CASE REPORT

THE ROLE OF OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN NON-ARTERITIC ISCHEMIC OPTIC NEUROPATHY: A CASE REPORT

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ABSTRACT

Introduction: *Non-arteritic ischemic optic neuropathy (NAION) is the second most common optic neuropathy in adults. Since circulatory insufficiency is presumed to have a role in pathogenesis of NAION, optical coherence tomography angiography (OCTA) is suggested as a tool in assessing NAION patients, while optical coherence tomography (OCT) can detect structural changes. This case report aims to describe the congruity of visual field defect with OCT and OCTA result in a case of bilateral NAION, highlighting the role of both OCT and OCTA in NAION.*

Case Report: *A 52-years-old male came due to painless, progressive blurry vision in both eyes, especially in lower visual field, for the past 7 months. Humphrey visual field examination revealed inferior visual field defects in both eyes. OCTA showed reduced retinal perfusion in the superior part bilaterally. OCT revealed ganglion cell loss in the superior part of his right eye and almost all parts of his left eye. Retinal nerve fiber layer (RNFL) thinning was found in the superior part bilaterally.*

Discussion: *In this case, the congruity of visual field defect, reduced perfusion, ganglion cell-inner plexiform layer (GCIPL), and RNFL thinning portrayed the connection of hypoperfusion as the presumed underlying mechanism of NAION, neuron loss as the result of the hypoperfusion, and the visual field loss as the presenting symptom in NAION.*

Conclusion: *This finding demonstrates the role of OCT-A and OCT in diagnosing and monitoring progression in patients with NAION.OCT-A is a useful tool to evaluate microvascular changes, while OCT can be used to evaluate RNFL and GCIPL thinning.*

Keywords: *non-arteritic ischemic optic neuropathy, visual field defect, optical coherence tomography angiography*

INTRODUCTION

Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common clinical manifestation of acute ischemic damage to the optic nerve.[1] NAION generally affects adults over 50 years of age with mean onset between 57 to 65 years, although there are reported cases in patients <40 years old. This disease frequently occurs in Caucasians with no gender predilection with an estimated annual incidence of 2.3 - 10.2 per 100.000 population in the United States.[2] In Asia, studies about NAION epidemiology are still limited. One study on the

South Korean population reported that the incidence rate was 11.35 per 100.000 person-years among adults older than 40 years old, similar to the incidence rate in Caucasian populations. The incidence rate seems to be increased with age.[3] To date, there is still no data on NAION incidence in the Indonesian population. Data from a study in Cipto-Mangunkusumo Hospital in Jakarta, Indonesia reported at least 272 cases of NAION from 2012-2017.[4]

Many studies have been performed to understand the pathophysiology of NAION, but the exact mechanism of this disease still remains unanswered.[2] Pathophysiologic processes involved in NAION are not firmly explained because histologic studies are rarely reported.[5,6] NAION is a multifactorial disease with many risk factors, including a small cup-to-disc ratio and various systemic diseases.[2,7] Disturbance in circulation to the optic nerve head leading to hypoperfusion and ischemia is thought to be the underlying mechanism for NAION, but the cause of this disruption is still unclear. Generalized hypoperfusion, nocturnal hypotension, thrombosis, and vasospasm are a few of many proposed theories explaining the cause of circulatory disruption in NAION.[2,8]

Since hypoperfusion is presumed to be the underlying mechanism of NAION, optical coherence tomography angiography can play a role in evaluating vascular conditions in this disease. A pilot study by Sharma et al suggested that optical coherence tomography angiography (OCT-A) is a useful tool in NAION. This study found a decrease in both retinal and choroidal peripapillary flow densities.[6] Optical coherence tomography (OCT) also plays an important role in diagnosing NAION considering its indefinite pathogenesis. While crowded discs or “disc-at-risk” are known as the biggest risk factor for developing NAION, OCT can reliably capture high-resolution images of the deep optic nerve to evaluate the structural loss such as the retinal nerve fiber layer and ganglion cell layer thickness.[1]

On that account, here we report a case of NAION that shows a corresponding visual field defect with vascular impairment and structural loss found with OCT-A and OCT, which demonstrates the role of OCT-A and OCT in diagnosing and monitoring progression in patients with NAION.

CASE ILUSTRATION

A 52-year-old male came to our hospital complaining of painless, progressive blurry vision in both of his eyes for the past 7 months. The patient complained that his lower visual field was blurrier in both eyes. Headache or pain on eye movement was denied. The patient has a history of type-2 diabetes mellitus and dyslipidaemia. History of hypertension, heart disease, sleep apnea, or autoimmune diseases was denied. The patient consumed glimepiride routinely

but did not take any medication for his high cholesterol level. He admitted that he used to smoke, but has stopped for the past 2 months. Any history of eye disease was also denied. The patient uses reading glasses in his daily activities. History of any systemic or eye diseases in his family was denied.

From the physical examination, the patient had uncorrected visual acuity of 6/60 and best-corrected visual acuity of 6/21 on both eyes. No abnormality was found on both the palpebral and anterior segments. Both lenses were cloudy. The relative afferent pupillary defect was positive in the left eye. Examination of the posterior segment of the eye revealed atrophy of the optic nerve head in both eyes. The optic nerve head was round with a clear margin. Both superior parts were pale and exudates were found in the peripapillary area of both eyes.

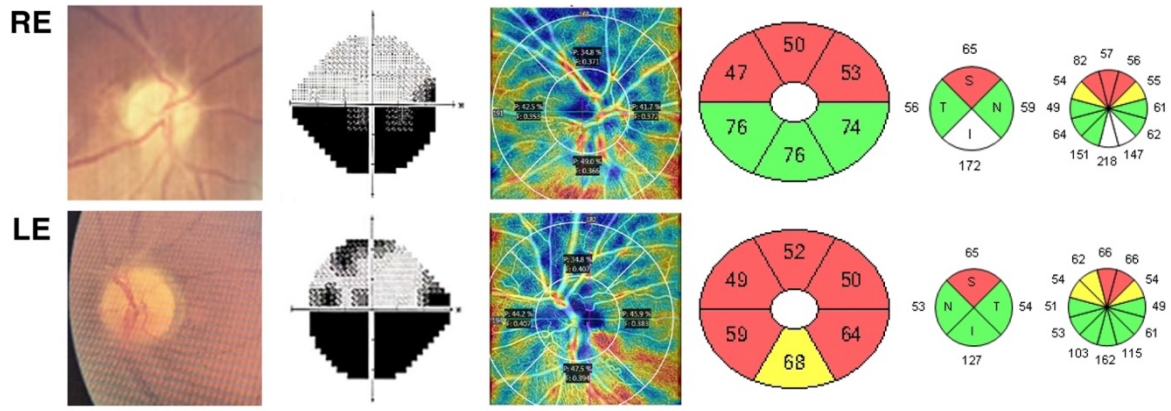

Figure 1. Spatial correspondence shown from the results of diagnostic examinations (from left to right: fundus photograph, Humphrey visual field examination, optic nerve head angiography, optic disc ganglion cell analysis, and optic disc RNFL analysis by quadrants and clock hours). Inferior visual field defect matched with the decreased perfusion and structural changes in the superior part of the optic nerve head.

Diagnostic assessments were performed and the results are presented in Figure 1. Humphrey visual field examination revealed inferior altitudinal visual defect in both eyes. Mean deviation (MD) was -19.69 dB on the right eye and -21.99 dB on the left eye. Visual field index (VFI) was 49% on the right eye and 33% on the left eye. OCT-A on the disc (4.5 x 4.5 mm) was obtained using Cirrus HD-OCT (Carl Zeiss Meditec, Inc). OCT for ganglion cell analysis and RNFL analysis were obtained using the same machine. OCT-A showed reduced retinal perfusion in the superior part bilaterally. Optical coherence tomography (OCT) revealed ganglion cell loss in the superior part of his right eye and almost all parts of his left eye. Decreased macular thickness was found in the superonasal part of his right eye and almost all parts of his left eye. Retinal nerve fibre layer thinning was found in the superior part bilaterally.

Laboratory examination revealed elevated total cholesterol levels (222 mg/dL), low density lipoprotein (143 mg/dL), and triglycerides (225 mg/dL). The patient also had a high HbA1c (7.9%) and a high postprandial glucose level (248 mg/dL). Erythrocyte sedimentation rate (37 mm), D-dimer level (820 µg/L), and fibrinogen (407.4 mg/dL) were all elevated, indicating a hypercoagulation state.

The patient was treated with a daily dose of 80 mg acetylsalicylic acid and 2 mg warfarin. After one month of treatment, the patient said his vision had remained stable with only a slight improvement in his right eye. Visual acuity had improved to 6/30 in his right eye but remained 6/60 in the left eye. Diagnostic examinations were performed again and the results are presented in Figure 2. From Humphrey visual field examination, progression of the visual field defect on both eyes was found. Both MD and VFI showed a decrease compared to the result one month prior. The mean deviation (MD) was -25.21 dB on the right eye and -25.37 dB on the left eye, while the visual field index (VFI) was 20% on the right eye and 25% on the left eye. Characteristical pattern of altitudinal visual field defects in the inferior part that were found in the first examination were less obvious in the one-month follow-up examination as the defect had progressed to be more generalised. Therefore, the spatial correspondence of visual field defect with the OCTA results was less pronounced. The OCT-A results showed worsening of the hypoperfusion in both of the superior quadrants, with decreasing capillary perfusion levels (34.8% to 26.7% in the right eye, 34.8% to 28.6% in the left eye). Other quadrants also showed decreasing capillary perfusion. OCT results showed slight decrease for both GCIPL and RNFL thickness.

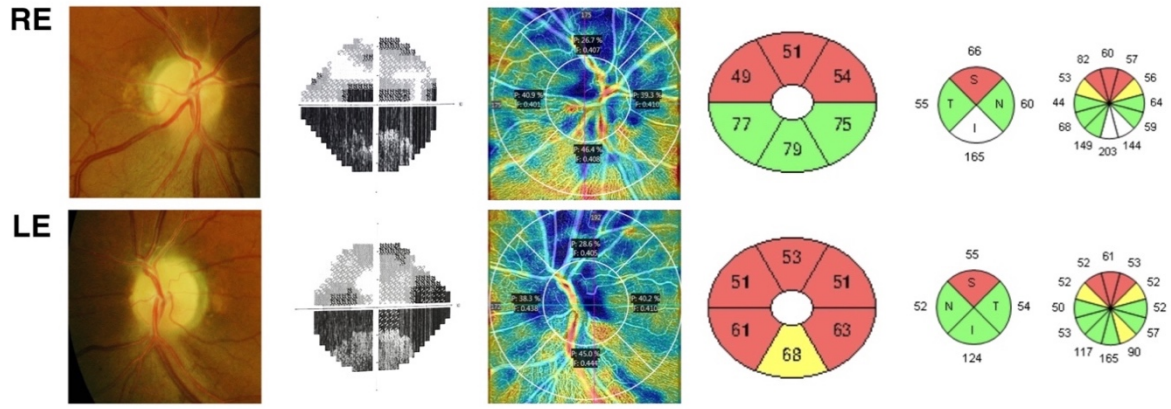

Figure 2. Results of diagnostic examinations performed at one-month follow-up (from left to right: fundus photograph, Humphrey visual field examination, optic nerve head angiography, optic disc ganglion cell analysis, and optic disc RNFL analysis by quadrants and clock hours). Spatial correspondence between visual field defect, hypoperfusion found in OCTA, and structural changes in OCT results was less obvious compared to the first examination.

DISCUSSION

NAION is a multifactorial disease with many risk factors that have been identified. At the time NAION patients lose vision, at least one underlying vascular risk factor may or may not be known during the disease development. Hypertension, nocturnal hypotension, diabetes mellitus, hyperlipidemia, anemia, obstructive sleep apnoea (OSA), coagulopathies, smoking, migraine, and cataract extraction are known risk factors of NAION.[8] In this case, our patient came with a typical symptom of painless visual field loss in the inferior part. The patient was a 52-years-old with a smoking habit and a history of diabetes mellitus and dyslipidemia thus corresponding to the age-onset predilection and known risk factors of NAION. The patient came 7 months after the initial onset, showing a long delay in seeking medical care which is also a challenge in the management of NAION.

OCT-A is a non-invasive tool that can evaluate microvascular changes in the optic nerve head and retinochoroidal layers.[9] The vascular structure was identified in OCT-A by detecting erythrocyte movement in blood vessels. Below the OCT-A threshold, non-visible capillaries may correspond to the flow velocities or to the ischemic areas.[5,6] OCT-A use in neuro-ophthalmology has great potential, including in NAION where hypoperfusion is involved in its pathogenesis. In acute NAION, OCT-A showed a significant segmental and global reduction in vascular flow density of the peripapillary vascular.[5,6] Flow to both retinal peripapillary capillaries (RPC) and peripapillary choriocapillaris (PCC) was affected in patients with NAION. Functional and structural impairment corresponded to these areas of flow deficits. Perfusion deficits in the RPC and superficial retinal capillaries in the macula were correlated to both GCC atrophy and HVF deficits and documented in OCT-A findings. On OCTA, areas of signal blockage are characterized by dark, hypo-reflective regions that appear as discrete areas of the same shape on both OCTA and structural en face OCT.[10] In our case, reduced retinal perfusion in the superior part bilaterally was shown in OCT-A. Compared to other quadrants, both capillary perfusion and flux index values were lowest in the superior area. This finding is consistent with the visual field loss in the inferior part of our patient.

Although the pathogenesis of NAION still requires more explorations and evidence, optic nerve head circulatory transient disturbance that leads to hypoperfusion and ischemia is thought to have a role. Many hypotheses have been suggested as the cause of this transient disturbance including generalized hypoperfusion, nocturnal hypotension, local autoregulation failure, vasospasm, venous occlusion, and thrombosis.[5,6] The finding in this case report may support the hypothesis that hypoperfusion plays an important part in the pathogenesis of

NAION.

NAION is often associated with retinal nerve fiber layer (RNFL) thinning and OCT is useful to monitor its thickness changes. RNFL thickness correlates with visual and neurological functioning as well as with paraclinical data and disease duration. A study by Contreras et al. showed that RNFL thinning occurred in more than 80% of patients with NAION. RNFL thinning in NAION patients is progressive which suggest ongoing process of atrophy until approximately 6 months after onset where a stable end point is reached.[11] Ganglion cell elements in the retina can be found in 3 layers: RNFL (ganglion cell axons), the ganglion cell layer (ganglion cell bodies), and the inner plexiform layer (ganglion cell dendrites). In OCT analysis, the ganglion cell layer and inner plexiform layer are analyzed as the ganglion cell-inner plexiform layer (GCIPL). In the acute phase, swelling of optic disc and axons masks the axonal loss measured by RNFL. Therefore, GCIPL is an alternative that can detect axonal loss earlier than RNFL.[12] GCIPL thickness is less likely to be affected by edema of the optic disc when compared to the RNFL. Therefore, changes in GCIPL thickness can be detected in the edema phase before RNFL changes appeared.[13] GCIPL is useful as a biomarker to predict the visual outcome in NAION patients. GCIPL thickness is correlated with BCVA, MD, and VFI at the chronic phase.[14] The criteria mentioned above matched our patient OCT result, it revealed ganglion cell loss in the superior part of his right eye and almost all parts of his left eye. Retinal nerve fiber layer thinning was found in the superior part bilaterally. Other than monitoring RNFL loss over time, OCT also measures optic disk edema.[12] Patients with NAION usually have a smaller optic disc area, a crowded optic nerve, and a smaller cup-to-disc ratio. Although crowded optic nerve does not always mean a small optic disc, hence the controversy. Almost all patients with NAION have disc-at-risks.[15] In this patient, the cup-to-disc ratio was difficult to evaluate since both eyes were involved.

This case showed an interesting finding from the result of diagnostic examinations performed. Inferior visual field defect found with the Humphrey visual field examination corresponded with the reduced perfusion in the superior part. The inferior visual field defect also corresponded to the thinning of GCIPL and RNFL in the superior area. The co-locality of visual field defect, reduced perfusion, GCIPL, and RNFL thinning portrayed the connection of hypoperfusion as the presumed underlying mechanism of NAION, neuron loss as the result of the hypoperfusion, and the visual field loss as the presenting symptom in NAION. Similar NAION cases that showed co-locality between the visual field defect and reduced perfusion and structural changes have also been reported. A case report by Giordano et al described a case where the persistent localized impairment of Radial Peripapillary Capillary (RPC)

appeared to be well-matched with visual field defects and with RNFL thinning at structural SD-OCT.[16] Higashiyama et al had also reported a case where a decrease in retinal perfusion was corresponding to the RNFL loss and GCC loss on OCTA.[17]

There are few other possibilities other than a primary hypoperfusion process that might explain the co-locality of visual field loss-reduced perfusion-structural changes in NAION cases. Sharma et al stated that reduced perfusion found in OCT-A might also be explained as the result of compressive edema. The decreased signal due to fluid build-up from edema might also explain the finding from OCT-A in NAION patients. When the edema has subsided, decreased metabolic needs due to tissue loss might explain the reduced perfusion in OCT-A.[18] It is also possible that a primary hypoperfusion process and edema-related findings in OCT-A contribute together to the result of OCT-A found in NAION. Since NAION is a multifactorial disease and its pathogenesis is still unclear, it is important to always consider all possible processes when interpreting the findings from OCT-A and OCT in NAION patients.

One month after the initial examination, the visual field defect had progressed and became more generalized. Hypoperfusion found with OCTA also showed to be worsening, not only in the affected quadrant but also in other quadrants. Progressive hypoperfusion found with OCTA is in concordance with previous reports by Rebolleda et al. Rebolleda et al found that superficial capillary density decreased from acute to the atrophic stage, although the decrease was only statistically significant in the temporal quadrant.[19] OCT findings were also slightly decreased for both GCIPL and RNFL thickness. In the one-month follow-up evaluation, the spatial correspondence between these results can still be found, although not as clear as in the initial examination, especially for the visual field defect. The slight decrease in RNFL thickness also supports the previous finding from Huang et al that stated RNFL continued thinning up to 12 months slowly in NAION. [20] Rebolleda et al also reported significant RNFL and GCIPL thinning from acute to atrophic stage, showing continuous structural changes in NAION. The GCIPL thinning also correlates to progressive vessel reduction.[19]

This case report has several limitations. First, this report only describes one case of NAION. The follow-up period reported for the patient was also relatively short. However, this report has described an interesting case of bilateral NAION portraying spatial correspondence of visual field defect with OCTA and OCT results, as well as the progression of this case.

CONCLUSION

OCT angiography is a safe diagnostic test that could detect the decrease of the retinal

perfusion due NAION. Decreased retinal perfusion in the retina was shown in OCT angiography of the disc and macula, corresponding to the RNFL loss and GCC loss due to NAION.

Conflict of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript.

Informed consent

Informed consent was obtained from the patient included in this report.

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