

Short Communication

Homonymous Hemimacular Ganglion Cell Layer Loss Detectable by SD-OCT: A Biomarker of Retrochiasmal Visual Pathway Lesion

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- Ischemic stroke
- Multiple sclerosis
- Optical coherence tomography
- Macular ganglion cell layer
- Retinal nerve fiber layer
- Retrograde degeneration
- Visual pathway

Abstract

In the retina, Ganglion Cell Layer (GCL) and their axons Retinal Nerve Fiber Layer (RNFL) representing the first-order neurons of the visual pathway can be affected by retrograde degeneration of the Central Nervous System (CNS) lesions. Thickness of GCL and RNFL can be quantified close to histological level using Spectral-Domain Optical Coherence Tomography (SD-OCT). We report two patients, one with previous ischemic stroke affecting left medial occipital lobe with permanent right homonymous hemianopia, and one with Multiple Sclerosis (MS) and a MS plaque at the right optic radiation but no homonymous hemianopia. Both patients had homonymous hemimacular GCL loss irrespective of visual field defect. Homonymous hemimacular GCL loss is consistent with ipsilateral retrochiasmal visual pathway lesions and represents imaging biomarker of retrochiasmal lesions which can be detected precisely and easily by OCT. This imaging biomarker can be of value in diagnosis, prognosis and clinical trials of developing novel therapies.

ABBREVIATIONS

CSF: Cerebrospinal Fluid; GCL-IPL: Ganglion Cell Layer - Inner Plexiform Layer; SD-OCT: Spectral-Domain Optical Coherence Tomography; RNFL: Retinal Nerve Fiber Layer; MRI: Magnetic Resonance Imaging; VEP: Visual Evoked Potentials; VF: Visual Field

INTRODUCTION

Optical Coherence Tomography (OCT) using intensity of back-reflected infrared light provides non-contact, real-time, high-resolution imaging of the retina. Spectral-Domain OCT (SD-OCT) with higher speed and broader wavelength improves image resolution to few micrometers and visualizes retinal microstructure with 10 distinct layers close to histologic level [1].

The first-order neuron of the visual pathway equal to the Ganglion Cell Layer (GCL) in the macula and their unmyelinated axons in the optic disc equal to the Retinal Nerve Fiber Layer (RNFL), provide a natural window to study the Central Nervous System (CNS). Thinning of macular GCL and peripapillary RNFL can occur through retrograde trans-synaptic degeneration of second-order neurons in the brain as detected by Magnetic Resonance Imaging (MRI). Thickness of GCL and RNFL may reflect global CNS damage [2,3], and has been suggested as biomarkers of brain atrophy [4].

Lesions of retrochiasmal visual pathway resulting from stroke [5] are characterized by homonymous Visual Field (VF) defect. In contrast, lesion of visual pathway caused by neuro-inflammation like Multiple Sclerosis (MS) may not lead to persistent visual field defects [6,7]. Impaired low-contrast letter acuity [8] and color

vision may be present in MS [9]. Irrespective of location and cause of lesion in retrochiasmal visual pathway, and degree of visual dysfunction, SD-OCT can visualize distinct homonymous hemimacular GCL loss which corresponds to ipsilateral lesions behind the chiasm. This unique pattern of GCL loss is a hallmark of primary CNS lesion and CNS damage-related visual disability. Here, we report 2 patients with homonymous hemimacular GCL loss on SD-OCT and lesion in ipsilateral retrochiasmal visual pathway on MRI, in presence or absence of homonymous VF defect.

CASES

Case 1 is a 56 years old woman who as teenager suffered from toxoplasma chorioretin it is diagnosed by ophthalmoscopy. Her visual acuity had been 4/20 in the left eye and 20/20 in the right eye. At age 20, she suffered from left hemispheric ischemic stroke with right homonymous hemianopia as sequel. At age 54, she developed loss of pain and temperature affecting left arm and leg over a few days. Brain MRI showed old ischemic lesion of the left medial occipital lobe (Figure 1A). Spinal cord MRI showed one spinal cord lesion at C3 (Figure 1B), diagnosed as myelitis. Cerebrospinal fluid (CSF) showed slight mononuclear pleocytosis, normal CSF/serum albumin ratio, no oligoclonal IgG bands and negative serology for viral and bacterial infection. Anti-aquaporin-4 antibody was negative at 2 occasions, tested 6 months apart. The sensory symptoms disappeared after 6 months without therapy. Follow-up with brain and spinal cord MRI, and repeated CSF analysis 1 and 2 years after onset, respectively, showed no new findings on MRI, and normal CSF.

Ophthalmological examinations revealed unchanged optic disk since many years, with normal fundus in the right eye (Figure C) and retinochoroidal scars in the left macula on ophthalmoscopy (Figure 1D). Intraocular pressure was normal (right 14, left 15 mm Hg). SD-OCT at 3 occasions during last 1.5 years showed unchanged nasal hemimacular GCL loss of right eye (Figure 1E), atrophy of left macula (Figure 1F), and bilaterally reduced RNFL thickness (Figure 1G and H). Automated Visual Field (VF) with Humphrey instrument showed right homonymous hemianopia (Figure 1I). Visual Evoked Potentials (VEP) showed normal latency of P100 (positive downwards) bilaterally (100 microseconds), normal amplitude in the right eye (15 microvoltages), and lower amplitude in the left eye (7 microvoltages).

Case 2 is a 34 years old woman with 10-year history of Multiple Sclerosis (MS) without history of optic neuritis. At age 24 she had vertigo, nausea, ataxia and diplopia lasting several days. CSF showed no mononuclear pleocytosis but oligoclonal IgG bands. MRI revealed multiple MS-like plaques in cerebral hemispheres, brain stem and spinal cord. One lesion was located in the right optic radiation (Figure 2A). The patient was since then on interferon-beta therapy. She had 4 normal childbirths at age 25, 27, 30 and 33. She had one MS-relapse after first childbirth. During second and fourth pregnancy, she was treated with intravenous immunoglobulin (IVIg) once per month. Last relapse was 6 months after fourth childbirth, when she had vertigo, nausea and diplopia lasting several days without sequel. In

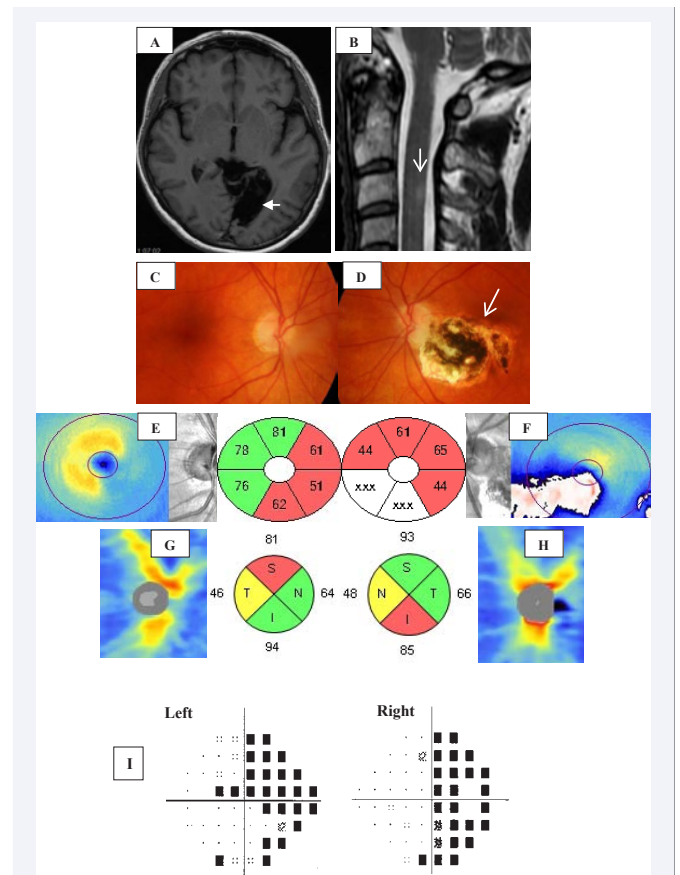


Figure 1 Images from 56 years old woman with a history of toxoplasma chorioretin it is in the left eye and ischemic stroke in the left occipital lobe. There is a T1-MRI lesion in left medial part of the occipital lobe (A, arrow), corresponding to right homonymous hemianopia. A T2 lesion in the spinal cord at C3 (B, arrow) is also seen. Fundus photography shows normal appearance in the right (C) and inactive retinochoroid scar in the left eye (D, arrow). Color-coded thickness map (red = thicker, blue = thinner) from SD-OCT showed loss of nasal hemimacular ganglion cell + inner plexiform layers (GCL-IPL) in the right eye (E) and diffuse macular atrophy of the left eye (F). Color-coded thickness map of optic disc showed slightly reduced retinal nerve fiber layers (RNFL) in the right eye (G, 76 μ m) and moderately reduced RNFL thickness in the left eye (H, 70 μ m). Automated visual fields (I) showed right homonymous hemianopia, consistent with T1-MRI lesion in the contralateral visual cortex.

addition, she experienced difficulties of vision and balance in the dark. EDSS was 0. The patient had high JCV titer, and therapy was switched from IVIg to rituximab 8 months after last childbirth.

Brain MRI during last relapse revealed gadolinium-enhancement of a previous lesion located in the left frontal lobe (Figure 2B). The lesion in right optic radiation on MRI remained unchanged. Ophthalmological examinations revealed normal-appearing optic discs (Figure 2C and D). Visual acuity was 20/20 in both eyes. Intraocular pressure and color-vision were normal. VEP showed delayed latency of P100 at 122 microseconds (ms) with normal amplitude in both eyes. SD-OCT at 4 occasions during last 1.5 years showed right homonymous hemimacular GCL-IPL loss (Figure 2E and F). Peripapillary RNFL thickness was normal in right eye (Figure 2G), and reduced temporally in left

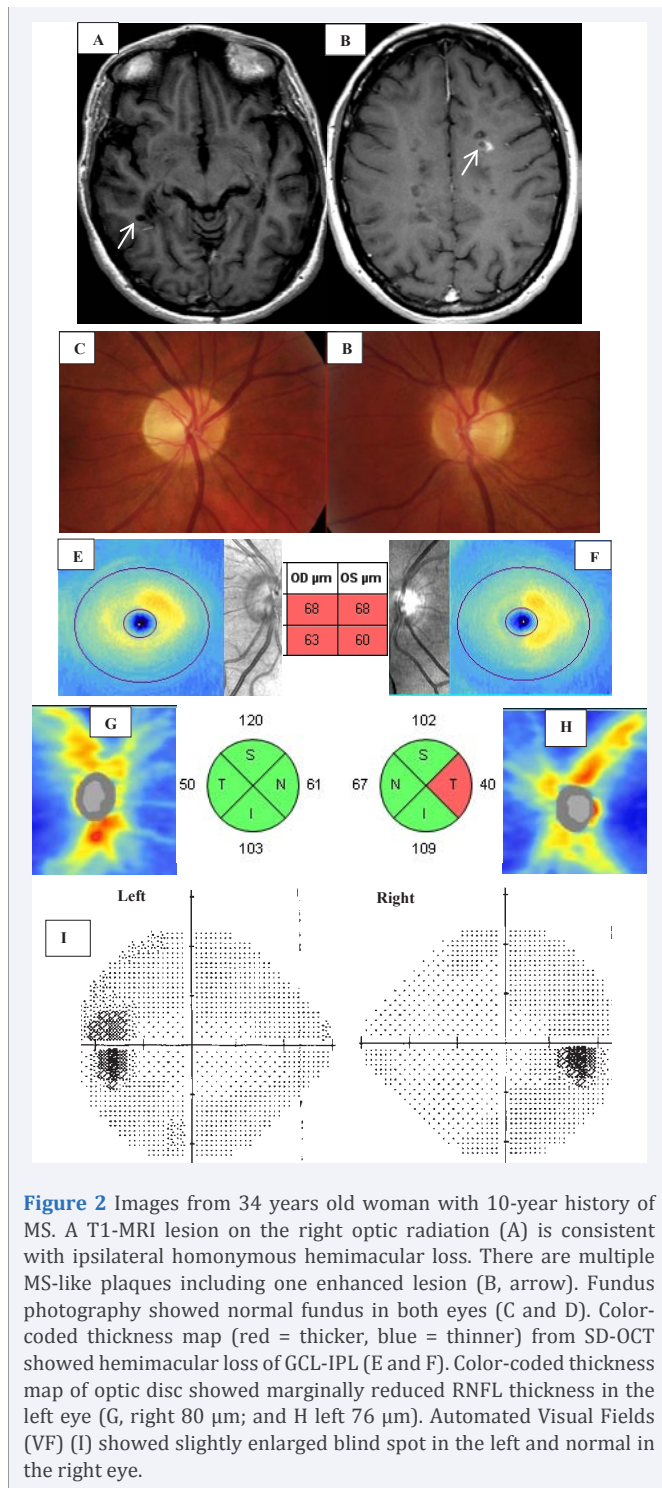


Figure 2 Images from 34 years old woman with 10-year history of MS. A T1-MRI lesion on the right optic radiation (A) is consistent with ipsilateral homonymous hemimacular loss. There are multiple MS-like plaques including one enhanced lesion (B, arrow). Fundus photography showed normal fundus in both eyes (C and D). Color-coded thickness map (red = thicker, blue = thinner) from SD-OCT showed hemimacular loss of GCL-IPL (E and F). Color-coded thickness map of optic disc showed marginally reduced RNFL thickness in the left eye (G, right 80 μm ; and H left 76 μm). Automated Visual Fields (VF) (I) showed slightly enlarged blind spot in the left and normal in the right eye.

eye (Figure 2H). VF showed enlarged central blind spot in left and normal in right eye (Figure 2I).

RESULTS AND DISCUSSION

We demonstrate that SD-OCT can visualize specific patterns of homonymous hemimacular GCL loss functioning as an imaging biomarker for primary lesion in retrochiasm visual pathway. SD-OCT with B-scan 512 x 128 pixels at macular cube acquires greater amount of data at higher speed and better

resolution and enables to generate microstructure of the retina close to the histological level [2]. Homonymous hemimacular GCL loss detected by SD-OCT corresponds to ipsilateral lesion behind chiasm as detected by MRI. Case 1 had infarction in the occipital lobe. VF defects of homonymous hemianopia persisted, corresponding to the remaining ipsilateral ischemic lesion in visual cortex. Case 2 had MS. Ophthalmologic examination revealed slightly enlarged blind spot in one eye and moderately delayed VEP latency bilaterally. Other visual functions were intact; fundus findings were unremarkable. Homonymous hemimacular GCL loss on SD-OCT is consistent with ipsilateral MS-plaque revealed by MRI in optic radiation.

Homonymous hemianopia has been used as hallmark for retrochiasm visual pathway damage [10]. Peripheral homonymous hemianopia caused by stroke [11] or surgical lobectomy [12] is consistent with persistent lesions in visual tract and visual cortex. Such lesions can be detected using diffusion tensor tractography [13]. Selective hemimacular thinning of each eye was also reported in a patient with neuromyelitis optica who had an ipsilateral optic tract lesion confirmed by diffusion-tensor tractography [14]. In a longitudinal study with SD-OCT, we recently observed one MS patient who developed hemimacular GCL-IPL loss over 4 months in relation to MS relapse [15]. One MS-plaque was detected in ipsilateral optic radiation by MRI, although the patient had no new visual dysfunction. Additional thinning of hemimacular GCL-IPL was registered in another patient with subclinical progressive MS who had ipsilateral optic radiation lesion on MRI since several years [15]. This patient also had unchanged visual dysfunction. In a longitudinal study of ON, we observed GCL-IPL thinning earlier than RNFL thinning, and not affected by optic disc swelling [16]. We believe that hemimacular GCL-IPL loss detected by SD-OCT is a sensitive and specific imaging biomarker for lesions in retrochiasm visual pathway, even in absence of VF defects.

CONCLUSION

These two cases illustrate existence of retrograde degeneration of visual pathway. Homonymous hemimacular GCL-IPL loss visualized by SD-OCT is consistent with ipsilateral lesions behind chiasm detectable by MRI, irrespective of VF defect. Such selective GCL-IPL loss can thus eventually serve as imaging biomarker to localize visual pathway lesions, monitoring disease progression and prognosis.

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Conflict of Interest

The authors declare no conflict of interests. The study was approved by the Ethics Committee Review Board of the University in Linköping, Sweden (reference number 2013/141-31).

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