CASE REPORTS

Retrogeniculate Lesion of the Visual Pathways: Retinal Optical Coherence Tomography Angiography Shows Evidence of Transsynaptic Retrograde Degeneration

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ABSTRACT

Transsynaptic retrograde degeneration (TSRD) of the visual pathways is the loss of retinal ganglion cells occurring upstream from a posterior visual pathway lesion. We present a case of a 54-year-old woman with an epidermoid cyst at the right temporo-occipital junction, in whom retinal optical coherence tomography angiography showed a reduction of the superficial retinal capillary density consistent with TSRD. While this reduction has been described in chronic optic neuropathies and *pregeniculate* lesions, to our knowledge, this is the first case report showing how a reduction in the superficial retinal capillary density occurs also for a *postgeniculate* lesion.

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Case report

A 54-year-old woman presented with an 18 month history of left-sided vision loss associated with moderate headache. Her best corrected visual acuity was 20/40 in both eyes (OU). Extraocular motility, intraocular pressure, pupil and slit lamp examination were normal OU. Fundus examination (Figure 1a) showed temporal pallor of the optic nerve in the right eye (OD) and a bow-tie optic atrophy in the left eye (OS) consistent with a right retrochiasmal lesion affecting the uncrossed fibres to the right and the crossed fibres to the left. Standard automated perimetry (Humphrey visual field) showed a left homonymous hemianopia (Figure 1b) consistent with a right retrochiasmal lesion. Magnetic resonance imaging (MRI) of the brain showed an epidermoid cyst at the right temporo-occipital junction. Homonymous macular ganglion cell complex loss (Figure 1c) was evident on optical coherence tomography (OCT). Interestingly, OCT angiography (OCTA) of the macula and optic nerve showed dropout of capillaries in the retinal

superficial vascular plexus consistent with the anatomical organisation of the retinal nerve fibre layer (RNFL) (Figure 1d,e).

Discussion

The retinal nerve fibre layer is composed of the axons of retinal ganglion cells (RGC); most of these axons project to the lateral geniculate nucleus (LGN). The axons subsequently form synapses in the LGN and reach the primary visual cortex.

Transsynaptic retrograde degeneration (TSRD) of the visual pathways is the loss of retinal ganglion cells occurring upstream from a posterior visual pathway lesion.¹ In 1963, Buren surgically induced a lesion in one occipital lobe of the adult macaque monkey.² Two years later, he was able to demonstrate homonymous thinning of the retina supporting the concept of TSRD. In humans, histological evidence of TSRD was first provided by Beatty *et al.* who reported this finding 40 years after occipital lobectomy.³

Figure 1. Colour retinography (a) shows minimal temporal pallor of the optic nerve OD (arrow), and a suggestion of bow-tie optic atrophy OS (dotted arrow). Standard computerised Humphrey visual field (30–2) shows left homonymous hemianopia consistent with a right postgeniculate lesion (b). Homonymous macular ganglion cell complex (c) loss occurs temporally to the fovea in the right eye and nasally in the left eye, consistent with the visual field defect. Peri-papillary and retinal capillary density reduction corresponding to the RNFL thinning (composite macula 6×6 mm and optic nerve 6×6 mm). In the right eye (d) the retrograde degeneration has affected the temporal retina causing a thinning of the RNFL temporally to the macula, which derives arcuately from the vertical poles of the optic disc (dotted arrows). In the left eye (e) the retinal capillary density reduction is evident in the area of RNFL which projects nasally to the macula (arrows).

Previously thought to occur only in congenital lesions, recent studies with OCT have demonstrated the possibility of TSRD in adult humans with acquired retrogeniculate lesions of the visual pathways. In fact, Jindahra *et al.* demonstrated thinning of the RNFL in both eyes in a series of 26 patients with both congenital and acquired homonymous hemianopia.⁴ Patients exhibited a significant loss of RNFL mean thickness compared with controls, and those with congenital lesions exhibited greater RNFL loss than individuals with acquired lesions.

The development of OCT has allowed measurement of the RNFL thickness, and this technology has provided evidence of TSRD even after occipital lesions.⁵ Furthermore, segmentation software of macular OCT provides thickness maps of the RGC layer–inner plexiform layer (IPL) complex. This approach allows discernment of the patterns of homonymous hemianopic visual field loss corresponding to TSRD from postgeniculate lesions.^{5,6}

Segmentation of retinal layers has in fact allowed the study of functional areas in greater detail. This is most evident at the macula where the RGCs density is maximal.⁷ In recent years, OCT of optic nerve and macula has assumed a relevant role in the study of many neurological

disorders, many of which possibly involve TSRD. In fact, the human visual pathway is characterised by its unique hierarchical architecture and, therefore, represents an ideal model to study TSRD.⁸ The study of TSRD is not only academic but may have therapeutic implications in the next future. For example, You *et al.* recently showed that myelin and glial pathology precedes axonal loss in many diseases, suggesting that the mechanism of TSRD may be at least partially mediated by glial components at the cellular level.⁸ RGCs are of particular interest because of their unique position and accessibility to direct *in vivo* measurement. Direct macular RGC thinning has been demonstrated in patients with optic tract lesions,⁹ or compression of the chiasm. Moreover, atrophy of the ganglion cell layer is a reliable predictor for poor visual function and correlates at the topographic level with the visual fields deficits.¹⁰

OCTA, moreover, allows vascular patterns to be demonstrated of acquired RNFL thinning. In chronic optic neuropathies, OCTA has shown a reduction in the superficial capillary density in a pattern corresponding to the acquired thinning of the RNFL.¹¹ Recently, Micieli *et al.* have described the same findings also in optic tract lesions, showing a bow-tie reduction in the superficial capillary density reflecting the bow-tie

atrophy of the *pre*geniculate optic pathways.¹² In our case, we were able to demonstrate that this reduction happens also for *post*geniculate (temporo-occipital) lesions and that capillary density reduction follows RNFL thinning independently from the site and cause of lesion. To our knowledge, this is the first case report in the English language ophthalmic literature showing how a reduction in the superficial retinal capillary density on OCTA occurs also for *post*geniculate lesions, thus suggesting a potential utility of OCTA also in other causes of TSRD associated with ganglion cell/inner plexiform complex (GCIP) thinning on OCT such as multiple sclerosis (MS) and Alzheimer's disease (AD).

In MS, Al-Louzi *et al.* described a cohort of patients in whom discrete areas of injury to the posterior visual pathway were related topographically to hemi-macular GCIP thickness reduction.¹³ This sheds light on mechanisms underlying the accelerated retinal neuronal loss seen in MS in the absence of optic neuritis. Hemi-macular GCIP thickness measurement might be useful in localising presumably destructive neuro-inflammatory pathology in the posterior visual pathway, which is in contradistinction to peripapillary RNFL thickness where hemi-macular axonal segregation is less distinct.

In preclinical AD, the foveal avascular zone, studied by means of OCTA, was increased compared with controls.¹⁴ In a recent review, Mardin *et al.* summarised that some neurological disorders such as AD, Parkinson's disease and MS are characterised by rarification of retinal vessels and atrophy of the retinal layers that cannot be appreciated with ophthalmoscopy.¹⁵ They concluded that OCTA parameters could serve in the future as supplementary biomarkers for assessment of the retinal-neurovascular coupling in these diseases. Possible technical limitations of OCTA machines now available though are the long acquisition times and relatively high sensibility to eye movements.

In conclusion, further studies are needed to fully understand the role and usefulness of OCTA in neurological disorders affecting the visual pathways, but OCTA will probably be useful as a non-invasive biomarker to assess the neurological dysfunction in these diseases.

Declaration of interest

Authors report no conflicts of interest.

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