Retrograde Transneuronal Degeneration: Homonymous Hemianopia and Associated Ganglion Cell Loss Following Cerebrovascular Accident

Abstract

Retrograde transneuronal degeneration occurs when injury to the central nervous system leads to loss of nerve fiber function and damage to presynaptic neurons. The damage could lead to ocular structural and functional impairment. Cerebrovascular accidents may lead to visual field defects. Clinical examination without imaging may not show structural damage. However, optical coherence tomography (OCT) exhibits retinal ganglion cell loss and associated field defects. This case presents a patient history of right-sided intracranial hemorrhagic stroke and associated left homonymous hemianopia corresponding to retinal ganglion cell loss due to transneuronal degeneration, indicating future management to include OCT.

Introduction

Transneuronal degeneration occurs when loss of neuron function leads to disruption of axonal transmission which can further damage associated neurons[1,2]. Anterograde degeneration leads to postsynaptic injury whereas retrograde degeneration causes presynaptic damage[1]. This case study focuses on retrograde degeneration. Trauma such as cerebrovascular accidents may lead to presynaptic damage and visual impairment. Visual deficits post-stroke is estimated at 65% which include ocular dysmotility, central or peripheral field loss, or visual perceptual disorder[3]. A common type of visual field loss due to post-chiasmal stroke damage is a homonymous hemianopia[4]. Peripheral field loss is typically measured using automated perimetry testing.

With retrograde degeneration, peripheral field loss may correspond to retinal ganglion cell loss. The long axons of these neuronal ganglion cells come together at the optic disc, exit the retina, and form the optic nerve[5]. The fibers travel to the optic tract and synapse to the lateral geniculate nucleus then leave as optic radiations that end in the visual cortex[5]. Many types of brain injuries can damage the fibers in this visual pathway to cause retrograde loss of ganglion cells. Retinal ganglion cell loss may be observed using optical coherence tomography (OCT). OCT shows cross-sectional images of the retina. With use of the Ganglion Cell Analysis (GCA) Cirrus OCT program, both the ganglion cell layer and inner plexiform layer are measured[1]. The GCA reduction is mapped in the macular region and may be compared to the associated visual field defect giving the clinician an objective way to measure the pathology over time.

Case Report

A 30-year-old African American male presented for a comprehensive examination November 15, 2018 complaining of blurred distance vision and worsening left side peripheral vision for the past couple months. He denied having ocular pain, flashes of light, or floaters. The patient's last eye examination was June 2017 at a blind rehabilitation optometry clinic. The exam notes stated the patient wanted to gain confidence driving with his peripheral vision loss. A confrontation visual field test was preformed which indicated the left sided hemianopsia appeared to split fixation. Thus, the patient was informed that driving was discouraged due to his visual field loss.

Medical history consisted of cerebral arteriovenous malformation, cerebrovascular accident, post-traumatic headache, joint pain, hemiparesis, insomnia, and depression. Blood pressure was normal. In July 2007, the patient sustained a right brain hemorrhage from the arteriovenous malformation so a craniectomy and ventriculostomy were performed. In 2017, CT and MRI results indicated encephalomalacia, or loss of brain tissue, near the posterior right middle cerebral artery involving the parietal and temporal lobes with some frontal lobe involvement.

Medications included zolpidem tartrate, diphenhydramine, glucosamine, ibuprofen, and multivitamins. Allergies included penicillin. Family medical and ocular history were unremarkable. He was alert and oriented to time, place, and person. His mood was appropriate.

Clinical Examination:

The patient's entering visual acuities with spectacle correction were 20/20 right eye and 20/20 left eye. Manifest refraction was -1.25-0.50x115 with 20/20+1 in the right eye and -1.750.75x026 with 20/15-2 in the left eye. Pupils were equal, round, and reactive to light without afferent pupillary defect. Extraocular muscles were full without restrictions in all gazes. Cover test at distance with correction was orthophoric. Confrontation fields indicated left sided restriction split to fixation in both eyes. Intraocular pressure was 13 mmHg right eye and 14 mmHg left eye with non-contact tonometry at 12:23 pm.

Anterior segment evaluation with slit lamp biomicroscopy was unremarkable for both eyes. Lids, lashes, conjunctiva, and cornea were clear. The irises were brown and flat. Anterior chamber was deep and quiet without cells or flare. Angles were deep with anterior chamber angles of 4/4 via the Von Herrick method.

The patient was dilated with 1.0% tropicamide and 2.5% phenylephrine at 12:30pm. Posterior segment evaluation with slit lamp biomicroscopy and binocular indirect ophthalmoscope were also unremarkable for both eyes. The lens and vitreous were clear. Optic nerves were pink and flat with distinct margins. Cup-to-disc ratio of right eye was 0.30 round and left eye was 0.35 round. The macula was flat and dry. Vessels were normal. The peripheral retina of each eye had no breaks or tears.

The Cirrus optical coherence tomography (OCT) retinal nerve fiber layer (RNFL) indicated an average reduction of RNFL thickness greater in the right eye compared to the left eye (Fig 1). The right eye had RNFL thinning superior-temporal and inferior while the left eye had RNFL thinning superior-nasal and temporal (Fig 1). In both eyes, RNFL OCT did not show association with ganglion cell analysis (GCA) or macular OCT findings. GCA OCT revealed diffuse loss on the right side of both eyes respecting the vertical midline (Fig 2). Macular OCT showed within normal limits of central thickness, but thinning on the right side corresponding to ganglion cell analysis (Fig 3).

	OD	OS
Average RNFL Thickness	75 µm	79 µm
RNFL Symmetry	46%	
Rim Area	1.35 mm²	1.17 mm²
Disc Area	1.58 mm²	1.72 mm²
Average C/D Ratio	0.38	0.55
Vertical C/D Ratio	0.46	0.47
Cup Volume	0.034 mm²	0.108 mm²

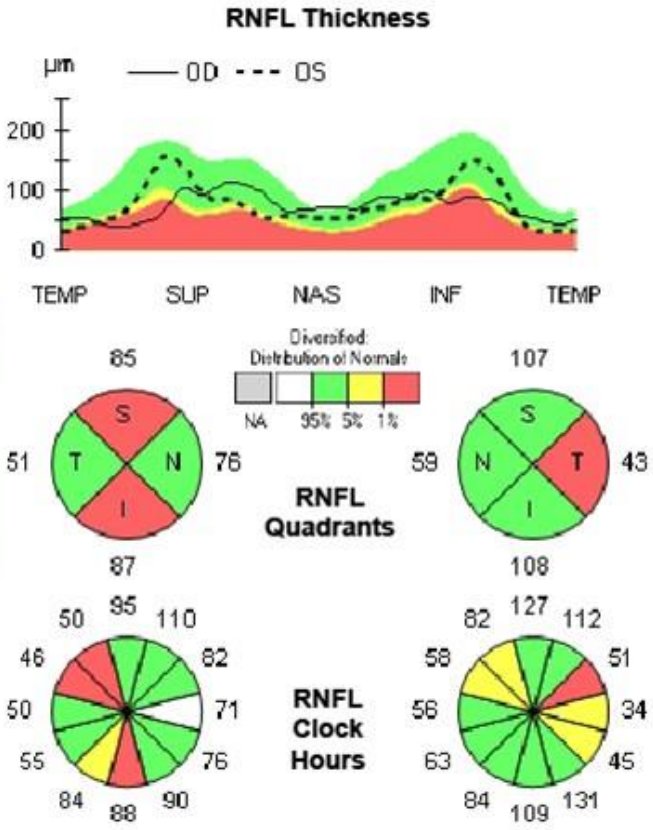

Figure 1. Optical coherence tomography indicated retinal nerve fiber layer (RNFL) thinning.

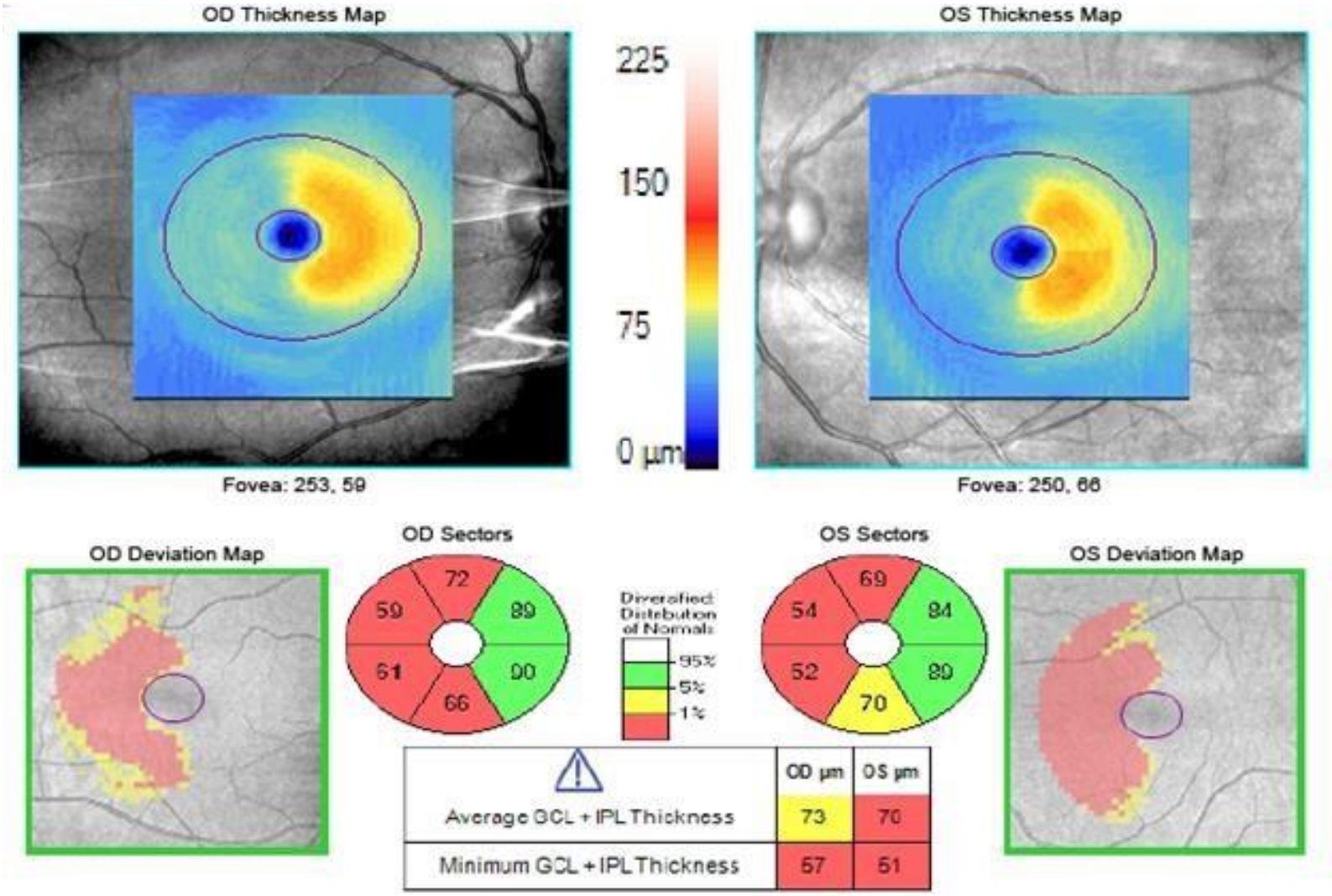

Figure 2. Ganglion cell analysis (GCA) using optical coherence tomography. Thickness, sectoral, and deviation maps showed thinning on the patient's right side of the macula in both eyes.

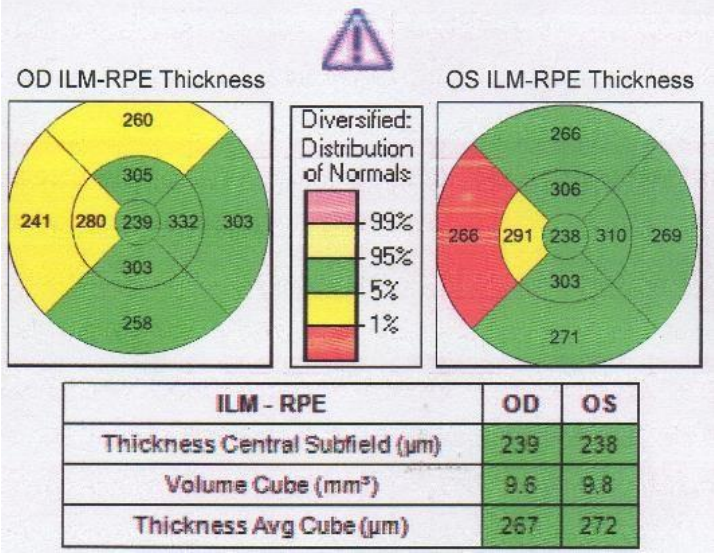

Figure 3. Macular optical coherence tomography demonstrated thinning on the patient's right side of the fovea with average central thickness in both eyes.

After showing the patient the thinning of the ganglion cell area of the macula, the patient better understood how his vision was impaired and why driving was contraindicated. The patient was given a finalized spectacle prescription for his myopia and astigmatism. Due to the left homonymous hemianopsia from the cerebrovascular accident, he was told to return for a 24-2 visual field at his next appointment in 1-2 months to check for further progression.

Differential Diagnosis:

The differential diagnoses included:

- Physical Trauma
- Neoplasm
- Glaucoma
- Cerebrovascular accident

- Physical Trauma is caused by blunt force, surgery, or an object penetrating the skin or body causing an open wound. The patient reported no history of trauma or brain injury.

- Neoplasm is an abnormal growth of cells sometimes called a tumor. Imaging did not indicate a neoplasm, but rather encephalomalacia (loss of brain tissue) secondary to the hemorrhagic stroke from the arteriorvenous malformation.

- Glaucoma is a progressive optic nerve disease that can also cause visual field defects and ganglion cell and retinal nerve fiber layer thinning. However, the visual field defects the

patient exhibited does not follow the typical glaucomatous pattern. Additionally, the patient's eye pressures were normal and there was no cupping of the optic nerve head.

-Cerebrovascular accidents are caused by either blockage or bleeding which prevents blood flow to the brain. Computerized tomography (CT) and magnetic resonance imaging (MRI) scans were performed which confirmed the patient had a hemorrhagic stroke or cerebrovascular accident. CT and MRI scans unavailable.

Follow Up #1

The patient returned on December 26, 2018 for a Humphrey visual field 24-2. He reported stable vision since his last visit. Visual acuity was stable with corrected distance acuities of 20/20 right eye and 20/20 left eye. Slit lamp biomicroscopy of the anterior segment and undilated posterior segment were stable in both eyes. Intraocular pressure was 12 mmHg right eye and 11 mmHg left eye with non-contact tonometry at 11:05 am. The Humphrey visual field (Fig 4) indicated a left sided homonymous hemianopsia which matched the macular OCT (Fig 3) and ganglion cell analysis OCT (Fig 2).

To minimize the chance of another stroke, the patient was advised to discontinue use of ibuprofen, which could cause bleeding, and switch to another medication with counsel from his primary care doctor for his headaches and joint pain. He was reminded that due to his arteriovenous malformation, the blood vessels in his brain were weak and could hemorrhage if there is any physical trauma. His primary care provider had cautioned him in the past about limiting use of alcohol. The patient was then scheduled for an appointment with the low vision rehabilitation optometrist for visual aids such as peli prisms to increase his visual field. Since his visual acuity was stable, he was instructed to return for a comprehensive vision exam with OCT in one year. If he notices vision changes, he was instructed to return sooner.

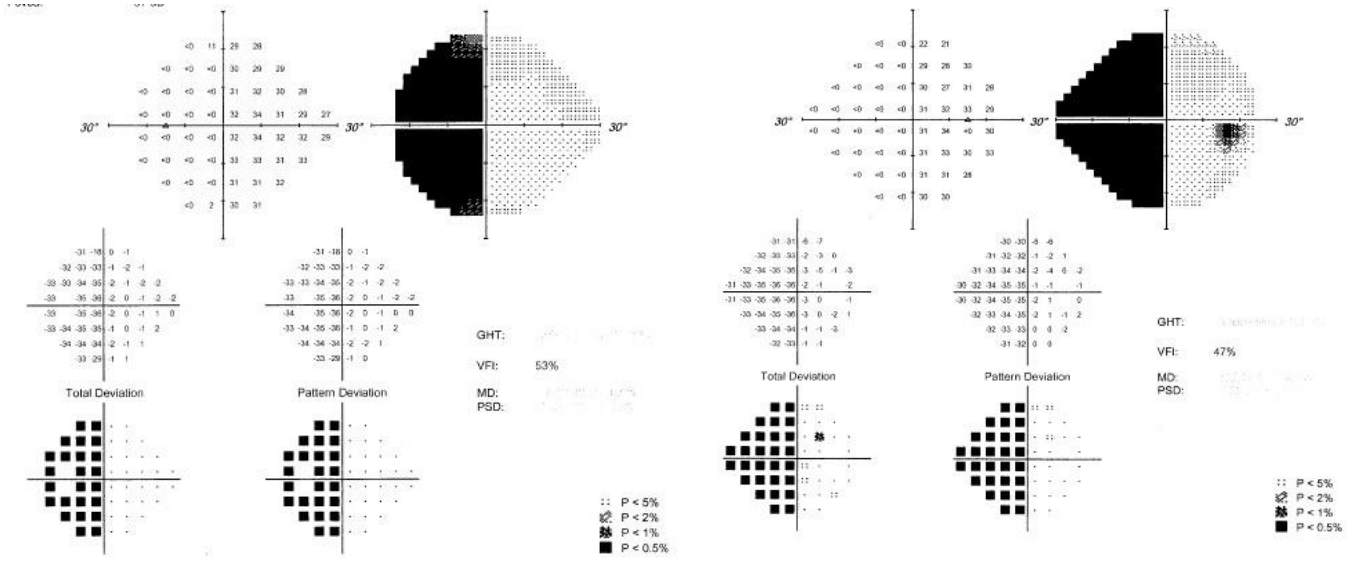

Figure 4. Humphrey visual field 24-2 displayed left sided homonymous hemianopsia respecting the vertical midline.

Follow Up #2

The patient was examined by another provider at the blind rehabilitation optometry clinic on January 18, 2019. The patient reported he does not drive, and uses Uber to get to different locations. While the patient was in clinic, a kinetic field was performed which indicated findings similar to the 24-2 visual field taken Dec. 2018 (Fig 5).

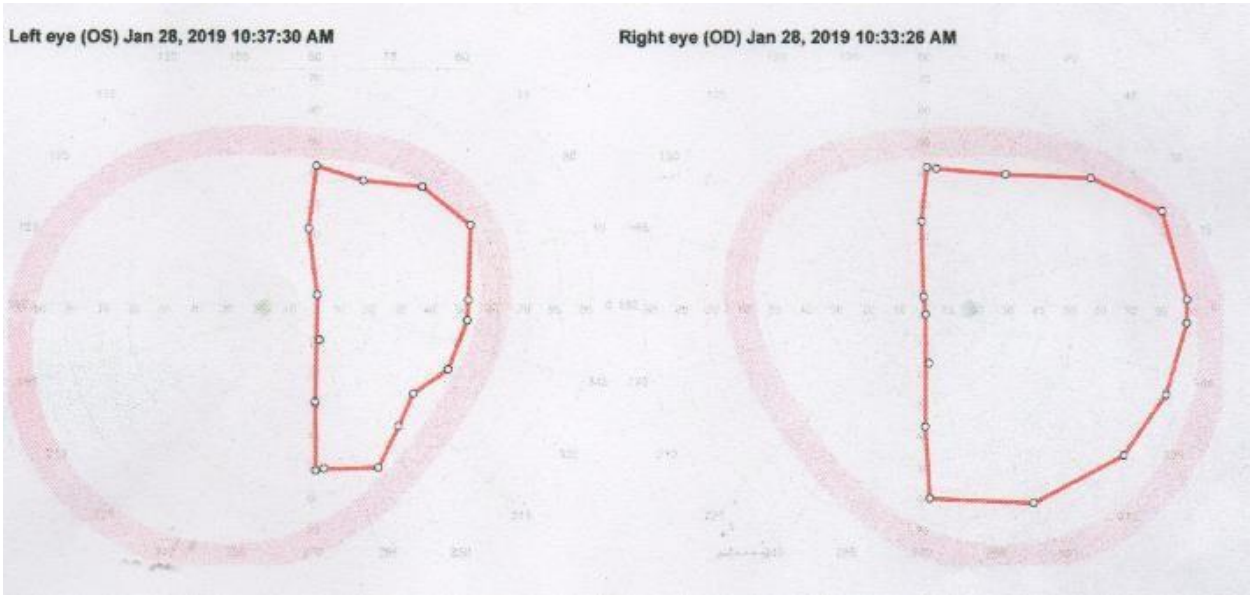

Figure 5. Kinetic visual field presented with left sided homonymous hemianopsia.

The blind rehabilitation optometrist discussed transportation options including the use of Catholic Community Services, Cowlitz Tribe Transportation, Dial-A-Lift, and intercity transit. No prisms were ordered as the patient declined visual aids.

Discussion

Arteriovenous malformation (AVM) are congenital defects which consist of the feeding arteries, the abnormal tangled connection of arteries and veins in the brain or spine called a nidus, and the draining veins. AVMs are not hereditary. There is a prevalence of 10-18 cases per 100,000[6]. Men and women are affected equally.[6] Absence of a capillary bed causes the blood to channel directly from the arterial to venous system through the nidus creating a higher than normal blood flow and hypertension on the venous side causing rupture.[7]

Cerebral AVMs may present with seizures, headaches, visual and neurological deficits. However, only 12% of AVMs are symptomatic. In patients who have experienced cerebral bleeding, the risk of a subsequent hemorrhage ranges from 9.65-32.9% within the first year and around 3.67% after five years from the initial hemorrhage[6]. AVM is the most common cause of non-traumatic cerebral bleeding in patients 35 years old and younger and account for 1.4-2% of hemorrhagic strokes[6].

Treatment of AVM with the goal to prevent hemorrhagic stroke includes[6,8]:

- Microsurgical resection-a craniotomy with a dural opening allows for a dissection and repair of the tangled nidus. A postoperative angiography is taken to confirm complete AVM excision. The advantage of this technique is the high rate of complete obliteration of the nidus. The drawbacks include limited accessibility depending on the location within the brain, intraoperative bleeding, post-op edema, and arterial thrombosis.
- Stereotactic radiosurgery- radiation to the AVM causes blood vessel sclerosis. This obliterates the bleeding vessels. It is considered when microsurgical resection is deemed too risky.
- Endovascular embolization – injected delivery of liquid embolics to block blood vessels to stop bleeding. It diminishes the size of the AVM. It may be used in conjunction with microsurgical resection and sterotactic radiosurgery. Ironically, a drawback is that since it is injected into fragile vessels, increased bleeding may occur.
- Conservative management- includes close monitoring to manage symptoms such as headaches, hypertension, and seizures.

Visual impairments after a cerebrovascular accident include ocular dysmotility, perceptual issues, and central or peripheral field defects. Eye movement defects include strabismus, cranial nerve palsies, gaze defects, and nystagmus[4]. Perceptual disorders post-stroke include

neglect, agnosia, and hallucinations[3]. The most common field defect is homonymous hemianopia. Other field defects include quadrantanopsia, scotomas, and constriction. Prevalence of visual field loss after a cerebrovascular accident varies from 8-25%,[4]. The defect is due to the ischemia at the visual pathway.

In this patient case, blood flow interruption occurred at the middle cerebral artery. The middle cerebral artery supplies optic radiations, also called the geniculocalcarine tract[5]. The geniculocalcarine tract receives information from the lateral geniculate nucleus which then receives information from the optic tract, optic chiasm, optic nerve, and retina[5]. When the geniculocalcarine tract was impaired from ischemia, the visual information could not be transferred to the primary visual cortex which led to the visual field defect.

Retrograde transneuronal degeneration at the retina may be viewed with optical coherence tomography (OCT) ganglion cell analysis[2,9]. Ganglion cells are located in the retina and their axons form the optic nerve[5]. The degeneration affecting the visual pathway may affect not only patients following stroke, but can be detected in patients with neurodegenerative systemic diseases. For example, visual impairment can be an early symptom of Alzheimer's disease. A study by Parisi *et al*. demonstrated a reduction of RNFL and total macular thickness and volume in patients who have cognitive impairment[10]. Unal Mutlu *et al.* in the Rotterdam Study found that thinner RNFL, ganglion cell layer, and inner plexiform layer are associated with smaller gray-matter and white matter-volume in patients with Alzheimer's disease[11]. These two studies demonstrated the usefulness of OCT for assessing the structural ocular system in patients with neurodegenerative systemic diseases such as Alzheimer's disease, Parkinson's, and diabetic peripheral neuropathy. The relationship between ganglion cell analysis and visual field defects indicate the benefits of optical coherence tomography use in neurological assessments because the visual impairments may not yet be noticeable to the patient.

Post-stroke visual impairment may be managed through physical training and vision devices. Ocular and head movement training as well as compensatory head posture may improve visual impairment[4]. Peli prisms help expand peripheral vision by shifting the patient's damaged visual field side to the unimpaired side. If patients have reduced central vision, then visual aids such as magnifiers may benefit. Typoscopes aid in keeping track of location while reading. Patients with diplopia may use Fresnel prisms or occlusion[12].

The retrograde degeneration in this patient's case resulted in left homonymous hemianopsia (Fig 4) which corresponded to ganglion cell disruption on the right side of the macula (Fig 2). Typically a person with concern of worsening left side peripheral vision, such as with this patient, would receive a comprehensive exam including visual field. In this case, the OCT was taken in conjunction with the 24-2 visual field to confirm the cause and extent of the damage resulting in the patient's symptoms. The OCT served as a patient education tool to explain why driving was discouraged.

Conclusion

The takeaway from this case is that OCT may be used as a supplement to visual field tests to manage and observe progression of visual impairment in patients post-stroke. It is a quick, noninvasive objective measurement which can also be used on patients who may give unreliable subjective answers for a visual field test for many reasons including fatigue, drug use, or disability. Thus, ganglion cell analysis may be used as an alternative to assess visual impairment if visual field testing cannot be performed.

Post stroke patients often do not realize the extent of their visual impairment. Patient education using images such as OCT send a powerful message by allowing the patient to see ganglion cell layer thinning and compare it to a normal cell layer. It seemed to increase this patient's compliance by wanting to avoid medications and activity which can increase blood pressure to prevent another cerebrovascular accident and further visual impairment.

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