

High-resolution MRI features of nonarteritic anterior ischemic optic neuropathy: a case series

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Abstract

• **AIM:** To demonstrate the imaging findings of nonarteritic anterior ischemic optic neuropathy (NAION) using high-resolution magnetic resonance imaging (MRI) sequences.

• **METHODS:** A retrospective review of 4y of medical records and MRIs of nine patients suspected of having NAION who underwent orbit protocol MRI was conducted. The orbit MRI protocol included high-resolution three-dimensional (3D) T2-weighted imaging (HR 3D T2WI), high-resolution 3D contrast-enhanced T1-weighted imaging (HR-CE 3D T1WI), and high-resolution 3D T2-fluid-attenuated inversion recovery imaging (HR-CE 3D T2-FLAIR) and diffusion-weighted imaging, if applicable. To rule out other causes of optic neuropathy such as inflammatory optic neuritis, we evaluated the presence of optic disc swelling, contrast enhancement at the optic disc, and other abnormal findings on these sequences.

• **RESULTS:** Among the 715 patients, 9 were diagnosed with NAION. The median age of the patients was 62y (range, 46–79y), and five patients (56%) were men. Two of these patients demonstrated optic disc swelling on HR 3D T2WI and focal contrast enhancement on HR-CE 3D T1WI. Eight patients showed focal contrast enhancement on HR-CE 3D T2-FLAIR imaging. Among these patients, five showed a focal contrast enhancement only on HR-CE 3D T2-FLAIR imaging. The most frequent location of the focal contrast enhancement was the superomedial ($n=5$, 56%) followed by the medial ($n=2$, 22%) and central ($n=2$, 22%), and superior ($n=1$) aspects. In all three patients for whom diffusion-weighted imaging was available, there was no evidence of diffusion restriction in the optic disc.

• **CONCLUSION:** This study demonstrates the imaging

finding of NAION using high-resolution MRI sequences. HR-CE T2-FLAIR imaging is particularly useful in detecting NAION when combined with other high-resolution MRI sequences. It can provide additional insights into the pathophysiology of NAION, which may aid in obtaining an appropriate diagnosis and follow-up.

• **KEYWORDS:** ischemic optic neuropathy; nonarteritic; magnetic resonance imaging

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INTRODUCTION

Ischemic optic neuropathy is a spectrum of conditions that affect the optic nerve as a result of ischemic injury^[1]. Anterior ischemic optic neuropathy typically arises from ischemia in the perilaminar region supplied by the posterior ciliary artery and can be classified as nonarteritic (NAION) or arteritic (AAION). NAION is characterized by microcirculatory hypoperfusion of the optic disc and is believed to be the leading cause of acute optic neuropathy in individuals older than 50y and the second most common optic neuropathy in adults^[2-3]. The growing population of older adults with higher risk factors for NAION, such as hypertension, diabetes, smoking, and atherosclerosis, makes understanding the pathophysiology and imaging findings of NAION necessary^[2-3].

Although advances have been made in understanding the clinical manifestations and natural history of NAION, differentiating between NAION and other common non-glaucomatous optic neuropathies, such as optic neuritis, remains challenging because of the clinical similarity of conditions, which is particularly apparent in cases in which optic disc edema obscures diagnostic clarity during the acute phase. Hence, in cases of clinical uncertainty, magnetic resonance imaging (MRI) is often recommended to rule out other potential causes of optic neuropathy, such as compressive optic neuropathy or inflammatory optic neuritis^[4]. High-resolution (HR) MRI sequences can offer enhanced

visualization of the optic nerve and surrounding structures, facilitating a comprehensive evaluation of the orbit. Therefore, understanding the MRI findings could be helpful for the diagnosis of NAION and exclusion of other causes of optic neuropathy. To date, there have been only a few case reports on the HR MRI findings of NAION, and there has been no comprehensive utilization of HR MRI sequences for NAION. In this study, we present nine patients with NAION in whom HR MRI sequences were applied.

PARTICIPANTS AND METHODS

Ethical Approval This retrospective study was approved by our institutional review board (Approval No. EMCS 2025-01-008) and the requirement for informed consent was waived.

Participants We reviewed the orbit MRIs of 715 patients who visited two university hospitals (Nowon Eulji University Hospital and Ewha Woman's University Seoul Hospital, Seoul, Republic of Korea) between May 2020 and April 2024. We included patients in this study who fulfilled the following requirements: 1) patients who underwent fundoscopy, visual field test, laboratory test including erythrocyte sedimentation rate, and C-reactive protein; 2) patients who did not meet the diagnostic criteria for giant cell arteritis, sarcoidosis, syphilis, or other inflammatory or infectious diseases; 3) patients who did not have compressive or infiltrative orbital lesions on MRI; 4) patients who underwent HR MRI with acceptable image quality.

Ophthalmic Exam All patients underwent fundoscopy and visual field test at the time of symptom presentation and during the follow-up periods. Ophthalmologists with 9 and 10y of experience, respectively, reviewed the funduscopy findings. The assessment of the visual field was performed on a Humphrey visual field analyzer (Carl Zeiss Meditec, Dublin, CA, USA) in two hospitals.

Magnetic Resonance Examination All MRI images were obtained with a 3-T MRI scanner (Signa Premier and Signa Architect; GE Healthcare, Milwaukee, WI, USA, and Magnetom Skyra, Siemens Healthineers, Erlangen, Germany) using a 16-channel head coil. We included precontrast isotropic three-dimensional (3D) T2-weighted sampling perfection with application optimized contrasts using different flip angle evolution (SPACE), contrast-enhanced (CE) 3D T2-fluid-attenuated inversion recovery (FLAIR), and CE axial 3D T1-weighted image (CE 3D T1WI) using gadoterate meglumine contrast [0.2 mL/kg; gadoterate meglumine (Dotarem, Guerbet, Paris, France) and gadobutrol (Gadovist, Bayer Schering Pharma AG, Berlin, Germany)]. The specific imaging parameters for the sequences were as follows: 1) for the diffusion-weighted image (DWI), repetition time (TR)/echo time (TE), 5250/53.2ms; section thickness, 3 mm; flip angle, 180°; field of view (FOV), 200×200 mm; matrix, 144×144, and b values 0 and 800 mm²/s; 2) for 3D T2-SPACE, TR/TE,

1190/131ms; effective section thickness, 0.66 mm; image display, 0.7 mm; flip angle, 140°; FOV, 180×180 mm; voxel size, 0.132 mm; number of excitations (NEX), 2; 3) for the CE 3D T2-FLAIR, TR/TE, 9000/383ms; inversion time (TI), 2500ms; effective section thickness, 0.66 mm; image display, 0.7 mm; flip angle, 120°; FOV, 180×180 mm; voxel size, 0.123 mm; NEX, 2; 4) for the CE 3D T1WI, TR/TE, 6.6/2.5ms; section thickness, 0.6 mm; flip angle, 9.0°; FOV, 180×180 mm; voxel size, 0.14 mm; NEX, 1. In all patients, the CE 3D T2-FLAIR sequence was acquired after the CE 3D T1-TFE. The CE 3D T2-FLAIR and T1-weighted images were acquired after the intravenous administration of gadobutrol (Gadovist, Bayer Schering Pharma) at a dose of 0.1 mmol/kg of body weight.

MRI Interpretation Two neuroradiologists (Yoon RG and Lee BE, with 12 and 8y of experience in the interpretation of head and neck MRI, respectively) evaluated the presence of signal abnormality and morphologic change on precontrast 3D T2-SPACE, abnormal enhancement on CE 3D T2-FLAIR images, CE 3D T1WIs, and DWI abnormality if applicable, while blinded to the clinical findings. In all cases, the evaluations were performed independently, and in cases in which a discrepancy in the evaluation occurred, the final decision was determined by consensus.

RESULTS

Among the 715 patients, after we excluded those who did not fulfill the requirements described above, such as patients with other ophthalmologic diseases, 9 were finally diagnosed as NAION (Figure 1). The median age of the patients was 62y (range, 46–79y), and five patients (56%) were men. Table 1 describes the detailed clinical features and ophthalmologic examination results of all nine patients. On the initial presentation, all patients had mono-ocular involvement with visual disturbance. Five patients (56%) had underlying risk factors including hypertension, diabetes, and dyslipidemia. Seven patients (78%) showed disc edema on the initial fundoscopy, which improved on follow-up fundoscopy examination. Five patients (56%) had an inferior altitudinal defect on the visual field test, and the other patients showed a small spot or diffuse defect.

Table 2 summarizes the MRI findings observed across HR sequences in patients with NAION. With regard to the MRI findings, two (22%) patients demonstrated optic disc swelling on HR 3D T2WI. On the CE images, a focal contrast enhancement was noted on HR-CE 3D T1WI in two (22%) patients, whereas eight (89%) patients exhibited the enhancement on HR-CE 3D T2-FLAIR imaging. Among these patients, five patients showed a focal contrast enhancement only on HR-CE 3D T2-FLAIR imaging. The most frequent location of the focal contrast enhancement was the superomedial ($n=5$, 56%), followed by the medial ($n=2$,

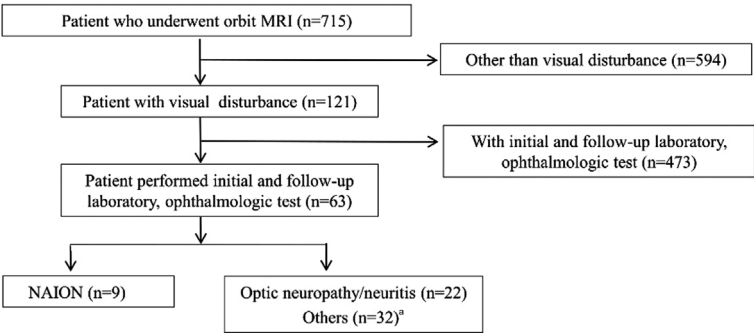


Figure 1 Flow chart of patient enrollment MRI: Magnetic resonance imaging; NAION: Non-arteritic ischemic optic neuropathy. ^aOthers includes sarcoidosis, diabetic optic neuropathy, arteritic ischemic optic neuropathy, anti-tuberculosis medication related optic neuropathy, or neuropathy not otherwise specified.

Table 1 Demographic characteristics, ophthalmic exam results of patients with NAION

Patient No.	Age, y	Sex	OD/OS	Clinical manifestation	Risk factor	Initial funduscopy	Follow-up funduscopy	Treatment
1	66	F	OS	Blurred vision	DM, HTN	Disc edema with hemorrhage	Resolved edema, Pallor (1mo)	Steroid pulse
2	79	M	OD	Visual discomfort	Dyslipidemia	Superior disc edema	Resolved edema (1mo)	-
3	49	M	OD	Pain	DM, HTN	Superior disc edema	Pallor (3mo)	Glucose control
4	70	F	OS	Blurred vision	-	Disc edema	Decreased edema (1mo)	-
5	53	F	OD	Visual discomfort	-	Disc edema	Pallor (1mo)	Oral steroid
6	63	M	OD	Blurred vision	-	Disc edema with hemorrhage	Pallor (6mo)	-
7	68	F	OS	Blurred vision	HTN	Drusen	N/A	-
8	46	M	OS	Visual discomfort	DM, HTN	Fovea focal hemorrhages	N/A	-
9	63	M	OD	Blurred vision	-	Disc edema with hemorrhage	Resolved edema (5mo)	-

NAION: Non-arteritic ischemic optic neuropathy; OD: Right eye; OS: Left eye; HTN: Hypertension; DM: Diabetes mellitus; N/A: Not applicable; -: Negative finding.

Table 2 Orbit MRI findings of patients with NAION

Patient No.	HR-3D T2WI	HR-CE 3D T1WI	HR-CE FLAIR	DWI
1	Optic disc swelling	Focal CE in optic disc	N/A	N/A
2	-	Focal CE in optic disc	Focal CE in optic disc	N/A
3	Optic disc swelling	-	Focal CE in optic disc	N/A
4	-	-	Focal CE in optic disc	N/A
5	-	-	Focal CE in optic disc	N/A
6	-	-	Focal CE in optic disc	N/A
7	-	-	Focal CE in optic disc	-
8	-	-	Focal CE in optic disc	-
9	-	Focal CE in optic disc	Focal CE in optic disc	-

MRI: Magnetic resonance imaging; NAION: Non-arteritic ischemic optic neuropathy; HR: High resolution; CE: Contrast-enhancement; T2WI: T2-weighted image; CE T1WI: Contrast-enhanced T1-weighted image; CE 3D FLAIR: Contrast-enhanced 3D-fluid-attenuated inversion recovery; N/A: Not applicable; -: Negative finding.

22%), central (*n*=2, 22%), and superior (*n*=1) aspects. In all three patients who had available DWI, there was no evidence of diffusion restriction in the optic disc. The MR images of the representative cases are illustrated in Figure 2 (case 1) and Figure 3 (case 2). Treatment options were determined based on the definite underlying risk factors and patients’ medical conditions. In our study, two patients received treatment with systemic corticosteroids, whereas seven patients received only conservative management, including glucose control or lifestyle modification.

CASE 1 A 70-year-old woman was referred to our hospital with a history of painless blurred vision in her left eye for 2wk. Her initial visual acuity was 20/25 in the right eye and 20/30 in the left eye. A left relative afferent pupillary defect was noted. Slit-lamp examination and intraocular pressure were normal in both eyes. The Humphrey visual-field test revealed an inferior altitudinal defect in the left eye, which was more prominent in the temporal side (Figure 2A). On funduscopy, the optic nerve head in the normal right eye was small and crowded without a definite visible cup, consistent with a disc at risk, and swelling

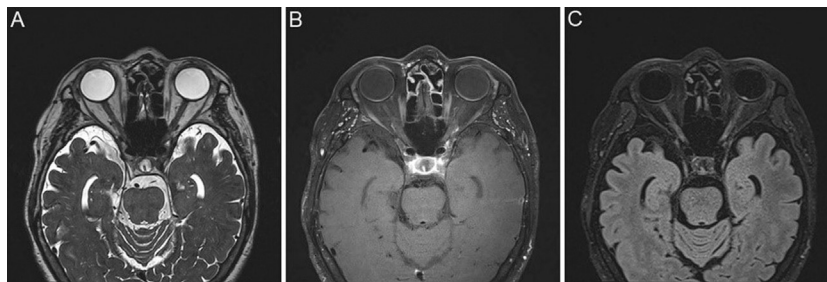


Figure 2 Orbit magnetic resonance imaging of a 70-year-old female patient with non-arteritic ischemic optic neuropathy (Case 1) Axial 3D T2-weighted SPACE and contrast-enhanced T1-weighted image demonstrate no definite optic disc swelling or contrast enhancement at the left optic disc (A and B, respectively). Axial contrast-enhanced 3D T2-fluid-attenuated inversion recovery image demonstrating definite focal contrast enhancement at left optic disc (C).

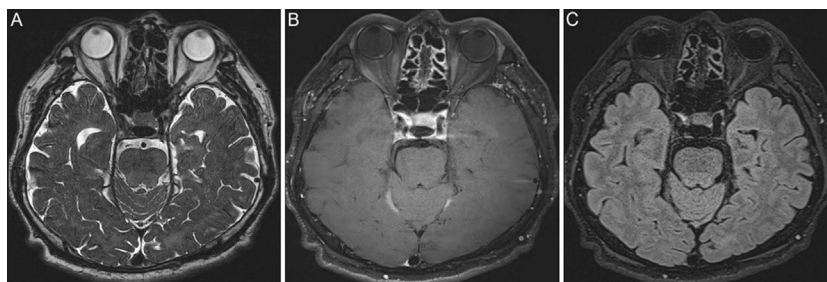


Figure 3 Orbit magnetic resonance imaging of a 79-year-old male patient with non-arteritic ischemic optic neuropathy (Case 2) Axial T2-weighted SPACE imaging demonstrating no definite optic disc swelling at the right optic disc (A). Axial 3D contrast-enhanced T1-weighted image shows a focal contrast enhancement at the right optic disc (B), which is more conspicuous on contrast-enhanced 3D T2-fluid-attenuated inversion recovery image (C).

of the optic disc was apparent in the affected left eye (Figure 2B). No other neurologic or systemic symptoms were found. The postcontrast 3D T2-FLAIR images revealed a focal area of contrast enhancement present in the superomedial aspect of the left optic disc, whereas the precontrast 3D T2 SPACE and CE 3D T1WI images showed no abnormality (Figure 2C). Two months later, the patient's visual acuity and visual fields were unchanged, but an improvement in the disc edema was observed.

CASE 2 A 79-year-old man visited our hospital with a history of painless visual discomfort in his right eye for 2wk. His underlying medical history included dyslipidemia. His initial visual acuity was 20/25 in the right eye and 20/30 in the left eye. Slit-lamp examination and intraocular pressure were normal in both eyes. The Humphrey visual-field test showed a constricted visual field in the right eye, with an inferior altitudinal defect (Figure 3A). On fundoscopy, the left optic disc exhibited no remarkable finding with a normal cup-to-disc ratio, and we noted segmental edema at the superior portion of the right optic disc with a relatively small, crowded optic nerve head (Figure 3B). No other neurologic or systemic symptoms were found. Postcontrast 3D T1 and FLAIR images of the orbits revealed focal bulging with contrast enhancement at the superomedial aspect of the right optic disc, which was more discernible on the CE 3D T2-FLAIR image, whereas the precontrast 3D T2 SPACE image showed no abnormality

(Figure 3C). One month later, the patient's visual acuity and visual fields were unchanged, but the disc edema had resolved.

DISCUSSION

In this study, we presented the HR MRI findings of nine patients with NAION. Notably, approximately 89% of the patients demonstrated a focal contrast enhancement in the optic disc on HR-CE 3D T2-FLAIR images, whereas only 22% showed discernible optic disc swelling on HR-T2WI. Our results may suggest the potential advantage of HR sequences, particularly HR-CE 3D T2-FLAIR imaging may offer a diagnostic advantage for detecting subtle abnormalities of the optic nerve head that might be missed on conventional sequences. The ability to clear visualization of characteristic changes, these findings on HR-sequences may support radiologists in making more accurate and timely diagnoses, and reducing the need for unnecessary additional or invasive diagnostic procedures.

Distinguishing NAION from AAION is clinically important, as the treatment strategies and prognoses for these two conditions differ significantly^[5-6]. AAION, most commonly associated with giant cell arteritis, often requires urgent corticosteroid therapy to prevent irreversible vision loss, whereas NAION can be managed more conservatively^[5-10]. To date, there have been few attempts to use different MRI sequences for the detection of AION, because it is challenging to differentiate between AAION, NAION and other optic

neuropathy, especially in patients without typical clinical features. Sommer *et al*^[11] suggested that HR 3D T1-weighted black-blood MRI and contrast enhancement may help to detect posterior ciliary artery involvement in patients with giant cell arteritis. Another recent study comparing 13 giant cell arteritis-associated AAION and eight with NAION found that optic nerve enhancement was significantly more extensive and intense in the AAION group, often involving both the sheath and intra-orbital segments, whereas NAION cases showed T2 hyperintensity usually involving the intra-orbital segment^[7]. In AAION, inflammation of the posterior ciliary arteries and optic nerve sheath compromise the blood-optic nerve barrier, resulting in robust gadolinium uptake and peri-neural sheath signal abnormalities that may be absent in NAION^[7,10]. In advance of the results of previous studies, our findings may further aid in differentiating NAION from AAION by using 3D CE-FLAIR imaging; focal T2 hyperintensity and mild disc-centered enhancement in NAION align well with non-arteritic ischemic patterns, lacking the sheath involvement or diffuse signal change typically found in AAION. However, as this preliminary study was not designed for direct comparison between AAION and NAION, further research is warranted to distinguish MRI characteristics of these two entities.

To date, few studies have explored the diagnostic value of different MRI sequences in detecting NAION. Conventional orbit MRI studies have shown that NAION cases demonstrate increased signal within the optic nerve on FLAIR, but no enhancement on CE T1WI^[7]. Another study using intravoxel incoherent motion showed *f* values derived from intravoxel incoherent motion could reflect the perfusion abnormality and impairment of visual function in patients with NAION^[12]. Adesina *et al*^[13] found that the presence of contrast enhancement on CE T1WI without diffusion restriction at the optic disc may be more indicative of NAION than optic neuritis. These findings align with our observations, in which subtle contrast enhancement at the optic disc was noted in the absence of diffusion signal changes. While earlier investigations used 2D sequences or 3D CE T1WI only, our study used HR-CE 3D-T2-FLAIR image, which has previously been validated for its good detectability of cranial nerve abnormalities. For instance, Chung *et al*^[14] demonstrated that HR-CE 3D T2-FLAIR could detect additional involvement in the inner ear, facial and vestibulocochlear nerves in patients with Ramsay Hunt syndrome. Similarly, Lee *et al*^[15] showed that HR-CE 3D T2-FLAIR provided high reliability and diagnostic accuracy in the evaluation of cranial neuropathies, including oculomotor nerve involvement in anti-GQ1b antibody syndrome. Given that the optic nerve head can be considered part of the cranial nerve system, we hypothesized that HR-CE 3D T2-FLAIR would be particularly well suited for identifying abnormalities

in NAION. Our study was therefore focused on this potential using HR-CE 3D T2-FLAIR sequences, and the relatively higher frequency of signal changes observed on this sequence in our cohort may indicate its potential value in the evaluation of NAION.

Regarding the utility of the FLAIR sequence in optic nerve evaluation, FLAIR is advantageous for detecting optic nerve abnormalities due to its combined fluid and fat suppression properties^[16]. Compared to 2D-FLAIR, 3D-FLAIR offers multiplanar reconstructions and superior spatial resolution^[17-18]. These properties allow for more precise localization of the enhancement, particularly when HR-CE 3D T2-FLAIR sequence are used. Additionally, CE T2-FLAIR is more sensitive to T1 shortening than conventional T1WI, especially at low gadolinium concentrations, making it particularly effective in visualizing faintly enhancing lesions^[19-21]. Moreover, CE T2-FLAIR images typically do not show contrast enhancement in normal vascular structures and meninges, improving lesion conspicuity at the CSF-tissue interfaces, such as orbital globe or optic nerve head. Our preliminary findings suggest that HR-CE 3D T2-FLAIR may be sensitive in detecting ischemic alterations in the optic nerve in NAION, as it can demonstrate both subtle fluid shifts and contrast enhancement. Based on these observations, our study adopted HR-CE 3D T2-FLAIR imaging, which has previously been validated for detecting cranial nerve abnormalities. However, while our findings support the potential utility of HR-CE 3D T2-FLAIR in the evaluation of NAION, further large-scale, controlled studies incorporating appropriate comparison groups and formal statistical validation will be essential to confirm its diagnostic performance.

As demonstrated in case 2 of our study, Yovel *et al*^[22] reported robust enhancement of the optic nerve head on CE-FLAIR imaging in NAION. The contrast enhancement of the optic nerve head can be attributed to an autoregulatory mechanism known as luxury perfusion, which is a vascular autoregulatory response to increase oxygenation in the ischemic portions of the optic disc^[22-24]. Although the exact pathogenic explanations remain uncertain, it is possible that venous stasis or selective shunting of blood flow to the ischemic portions of the optic disc, where there is a breakdown of the blood-brain barrier, underlies the observed contrast enhancement.

This study has several limitations. First, because performing MRI specifically for this condition is rare, this study included a small number of patients. In addition, this retrospective observational study did not include a control group of healthy subjects for comparison. We did not routinely perform precontrast FLAIR; therefore, there is limited information for detecting the exact enhancement of the optic nerves. Lastly, the timing of contrast enhancement might affect the positive

finding of each HR sequence. The most delayed scan time of T2-FLAIR imaging may have played a role in the more apparent contrast enhancement on 3D T2-FLAIR than T1WI. Further studies with larger sample sizes with control groups are warranted to confirm the diagnostic accuracy of FLAIR imaging in NAION and to compare its performance with other MRI sequences.

In conclusion, we reported a case series of HR MRI findings in patients with NAION. HR-CE 3D T2-FLAIR imaging is particularly useful for detecting NAION, especially when other HR MRI sequences show no abnormal finding. The utility of various HR MRI sequences and awareness of these MRI findings in patients presenting with undetermined optic neuropathy could help clinicians make an appropriate diagnosis and management plan.

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Conflicts of Interest: Lee BE, None; Yoon RG, None.

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