposed that it could be due to chance co-occurrence of the two disorders (1). However, there is discussion about the possible reciprocal modifying influence on natural history of both diseases.

In the light of mounting evidence of mitochondrial dysfunction in MS and clear mitochondrial involvement in LHON, we present a case with a peculiar involvement of optic radiations.

Methods: Axial and multiplanar FLAIR T2-weighted sequences were obtained on a high-field 3T MRI. Assessment of the anterior visual pathway was performed through Optical Coherence Tomography (OCT, Stratus Zeiss) evaluating retinal nerve fibre layer (RNFL) thickness and computerized Humphrey Visual Fields.



Case report

We report a 51 year-aged male patient with LHON-MS disease carrying the m.11778A>G mitochondrial DNA mutation.

He presented disease onset at 24 years of age with loss of central vision in the left eye, rapidly followed by right eye involvement, unresponsive to corticosteroid treatment.

At 29 years he developed spastic paraparesis. Brain MRI white matter lesions were documented since the optic neuropathy onset, with periventricular and subcortical distribution on T2 images highly suggestive of MS. Spinal MRI revealed multiple demyelinating lesions both at cervical and thoracic level. Oligoclonal bands on CSF analysis were also demonstrated.

The patient presented a slowly progressive course of SM with a gradual worsening of visual, motor and sensitive functions, with urinary dysfunction.

The last neurological examination disclosed severe visual loss, diffuse muscle hypotrophy, spastic paraparesis with brisk deep tendon reflexes and bilateral clonus achilleus, mild hyposthenia at the upper limbs, tactile hypoesthesia on the right side.

The patient is now on wheel-chair.

Figure 1 legend:

A: Axial FLAIR T2-weighted sequence displaying widespread hyperintensity with black holes along the whole optic radiations.

B: Multiplanar reformatted FLAIR T2-weighted images showing demyelinating lesions in the cerebral deep white matter and in the corpus callosum.

C: Optical Coherence Tomography (Stratus Zeiss) showed diffuse reduction of the retinal nerve fibre layer thickness.

D: Computerized Humphrey visual fields revealed diffuse loss of sensitivity bilaterally, more dense centrally.

Results

Last brain MRI control revealed an overall involvement of the posterior visual pathway, as shown by the hyperintense signal in FLAIR depicting the entire length of optic radiations from the lateral geniculate nucleus to the occipital cortex **(Figure 1A)**. This is unusually seen in MS patients and contrasts with the less severe involvement of the remaining white matter, otherwise showing the typical demyelinating lesions pattern **(Figure 1B)**. The assessment of the anterior visual pathway showed a bilateral optic atrophy with a diffuse visual field defect (more dense centrally) , typical of severe chronic LHON optic atrophy **(Figure 1C-1D)**.

Discussion

The trans-synaptic involvement of the post-geniculate pathways has been demonstrated in LHON by diffusion-weighted imaging or post-mortem studies; however, it does not reflect into visible signal changes at MRI (2). Conversely, trans-synaptic degeneration secondary to optic neuritis and Wallerian degeneration due to local demyelinating lesions have both been reported to contribute to optic radiation damage in MS (3). A common denominator for LHON and MS is the mounting evidence that primary and secondary mitochondrial dysfunction contribute to neurodegeneration in both diseases (1).

In conclusion the unusual MRI appearance of visual pathways in our patient suggests the existence of a reciprocal and synergistic interaction between the pathogenic mechanisms of LHON and MS, probably mediated by mitochondrial dysfunction. This leads to a distinct phenotype with a more aggressive course and, in our patient, to this up to now unreported severe signal changes involving the visual pathways.

References:

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Sin XLVII CONGRESSO NAZIONALE
22-25 OTTOBRE 2016 – VENEZIA