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Case report
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Evidence of retrograde trans-synaptic degeneration: retinal ganglion cell atrophy following occipital stroke

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Abstract

Background: Trans-synaptic degeneration (TSD) is an uncommon phenomenon wherein the degeneration of one neuron leads to the subsequent degeneration of interconnected neurons.
Case report: A 50-year-old woman experienced sudden bilateral visual field loss for 10 days, accompanied by right-sided headache, numbness, tingling, and a sensation of tingling and heaviness in the tongue. The confrontation visual field indicated right homonymous hemianopia field loss, and automated static perimetry confirmed this finding. Magnetic resonance imaging showed recent acute infarcts on the left occipital lobe and optical coherence tomography of the ganglion cell layer revealed contralateral thinning, thus confirming retrograde TSD, as the post-synaptic damage in the occipital lobe was mirrored in the pre-synaptic neurons, *i.e.*, ganglion cells.
Conclusion: This case report demonstrated evidence of TSD in the retinal ganglion cell layer of a patient with acute occipital stroke.

Keywords: occipital stroke, retinal ganglion cells, trans-synaptic degeneration

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Bukti degenerasi trans-sinaptik retrograd: atrofi sel ganglion retina selepas strok oksiptal

Abstrak

Latar belakang: Degenerasi trans-sinaptik (trans-synaptic degeneration, TSD) merupakan fenomena yang jarang berlaku, di mana degenerasi satu neuron menyebabkan degenerasi seterusnya pada neuron-neuron yang saling berhubung.
Siri kes: Seorang wanita berusia 50 tahun mengalami kehilangan medan penglihatan bilateral secara tiba-tiba selama 10 hari, disertai sakit kepala di bahagian kanan, kebas, rasa mencucuk-cucuk, serta sensasi kesemutan dan berat pada lidah. Pemeriksaan medan penglihatan secara konfrontasi menunjukkan kehilangan medan penglihatan hemianopia homonim kanan, dan perimetri statik automatik mengesahkan dapatan tersebut. Pengimejan resonans magnetik menunjukkan infark akut terkini pada lobus oksipital kiri, manakala tomografi koheren optik lapisan sel ganglion menunjukkan penipisan pada bahagian kontralateral. Dapatan ini mengesahkan TSD retrograd, apabila kerosakan pascasinaptik pada lobus oksipital dicerminkan oleh perubahan pada neuron prasinaptik, iaitu sel ganglion retina.
Kesimpulan: Laporan kes ini menunjukkan bukti berlakunya TSD pada lapisan sel ganglion retina pada seorang pesakit yang mengalami strok oksipital akut.

Kata kunci: degenerasi trans-sinaptik, sel ganglion retina, strok oksipital

Introduction

Trans-synaptic atrophy, also referred to as trans-synaptic degeneration (TSD), is a condition in which the degeneration of one neuron causes the subsequent degeneration of connected neurons. This phenomenon is an uncommon condition with limited evidence, theoretically seen in neurodegenerative diseases such as multiple sclerosis, stroke, and optic neuritis.[1,2] The proposed mechanism of TSD is that synaptic dysfunction and pathology of synaptic adhesion molecule in the synaptic space leads to axonal and dendritic damage in postsynaptic neurons.

In theory, presynaptic to postsynaptic neuronal degeneration in the visual pathway is anterograde TSD, *i.e.*, degeneration in the posterior visual pathway, which results in changes in the lateral geniculate nucleus, optic radiation, and visual cortex. Postsynaptic to presynaptic degeneration is called retrograde TSD, *i.e.*, degeneration in the posterior visual pathway that results in changes or potential damage to the inner retina. This case report presents retrograde TSD.

Case presentation

A 50-year-old woman was referred to the ophthalmology clinic at Dr. Sardjito General Hospital, Yogyakarta, Indonesia with complaints of bilateral blurred vision, worse in the right eye and resembling white mist, for 10 days prior to her visit to the eye clinic. The incident occurred in the afternoon while the patient was sewing clothes, as this is her daily work. The blurred vision was accompanied by a right-sided headache, without dizziness, nausea, or vomiting. Other positive symptoms included numbness on the right side of her body, and a tingling and heavy feeling in the tongue. These symptoms started around the same time as the vision loss and worsened gradually.

The patient denied any history of head injuries or illnesses, and her past ocular history was unremarkable for any eye diseases or surgeries. She had a history of uncontrolled hypertension without medication. The patient's social history revealed that she was a passive smoker and denied any recent use of illicit drugs or any systemic diseases. She is the third of 4 siblings, all female, and 2 of which had a history of stroke. There was no family history of congenital anomalies.

Upon presentation at the clinic, the patient's peripheral pulse rate was measured at 78 beats per minute, respiratory rate was 18 cycles per minute, and blood pressure was 154 mmHg/75 mmHg. The patient was alert and oriented to person, place, and time, with no focal neurological deficits. Uncorrected distance visual acuity was 6/15 (20/50) bilaterally. With the pinhole test, the visual acuity improved to 6/12 (20/40) in the right eye and 6/9 (20/30) in the left eye. The best-corrected visual acuity with a +0.50 spherical lens improved to 6/6 E (20/20) in both eyes. Intraocular pressure was 15 mmHg in the right eye and 11 mmHg in the left eye.

On the slit lamp examination, the anterior segment was unremarkable, and no eyelid ptosis was present. The conjunctiva and anterior chamber were quiet. Pupils were equal, round, and reactive to light with no relative afferent pupillary defect. On posterior segment examination, both optic discs had well-defined borders, with a cup-to-disc ratio of 0.6 in the right eye and 0.5 in the left eye. The foveal reflex was present, and the arteriole-to-venule ratio was 2:3, with the presence of arteriolar copper wiring noted in both eyes. Extraocular muscles were intact with no restrictions. Upon contrast-sensitivity testing, the right eye had 19.2% and the left eye had 14.6%. There was red-green dyschromatopsia observed on colour vision testing with the Ishihara test. Confrontation visual fields revealed right homonymous hemianopia field loss.

The macular thickness measured by spectral-domain optical coherence tomography (OCT) revealed thinning of the superonasal [66 µm (normal mean: 81 ± 6 µm; range: 69–93 µm)] and inferonasal [62 µm (normal mean: 80 ± 6 µm; range: 68–92 µm)] regions of the circumferential sectors of the retinal ganglion cell layer (GCL) and plexiform layers in the right eye, and thinning of the superotemporal [65 µm (normal mean: 83 ± 7 µm; range: 70–96 µm)] and inferotemporal [64 µm (normal

mean: 84 ± 6 µm; range: 72–96 µm)] regions in the left eye (Fig. 1). The retinal nerve fibre layer (RNFL) thickness measurement showed no significant thinning in either eye. Automated static perimetry revealed right homonymous hemianopia (Fig. 1). Laboratory workup included a complete blood count and metabolic panel, but the results were unremarkable. Additional testing with magnetic resonance imaging (MRI) revealed recent acute infarcts, predominantly involving the left occipital lobe (Fig. 1). Based on the MRI findings, the patient was admitted to the neurology stroke service. The patient was prescribed 30 mg of aspirin daily, 5 mg of amlodipine daily, and 500 mcg of mecobalamin twice a day. The patient was regularly followed up every month at the eye clinic.

Discussion

The visual system is a good model for studying TSD because of its well-defined structure and strong connectivity between the retina and visual cortex.[3] These visual pathways can undergo neurodegenerative processes, which are bidirectional in nature. The defects might be detected through several techniques including OCT, advanced MRI techniques, electrophysiology, high- and low-contrast visual acuity tests, automated perimetry, and colour vision assessments.[4]

The degeneration process in the present case report is a retrograde TSD, in which the degeneration in the posterior visual pathway causes retinotopic changes in the anterior visual pathway (retinal ganglion cells), as shown in the OCT image (Fig. 1). Thinning of the homonymous hemimacula following damage to the optic radiation (a reduction in RNFL thickness was demonstrated in the nasal side of the contralateral eye and the temporal side of the ipsilateral eye in patients with cerebral infarction). The occipital stroke location is consistent with the thinning of the circumferential RNFL, GCL, and plexiform layers. It is hypothesized that the severity and location of RNFL thinning correlate with the site of damage and the region of infarcted arteries.5 When a neuron is damaged, its ability to transmit signals diminishes, leading to reduced synaptic inputs to connected neurons, causing apoptosis and degeneration process by releasing pro-inflammatory cytokines that can exacerbate neuronal injury and promote degeneration.[4,6,7] A prior study discussing homonymous visual field deficits in occipital lobe stroke patients mentioned varying rates of retrograde TSD manifestation. These patients had at least 10% of relative hemifield atrophy 2.5 years after experiencing a stroke. One case had the earliest onset, occurring 5.5 months post-stroke.[8]

Optic nerve atrophy can be evaluated using OCT measurements of the macular ganglion cell-inner plexiform layer (GC-IPL), optic nerve head, and peripapillary RNFL. This approach allows for non-invasive and repeatable evaluations. Upon understanding the TSD mechanism, GCL thickness can be used to analyse disease progression and help formulate treatment strategies.[8] OCT-detected TSD may

provide valuable information regarding the extent and chronicity of retrograde neuronal damage. Greater thinning generally indicates more extensive neuronal loss. Furthermore, reduced retinal layer thickness on OCT correlates with persistent visual field deficits and limited functional recovery, suggesting that the potential for neural regeneration is minimal once degeneration has stabilized.

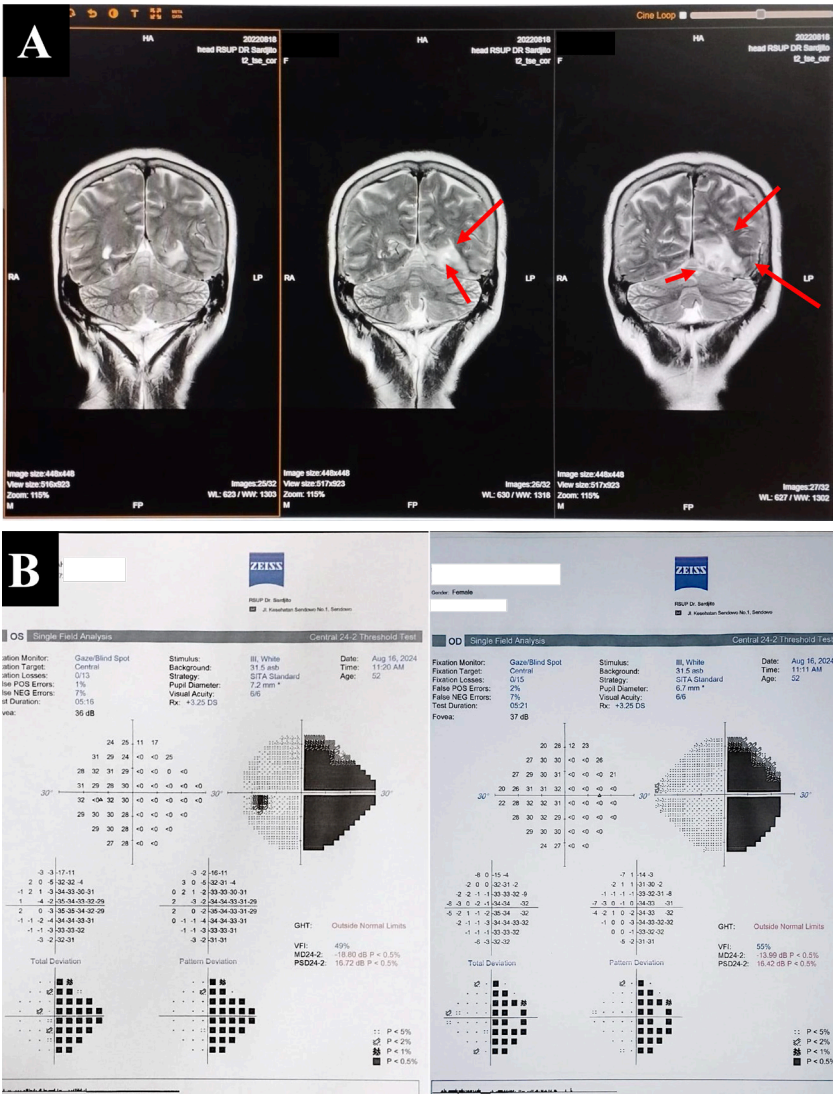

Fig. 1. (A) MRI shows acute infarcts on the left occipital lobe. *(B)* Automated static perimetry shows right homonymous hemianopia.

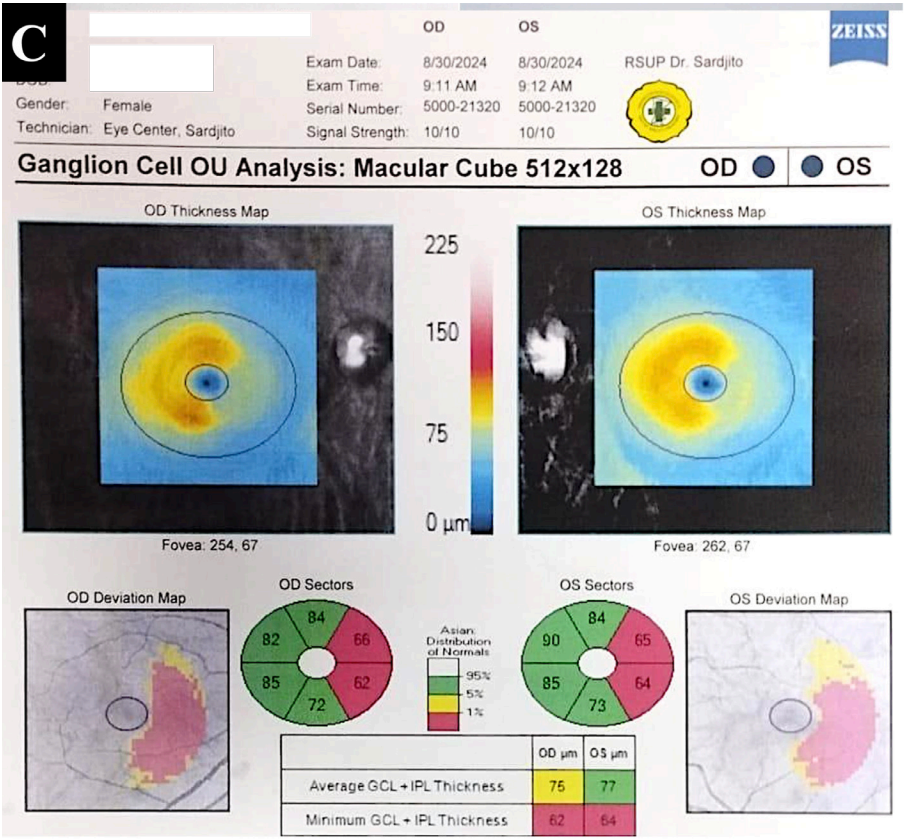

Fig. 1. (C) Superonasal and inferonasal regions of the circumferential ganglion cell layer.

Conclusion

Although TSD has been proposed theoretically, direct clinical evidence remains limited. This case provides supportive evidence of retrograde degeneration in the retinal ganglion cell layer following occipital stroke.

Declarations

Informed consent for publication
The patient provided informed consent for the publication of the clinical data and images contained in this case report.

Competing interests
None to declare.

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