PHOTO ESSAY

Trans-synaptic Retrograde Degeneration Following Hemispherectomy in Childhood

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ABSTRACT

Trans-synaptic retrograde degeneration (TRD) in the human visual system has been established. However there are few studies demonstrating macular thinning of the Retinal Ganglion cell Layer and/or Inner Plexiform layer (RGCL-IPL), corresponding to an acquired homonymous hemianopia. We report a 17 year old with a homonymous hemianopia, secondary to a hemispherectomy for intractable epilepsy. Three years following hemispherectomy, Optical Coherence Tomography (OCT) revealed evidence of TRD, corresponding to his complete homonymous hemianopia. Macular maps of the RGCL-IPL thickness provides useful additional information to measurements of optic nerve Retinal Nerve Fibre Layer Thickness (RNFL) in identifying TRD in acquired homonymous hemianopia.

ARTICLE HISTORY

Received 17 November 2016
Revised 21 December 2016
Accepted 22 December 2016

KEYWORDS

Hemispherectomy;
homonymous hemianopia;
inner plexiform layer; optical
coherence tomography;
retinal ganglion cell layer;
trans-synaptic retrograde
degeneration

A 17-year-old male with Rasmussen's encephalitis was reviewed for a full ophthalmological assessment 3 years following a left image-guided hemispherectomy at the age of 14, for intractable epilepsy. He was also reviewed prior to his surgery as part of his epilepsy surgery work up. Post-operative T1- and T2-weighted magnetic resonance imaging (MRI) images demonstrating the disconnected left hemisphere are shown in [Figure 1](#). Despite post-operatively developing a right hemiplegia, he remained independently mobile. He had a moderate learning disability (full-scale IQ = 50) and had been diagnosed with autistic spectrum disorder. His unaided visual acuity was on the right eye 0.000 and on the left eye 0.100 with LogMAR acuity test. His near vision was N4.5 print in either eye. There was no relative afferent pupillary defect (RAPD) present, and fundoscopy showed mild bilateral temporal optic disc pallor. As expected, he had a complete right homonymous hemianopia on kinetic visual field testing to the Goldmann I2e, I4e, and V4e targets, which had not been present on pre-operative assessment.

Infrared and macular/optic disc optical coherence tomography (OCT) images were obtained using the

Spectralis system (Heidelberg Engineering, Germany). Global retinal nerve fibre layer (RNFL) thickness was outside normal limits in both eyes (right eye: 62 μ m, left eye: 67 μ m; normal: minimum 99 μ m), with additional thinning affecting the temporal (T: 36 μ m; normal: minimum 78 μ m), inferior-temporal (TI: 102 μ m; normal: minimum 147 μ m), superior-temporal (TS: 94 μ m; normal: minimum 138 μ m), and superior-nasal (NS: 52 μ m; normal: minimum 102 μ m) sectors of the right eye and the temporal (T: 51 μ m; normal: minimum 78 μ m), superior-temporal (TS: 76 μ m; normal: minimum 138 μ m), and inferior-temporal (TI: 73 μ m; normal: minimum 147 μ m) sectors of the left eye ([Figure 2](#)).

The central macular profiles were segmented using the inbuilt HEYEX software (Heidelberg Engineering, Germany). Each layer was visually inspected for artefactual segmentation and then for asymmetries in thickness on either side of the fovea centralis. Homonymous asymmetries of the total retinal thickness ([Figure 3a](#) and [b](#)) were evident, affecting the nasal retina of the right eye (measuring 307 μ m) and the temporal retina of the left eye (measuring 298 μ m). Raster scans of the layers also showed neuronal loss

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Figure 1. MRI at 3 years post op [(a) T1 coronal (b) T1 sagittal and (c) T2 axial] showing the complete disconnection of the left hemisphere and diffuse left cerebral hemisphere atrophy.

Figure 2. (a) Infra-red images of the right (i) and left (ii) eyes showing the optic disc appearance. (b) OCT of the RNFL of both nerves and (c) the segmental measurements.

throughout the maculas (Figure 3c and 3d), corresponding to the distribution of the complete dense homonymous hemianopia, hence respecting the vertical meridian on both eyes.

Unilateral cortical pathologies result in homonymous hemianopia. Trans-synaptic retrograde degeneration (TRD) of the visual pathways is a previously described phenomenon

Figure 3. (a) OCT scans through the fovea centralis with red lines outlining the total retinal thickness in the right (i) and left (ii) eye. Thickness maps of (b) the total retinal thickness, (c) Ganglion Cell Layer and (d) Inner Plexiform Layer. Note the homonymous distribution in the Ganglion Cell and Inner Plexiform Layers as a result of the trans synaptic degeneration.

leading to a loss of retinal neuronal cells and can occur in various neurological diseases, affecting posterior visual pathways. This phenomenon has been reported in both experimental conditions with variable expression in primates and monkeys^{1,2} and in humans³.

Although it was previously thought to occur only in congenital lesions,^{3,4} it has now also been well demonstrated in acquired posterior visual pathway damage,⁵⁻⁸ including unilateral occipital strokes and lesions of the retrogeniculate visual pathway. Further evidence of TRD in

humans has been provided both histologically⁹ and by MRI.¹⁰ With the use of T1-weighted scans, TRD of the optic tract was found to occur in correlation with the size of the field loss in congenital and acquired hemianopia and was most severe in congenital cases.¹⁰

It is well known that pathologies affecting the posterior visual pathways unilaterally can result in a typical pattern of temporal atrophy of the optic disc ipsilaterally to the lesion and band atrophy on the contralateral side.³ This pattern is associated with loss of non-crossing fibres in the ipsilateral eye and loss of crossing fibres in the contralateral eye and can often be very subtle clinically and therefore easily overlooked on ophthalmoscopy. OCT demonstrating RNFL loss has been recently proven a very useful, non-invasive tool of TRD evidence in patients with congenital and acquired homonymous hemianopia.^{4–8} These studies suggested abnormalities in the RNFL pattern corresponding to the visual field defect, with significant RNFL thinning affecting the temporal (T) and vertical (TI, TS) sectors of the ipsilateral eye and the nasal (N, NS, NI) and temporal (T) sectors of the contralateral eye.^{4,5,7} Time course of TRD with the use of RNFL thickness in acquired homonymous hemianopia was characterised: occurring early after the onset of the occipital injury, and at a maximal rate in the first few years, followed by a much slower rate in ensuing years.^{6,8}

There are, however, very few studies that demonstrate macular retinal ganglion cell layer–inner plexiform layer (RGCL-IPL) complex atrophy as evidence of TRD in patients with homonymous hemianopia.^{11–13} These studies have demonstrated a significantly stronger correlation between the visual field defect and the thickness of macular RGCL, rather than that of the peripapillary RNFL in patients with lesions in the posterior visual pathway.¹³ This was attributed to the fact that at the macula, the bodies of the neurons are more numerous and topographically organised in such a way to correspond to the visual field. On the contrary, the peripapillary RNFL structure is more complex in its anatomical distribution of fibres and therefore is more difficult to correlate RNFL loss to visual field defect. Moreover, Goto et al., in a group of seven patients with acquired unilateral occipital lesions, found reduced RNFL thickness in all temporal sectors (T, TI, TS) of the ipsilateral eye, corresponding to the nasal hemianopic field and predominantly

temporal (T, TI, TS) and superior-nasal (NS) sector thinning in the contralateral eye, which was contradictory to previous studies.⁸ In the present case report, a very similar distribution of the RNFL thinning was detected. One reason suggested for this discrepancy to most previous studies could be that the contributing crossing fibres to the nasal sector of the optic disc correspond to ganglion cells from the nasal peripheral retina, whereas those contributing to the temporal sector correspond to the ganglion cells from the central retina, including the papillomacular bundle.⁸ This could reflect the proportion of ganglion cell loss, predominantly located in central retina and projecting to the parvocellular layer of the lateral geniculate nucleus, which has been previously proven by animal studies as selectively degenerated following striate cortex lesions.² In conclusion, in this case report, despite clinically subtle findings, and a more atypical distribution of RNFL loss, RGCL-IPL thinning was strikingly significant and corresponded to the dense homonymous visual field loss.

The segmentation software for macular OCT can provide thickness maps of the RGCL-IPL complexes and appears to be of an additive value to RNFL measures in the assessment of TRD. We report a case of homonymous thinning of RGC-IPL in the macula of a patient who suffered right acquired homonymous hemianopia. We believe this case demonstrates in vivo evidence of severe TRD at a young age, as a result of functional hemispherectomy.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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