Retrograde retinal damage after acute optic tract lesion in MS

The anterior visual pathway is frequently affected in multiple sclerosis (MS), but how axonal damage extends from the site of the lesion to neuronal bodies in the retina or lateral geniculate nucleus is poorly understood. Thanks to optical coherence tomography (OCT), it is possible to map and quantify the retrograde diffusion of axonal damage to the retina.1 Lesions in the anterior optic pathway promote significant atrophy of retinal nerve fibre layer (RNFL), which develops in the first 3 months after damage and remains stable after 3 months. Moreover, it has been recently demonstrated that retinal damage in MS is complex and may distinctly affect retinal layers, combining either layer thinning (suggesting the presence of synapse loss and neuronal loss) or layer thickening (suggesting the presence of oedema and inflammation). In fact, the analysis of the ganglion cell/inner plexiform layer (GCL+IPL) and inner nuclear layer (INL) better correlates with functional disability and prognosis than with RNFL atrophy.2 Acute focal lesions of the optic tracts are infrequently recognised in MS, and they constitute an excellent opportunity to study retrograde axonal degeneration. Previous studies with OCT have shown the homonymous hemimacular atrophy ipsilateral to the optic tract lesion as a specific pattern of retinal atrophy in optic tract lesions,3 with a preferential impact on the GCL.4

METHODS

A patient with relapsing–remitting MS presented with non-painful, new onset, acute bilateral visual deficit. Automated visual field tests demonstrated non-congruent bilateral homonymous right hemianopsia (figure 1A). Visual acuity (Snellen chart) and colour test (Hardy Rand and Rittler plates) were normal. 3T brain MRI showed a new 10-mm lesion on fluid attenuated inversion recovery in the area corresponding to the left optic tract that showed gadolinium enhancement (figure 1B). She was treated with intravenous methylprednisolone. Before starting the prospective evaluation, we obtained written informed consent from the patient.

We performed OCT (Spectralis, Heidelberg Engineering) for each eye with macular raster scan centred on the fovea (matrix size 20°×20°, 25 sections of 240 μm; 6-mm ring area was used to calculate sector retinal thickness). Central 1-mm diameter area corresponding to the fovea was excluded to facilitate the calculation of average measurements at baseline, 5th and 10th month after onset. Retinal layers were automatically segmented by the in-built software of the equipment (Spectralis Viewer software, V5.7, with Segmentation Editor (β version)) and manually corrected by a trained neurologist (IG). GCL and IPL layers were considered as a single complex (GCL+IPL) as
described by Saidha et al. The thicknesses of RNFL, GCL+IPL and the entire retina were measured for every macular sector of each eye. INL, layers accounting for photoreceptors (PHRP), pigment epithelium and Bruch’s membrane were considered as a single complex (INL+PHRP), the thickness of which was calculated by subtracting the RNFL and GCL+IPL thicknesses from the retinal thickness.

**RESULTS**
At 10-month follow-up, we observed a mean reduction of 4.7% (13.3 μm) in bilateral mean macular thickness: 4.7% (11.6 μm) in the right eye (contralateral to optic tract lesion) and 5.2% (15 μm) in the left eye (ipsilateral to the lesion) (figure 1C and online supplementary figure S1). This atrophy reproduced the specific pattern observed in optic tract...
lesions with homonymous hemimacular atrophy that was congruent with the left optic tract lesion. This atrophy was mainly due to GCL+IPL thinning (13.6 μm reduction (18.4%) in bilateral average thickness compared to baseline) with the same homonymous hemimacular pattern seen for the entire retina. RNFL atrophy (5.05 μm reduction bilaterally (14.8%) compared to baseline) was more severe in the nasal sector of the right macula (26.4% reduction compared to baseline) and in the inferior and superior sectors of the left macula (25.8% and 22.2%, respectively, compared to baseline). We observed that most of the macular atrophy (9.6 μm, 75.6% of total thinning) happened during the first 5 months (figure 1D). Interestingly, while most of the GCL+IPL atrophy (11.9 μm, 87.5% of total thinning) happened in the first 5 months, RNFL atrophy developed more slowly and progressively along 10 months (54.4% of the reduction happened in the first 5 months). In addition, we found an increase in the INL+PHRL thickness (4.3 μm (2.5%) reduction in bilateral average thickness compared to baseline) in the first 5 months that remained stable until month 10. This increase was particularly notable in the temporal sectors, with a mean thickening of 9 μm (4.9%) after 10 months. No microcystic macular oedema was observed in the INL or PHRL at any time.

DISCUSSION

This case illustrates that axonal damage due to optic tract lesion may extend in a retrograde manner to the retina with different dynamics and effects into the different retinal layers. The fact that most of the thinning of GCL+IPL happens in the first months when RNFL atrophy extends longer suggests that functional axonal abnormalities may influence neuronal survival even before axons are definitively lost in the RNFL. If true, this clearly indicates that early monitoring of ganglion cell loss would be relevant to evaluate dynamics of neuronal damage. Finally, we observed a thickening of macular INL+PHRL layers that would be, especially for temporal sectors, above the expected axial resolution (3.9 μm) and test–retest variability of total macular thickness segmentation (1 μm) of our equipment. This finding may suggest the presence of pathological abnormalities like oedema or inflammation in these layers, a phenomenon that could constitute the response of glial cells to axonal and neuronal loss in the neighbouring layers. These results would require further validation.

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Contributors IG, EF and SOP performed OCT studies and analysis; MS, SL, NS and AS performed patient evaluation; PV and BSD reviewed data and wrote the manuscript.

Funding This work was supported by grants to PV from the Instituto de Salud Carlos III, Spain (FIS PS09/00259 and RETICS program RD07/0060/01) and by an unrestricted grant from Roche Postdoctoral Fund (RPF-ID046). IG was supported by a fellowship from the Instituto de Salud Carlos III, Spain (Rio Ortega program CM11/0240).

Competing interests Ilígito Gabiñolón has received travel and accommodation expenses from Novartis for national and international congresses. María Sepúlveda has no conflicts of interest to disclose. Santiago Ortiz-Pérez has received consultancy fees from Novartis.

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Ethics approval IRB of the Hospital Clinic of Barcelona.

Provenance and peer review Not commissioned; externally peer reviewed.

Accepted 1 May 2013

Published Online First 28 May 2013

J Neurol Neurosurg Psychiatry 2013;84:824–826.

PostScript
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J Neurol Neurosurg Psychiatry 2013 84: 824-826 originally published online May 28, 2013
doi: 10.1136/jnnp-2012-304854

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