NON-ARTERITIC ANTERIOR ISCHEMIC OPTIC NEUROPATHY IN SMOKER ADULTS

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ABSTRAK

Neuropati optik iskemik anterior non-arteritik (NAION) dikenal sebagai neuropati optik akut yang paling umum dan penyebab utama kehilangan penglihatan mendadak tanpa rasa sakit di seluruh dunia, dengan perkiraan kejadian tahunan berkisar antara 2,3 hingga 10,2 per 100.000 individu >50 tahun. Meskipun asal pasti NAION masih belum diketahui, patofisiologinya melibatkan infark iskemik kepala saraf optik karena aliran darah yang terganggu melalui arteri siliaris posterior pendek, dengan beberapa faktor risiko vaskular sistemik yang berkontribusi terhadap perkembangannya termasuk peran merokok tembakau yang kontroversial tetapi semakin dikenal. Untuk mencegah kebutaan seumur hidup, penelitian ini menekankan pentingnya diagnosis dini dan manajemen NAION yang menyeluruh pada pasien perokok berat. Dilaporkan seorang pria berusia 45 tahun mengeluhkan penglihatan mata kanan kabur sejak 1 minggu yang lalu. Penglihatan kabur dirasakan terutama hanya ketika melihat ke kanan dan ke bawah. Dia memiliki riwayat sakit kepala 1 minggu yang lalu. Dia juga merupakan seorang perokok aktif dengan kebiasaan merokok 1 bungkus/hari sejak 15 tahun yang lalu. Pemeriksaan visus jauh 0,5 pada kedua mata. Hasil tes konfrontasi menunjukkan penyempitan lapang pandang temporo-inferior OD. Pemeriksaan tonometri OD > 50 mmHg dan OS 17 mmHg. Pemeriksaan funduskopi langsung menemukan OD diskus optikus bulat dengan batas tidak jelas, berwarna kuning kemerahan, rasio C/D 0,3, rasio A/V 2/3.

Kata kunci : dewasa, neuropati optik iskemik anterior non-arteritik, perokok, perokok terkait NAION

ABSTRACT

Non-arteritic anterior ischemic optic neuropathy (NAION) is recognized as the most common acute optic neuropathy and a leading cause of sudden and painless vision loss worldwide, with an estimated annual incidence ranging from 2.3 to 10.2 per 100,000 individuals >50 years old. Although the exact origin of NAION is still unknown, obstruction of blood flow through the short posterior ciliary arteries, resulting in an ischemic infarction of the optic nerve head, with multiple systemic vascular risk factors contributing to its development including the controversial but increasingly recognized role of tobacco smoking. In order to prevent lifelong blindness, this study emphasizes the importance of early diagnosis and thorough management of NAION in patients who smoke heavily. Presented a 45-year-old man with a major complaint of blurry vision in his right eye since 1 week ago. The blurred vision was felt mainly only when looking to the right and down. He had a history of headaches 1 week ago. He also an active smoker with a habit of smoking 1 pack/day since 15 years ago. Distant vision examination was 0.5 in both eyes. The results of the confrontation test showed a narrowed temporo-inferior visual field OD. tonometry examination were OD > 50 mmHg and OS 17 mmHg. Direct fundoscopy examination found a round optic disc OD with indistinct borders, reddish yellow in color, C/D ratio 0.3, A/V ratio 2/3.

Keywords *: non-arteritic anterior ischemic optic neuropathy, smoker, NAION-related smoker, adult*

INTRODUCTION

Non-arteritic anterior ischemic optic neuropathy (NAION) is a leading cause of sudden, painless vision loss worldwide. Globally, in middle-aged and older populations (those over 50), NAION is acknowledged as the most prevalent acute optic neuropathy, with an estimated annual incidence ranging from 2.3 to 10.2 per 100,000 individuals, and for all ages, it was

0.54/100,000 (Wu KY & Evoy F, 2022; Raizada K & Margolin E, 2025). According to recent population-based studies, the incidence may be higher than previously thought; estimates for patients over 67 years old approach 82 per 100,000 annually (Lee MS et al., 2011). The condition demonstrates a clear age-related pattern, with prevalence increasing substantially after age 50, with the seventh and eighth decades of life having the highest incidence (Hattenhauer MG, et al., 1997; Lee MS et al., 2011).

Studies show that men reported 57% of instances, indicating a higher frequency of impact than women (Foster R et al., 2019). Racial disparities have been documented, with Caucasians experiencing higher incidence rates compared to Black and Asian populations (Raizada K & Margolin E, 2025; Lee MS et al., 2011). An estimated 6,000 new cases are reported each year in the United States alone, contributing to the global burden, highlighting the significant public health impact of this sight-threatening condition (Howard L, 2023; AAO, 2025). The pathophysiology involves obstruction of blood flow through the short posterior ciliary arteries, resulting in an ischemic infarction of the optic nerve head, with multiple systemic vascular risk factors contributing to its development (such as diabetes mellitus, hypertension, and hyperlipidemia), including the controversial but increasingly recognized role of tobacco smoking (Lee MS et al., 2011).

The relationship between tobacco smoking and NAION development has generated significant scientific debate, with conflicting evidence from various international epidemiological studies. While some large-scale investigations have found no significant association between tobacco smoking and NAION incidence overall, compelling evidence suggests that current smokers develop NAION at significantly younger ages compared to former smokers and never-smokers (Hayreh SS, et al., 2007). A comprehensive study of 624 patients revealed that current smokers developed NAION at a mean age of 57.8 years, compared to 64.0 years for former smokers and 60.4 years for never-smokers, indicating that smoking may accelerate disease onset in susceptible individuals (Hayreh SS, et al., 2007). Conversely, several studies have identified smoking as an important risk factor, with some research demonstrating that cigarette smoking significantly increases NAION risk, particularly in younger patients (Chung SM et al., 1994; Kim DH et al., 2017).

Asian populations, particularly in South Korea, have provided valuable insights into NAION epidemiology with distinctive patterns compared to Western populations. A nationwide Korean study reported a prevalence of 102.87 per 100,000 among adults over 40 years old, with incidence rates of 11.35 per 100,000 person-years, comparable to Caucasian populations (Lee JY et al., 2018). However, Korean studies have identified smoking as a significant risk factor with an OR of 3.58 ($p = 0.014$), with 35.5% of NAION patients being current smokers (Kim DH et al., 2017). This finding contrasts with some Western studies and highlights potential ethnic or regional differences in risk factor profiles. The Korean data also revealed gender-specific patterns, with males more frequently affected, likely reflecting higher smoking rates among Korean men and potential genetic or environmental factors specific to Asian populations (Lee JY et al., 2018; Kim DH et al., 2017).

These international differences may reflect genetic predisposition, environmental factors, healthcare access patterns, and varying diagnostic criteria across different medical systems. In Indonesia, NAION epidemiology reveals unique characteristics that differ from both Western and other Asian populations. A comprehensive five-year study at Cipto Mangunkusumo Hospital in Jakarta documented 272 NAION cases, showing that 54.5% of patients smoked, making it one of the most common risk factors (Zulkarnaen M et al., 2021). This high prevalence of smoking among Indonesian NAION patients was accompanied by other significant risk factors, such as 73.9% with hypertension, 63.5% with obesity, and 54.6% with diabetes mellitus (Zulkarnaen M et al., 2021). The mean age of Indonesian NAION patients was 52.6-53.69 years, which appears younger than typical Western populations, with males

comprising 54.1% of cases (Dwipayani NM et al., 2017). Indonesian studies have documented that patients typically present with advanced visual impairment, with the majority having initial visual acuity worse than 3/60 and an average delay of 15.16 weeks before seeking specialized care, suggesting challenges in healthcare access and awareness (Zulkarnaen M et al., 2021). In order to prevent lifelong blindness, this study emphasizes the importance of early diagnosis and thorough management of NAION in patients who smoke heavily.

METHODS

This study, which was conducted at Bhayangkara Hospital in Semarang from September to Octotober 2024, is based on case report studies. In order to gather information for this case report, the patient's history, basic physical tests of the eyes, and additional supporting examinations of the eyes being investigated.

CASE REPORT

A 45-year-old man came to the eye clinic of Bhayangkara Hospital Semarang with a major complaint of blurry vision in his right eye since 1 week ago. The patient continuously experienced blurry vision in his right eye, which interfered with his daily activities. The patient admitted that the complaint did not improve even though he had been given chloramphenicol eye drops that he bought himself at the pharmacy. The patient admitted that the blurred vision was felt mainly only when looking to the right to see the rearview mirror when driving a car and down to step on the brake. The patient had a history of headaches 1 week ago. Complaints of headaches on the right side, especially after waking up in the morning, felt throbbing continuously with a duration of about 15 minutes and improved by taking paracetamol. The headache was only felt once and has not recurred. Complaints of fever, seeing flashes of light, red eyes, watery eyes, pain, seeing black dots, foggy eyes, and vision as if covered by a curtain were denied.

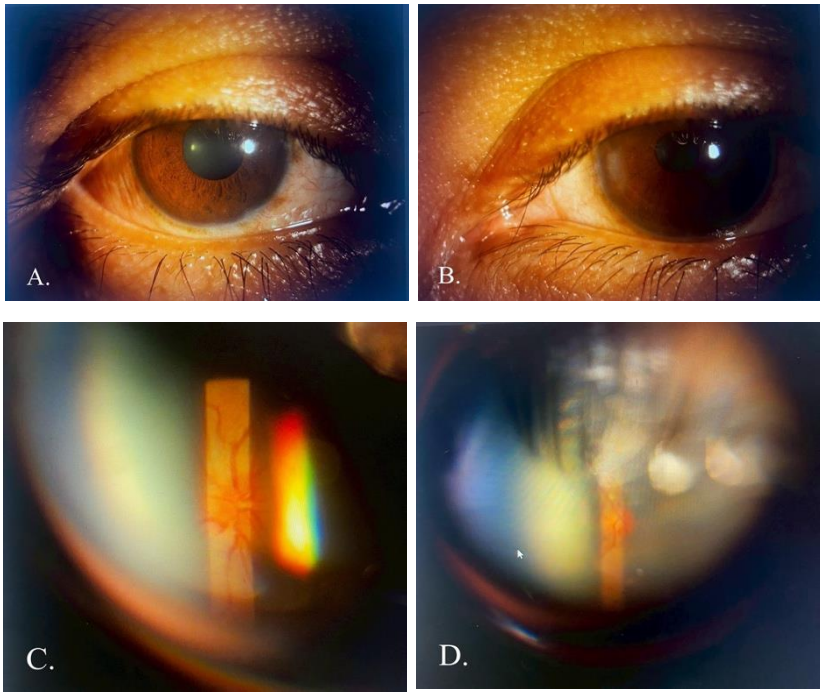

Figure 1. Ocular Examinations (a) OD with slit-lamp; (b) OS with slit-lamp; (c) Direct funduscopy OD; (d) Direct funduscopy OS

The patient had a habit of smoking 1 pack/day since 15 years ago. History of similar complaints, eye trauma, and previous use of glasses were denied. A history of previous eye surgery was denied. History of having diabetes mellitus, hypertension, and malignancy was denied. Family history of similar complaints, diabetes mellitus, and hypertension were denied. Allergies and alcohol consumption were denied. Vital signs examination was within normal limits. Distant vision examination was 0.5 in both eyes. The results of the confrontation test showed a narrowed temporo-inferior visual field OD. Physical examination of the eyes was within normal limits. The results of the tonometry examination were OD > 50 mmHg and OS 17 mmHg. Direct fundoscopy examination found a round optic disc OD with indistinct borders, reddish yellow in color, C/D ratio 0.3, A/V ratio 2/3, no scars, bleeding, ablation, neovascularization, or exudates on the retina.

NAION OD was identified as the patient's diagnosis. Given treatment to reduce intraocular pressure in the form of acetazolamide 3x500 mg, timolol eye drops 2x1 gtt, and KSR 2x600 mg. The patient was given drugs to suppress inflammation in the form of methylprednisolone 3x4 mg. In addition, the patient also received mecobalamin 3x500 mcg, zinc 2x20 mg, and citicoline 1x500 mg as neuroprotection. The patient was educated to stop smoking.

DISCUSSIONS

One of the main causes of abrupt, painless vision loss in the world is NAION. Globally, NAION is recognized as the most common acute optic neuropathy in middle-aged and elderly populations (Wu KY & Evoy F, 2022; Raizada K & Margolin E, 2025). Although the exact origin of NAION is still unknown, it has been proposed that acute ischemia of the optic nerve head (ONH) due to transitory hypoperfusion of the small posterior ciliary arteries results in axonal swelling. By impairing axoplasmic flow, this swelling leads to an increase in axonal swelling, which in turn compresses ONH microcirculation and exacerbates ischemia. This vicious cycle results in comEvoy F, 2022). The patient's age of 45 years is younger than the typical NAION demographic, as most cases occur in individuals >50 years (Wu KY & Evoy F, 2022; Raizada K & Margolin E, 2025). Although NAION can occur at any age, research indicates that between 10.5% and 23.2% of cases start before the age of 50 (Guyer DR et al., 1985; Preechawat P et al., 2007). According to a different study, 12.7% of NAION cases in individuals <50 years old (Arnold AC et al., 2013).

Recent meta-analyses have identified significant risk factors for NAION, including male gender (OR = 1.67), hypertension (RR = 1.28), hyperlipidemia (RR = 1.43), diabetes mellitus (RR = 1.53), coronary heart disease (RR = 1.68), and sleep apnea (RR = 3.28) (Liu B et al., 2021). Men appear to be affected more frequently than women, with studies reporting a male predominance in 57% of cases (Foster R et al., 2019). Another study reported smoking can increase the risk of experiencing NAION 3.58 times (Kim DH et al., 2017). These findings align with our case, where the risk factors for NAION of the patient were that he was a man and an active smoker.

The relationship between smoking and NAION remains controversial in the literature. However, some research, such as a large cohort study conducted by Hayreh et al found no relationship between tobacco use and NAION but according to other studies, smoking is a significant risk factor, especially for younger individuals (Hayreh SS et al., 2007). In contrast, smokers with NAION were statistically younger at onset (mean age 51 years) than nonsmokers (mean age 64 years), as shown by Chung et al (Chung SM et al., 1994). This finding aligns with our case, where the 45-year-old patient had a substantial smoking history. The potential mechanisms by which smoking may contribute to NAION include vascular endothelial dysfunction, increased thrombogenicity, and reduced oxygen-carrying capacity (Chung SM et al., 1994). Potential role also includes nicotine-induced vasoconstriction, increased platelet

aggregation, elevated blood cell counts, and enhanced atherosclerotic processes that may compromise optic nerve head perfusion (Kim DH et al., 2017; Lee MS et al., 2011).

The clinical presentation in this case was classic for NAION, presenting acute, painless, unilateral vision loss with characteristic optic disc swelling and altitudinal visual field defect (Wu KY & Evoy F, 2022; AAO, 2025). Around 10% of patients reported headache, ocular discomfort, and periocular pain but those symptoms were not typical in NAION (Wu KY & Evoy F, 2022).The temporo-inferior visual field defect pattern observed is consistent with the most common visual field defect in NAION, which typically presents as inferior altitudinal loss (Wu KY & Evoy F, 2022). The absence of pain, light perception, inflammatory signs, or systemic symptoms helps differentiate this case from arteritic anterior ischemic optic neuropathy (AAION) and optic neuritis (Wu KY & Evoy F, 2022). NAION doesn't have any effective treatment (AAO, 22025). The significantly elevated intraocular pressure (>50 mmHg) in this case is noteworthy and requires immediate intervention. This likely represents secondary glaucoma due to optic disc swelling rather than primary angle-closure glaucoma (Aranti A et al., 2024; Wanichwecharungruang B & Chantra S, 2009). Several case reports have documented the association between NAION and elevated IOP, with blood flow autoregulation in the human optic nerve potentially maintained at IOPs up to 30-40 mmHg (Wanichwecharungruang B & Chantra S, 2009). When IOP exceeds this threshold, NAION can develop because the optic nerve cannot maintain adequate circulation.

The combination of acetazolamide and timolol used in this case represents standard care for acute IOP elevation. Acetazolamide, a carbonic anhydrase inhibitor, can reduce IOP by 18.8% to 26.9% within the first 6 hours (Van den Heever H & Meyer D, 2016). Timolol, a beta-blocker, demonstrates IOP reduction of 21.3% to 31.2% and is highly effective as a topical agent (Van den Heever H & Meyer D, 2016; Cheng JW et al., 2012). The concurrent use of potassium supplementation (KSR) was appropriate to prevent hypokalemia associated with acetazolamide therapy. The neuroprotective approach using citicoline, mecobalamin, and zinc represents emerging therapeutic concepts in NAION management. Citicoline has shown promise, with a randomized pilot study demonstrating that 500 mg daily for six months improved visual function and provided neuroprotection in NAION patients (Parisi V et al., 2019). The mechanism of citicoline's neuroprotective effect involves enhancement of retinal ganglion cell metabolism, stabilization of cell membranes, and promotion of neural regeneration (Parisi V et al., 2019; MedPath, 2017).

The use of methylprednisolone in this case reflects the ongoing controversy surrounding corticosteroid therapy in NAION treatment. The evidence for corticosteroids remains mixed and controversial. According to some preliminary research, 75% of individuals treated with 40–80 mg of oral prednisone had improved visual acuity, compared to 17% of patients who were not treated (Hayreh SS, 1974). According to a research by Hayreh and Zimmerman, when treatment was started within two weeks of the commencement, visual acuity and visual fields significantly improved (Hayreh SS & Zimmerman MB, 2008). However, randomized controlled trials have shown conflicting results. Rebolleda et al found no beneficial effect of high-dose systemic steroids on visual or anatomical outcomes and reported serious complications in 30% of treated patients, leading to early study termination (Rebolleda G et al., 2013). A more recent randomized double-masked trial showed faster resolution of optic disc edema with prednisone but no difference in final visual acuity between groups (Chen JJ, 2018). The decision to use methylprednisolone in this case was likely based on the acute presentation with significant disc swelling and the markedly elevated IOP, where anti-inflammatory effects might help reduce compartment syndrome pressure.

The prognosis for NAION varies considerably, with visual improvement occurring in 22-32% of patients, although improvement is often modest. Several factors influence visual outcomes in NAION patients. Age appears to be a significant prognostic factor, with older

patients having worse visual recovery outcomes. A Thai population study found that older adults were 4,041 times more likely to experience poorer vision recovery, as did having diabetes mellitus (OR: 3.809) and hypertension (OR: 4.577) (Kemochoknateee P et al., 2022). According to a study from Kuwaitt, patients under 50 had a 2.8-fold higher chance than older patients of having final visual acuity of 20/40 or higher. (Behbehani R et al., 2021). Smoking cessation counseling is essential given this patient's significant tobacco history. While the relationship between smoking and NAION remains debated, the potential vascular effects of smoking and the observation that smokers develop NAION at younger ages support the importance of cessation counseling (Chung S et al., 1994).

CONCLUSION

The most prevalent acute optic neuropathy and a major contributor to abrupt, painless vision loss globally is NAION. This study underscores NAION's occurrence in younger patients with vascular risk factors (e.g., smoking). Acute vision loss mandates urgent ophthalmic assessment to exclude arteritic causes. NAION doesn't have any effective treatment. Management hinges on IOP reduction, anti-inflammatories, neuroprotection, and aggressive risk-factor modification. Despite intervention, visual recovery is often incomplete, highlighting the need for early diagnosis and patient education on recurrence prevention.

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