American Journal of Ophthalmology Case Reports 34 (2024) 102057

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Video

Non-arteritic anterior ischemic optic neuropathy secondary to idiopathic intracranial hypertension

Ryung Lee [a], Saif Aldeen Alryalat [b,c], Osama Al Deyabat [b], Noor Laylani [b], Peter Mortensen [b], Andrew G. Lee [b,d,e,f,g,h,i,*]

[a] Touro College of Osteopathic Medicine, New York, NY, USA
[b] Department of Ophthalmology, Blanton Eye Institute, Houston Methodist Hospital, Houston, USA
[c] Department of Ophthalmology, The University of Jordan, Amman, Jordan
[d] Department of Ophthalmology, University of Texas Medical Branch, Galveston, TX, USA
[e] Department of Ophthalmology, Cullen Eye Institute, Baylor College of Medicine, Houston, TX, USA
[f] Departments of Ophthalmology, Neurology, and Neurosurgery, Weill Cornell Medicine, New York, NY, USA
[g] Department of Ophthalmology, University of Texas MD Anderson Cancer Center, Houston, TX, USA
[h] Texas A&M College of Medicine, Bryan, TX, USA
[i] Department of Ophthalmology, The University of Iowa Hospitals and Clinics, Iowa City, IA, USA

ARTICLE INFO

Keywords:
Non-arteritic anterior ischemic optic neuropathy
Idiopathic intracranial hypertension
Diffusion-weighted imaging

ABSTRACT

Purpose: Patients with increased intracranial pressure and underlying hypertensive emergency may present with optic disc edema. Papilledema in this setting may be a predisposing risk factor for superimposed non-arteritic anterior ischemic optic neuropathy (NAION). We highlight the role of neuroimaging including diffusion-weighted imaging in magnetic resonance imaging that can help to differentiate visual loss from NAION versus papilledema in fulminant IIH with and without hypertension.

Observations: A 46-year-old female presented with acute vision loss in the right eye and transient right hemiparesis. Neuro-ophthalmic examination revealed optic disc edema in both eyes. Magnetic resonance imaging (MRI) of the brain with diffusion-weighted imaging (DWI) sequences showed restricted diffusion in the optic nerve head of the affected eye. Lumbar puncture revealed an elevated opening pressure of 34.8 cm H2O confirming increased intracranial pressure. Additionally, literature searches were conducted in the PubMed, Google Scholar and Embase databases to uncover previous cases of patients with ischemic optic neuropathy and restricted diffusion on MRI.

Conclusions and importance: We highlight the shared pathophysiology between optic disc edema related visual loss in NAION and papilledema in IIH. We review the overlapping clinical and radiographic findings in these two conditions which may occur simultaneously. The presence of restricted diffusion in the optic nerve head versus in the optic nerve parenchyma may support a diagnosis of superimposed NAION and might influence the decision to perform surgery in cases of IIH with fulminant visual loss. Although restricted diffusion on MRI DWI sequences is often used to define cytotoxic edema related to ischemic infarction in the brain, this radiographic finding alone should not be used to determine the indication for surgery for papilledema related visual loss in fulminant IIH.

1. Introduction

Idiopathic intracranial hypertension (IIH) is a disorder predominantly affecting obese, young females and is characterized by symptoms and signs (e.g., papilledema) confined to increased intracranial pressure (ICP); negative neuroimaging (except for radiographic signs of increased ICP); normal cerebrospinal fluid analysis; and an elevated ICP on opening pressure by lumbar puncture. Visual loss in IIH can occur gradually or suddenly (i.e., fulminant IIH) and is typically due to papilledema.

Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common optic neuropathy in older patients and is associated with various vasculopathic risk factors (e.g., hypertension, obstructive sleep apnea, diabetes mellitus). In contrast to the visual loss of papilledema in

* Corresponding author.
E-mail address: aglee@houstonmethodist.org (A.G. Lee).

https://doi.org/10.1016/j.ajoc.2024.102057
Received 22 August 2023; Received in revised form 25 February 2024; Accepted 14 March 2024
Available online 16 April 2024

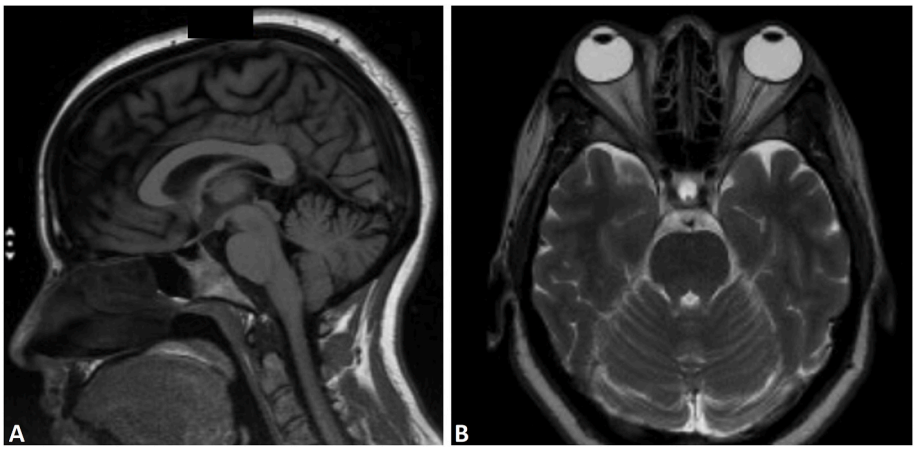

Fig. 1. (A, B): A) T1 weighted scan in the sagittal plane demonstrating partial empty sellae due elevated intracranial pressure. B) T2 weighted MRI transverse of flattened posterior globes.

IIH (chronic, bilateral, headache), the visual loss in NAION is typically acute, unilateral, and painless. Diffusion weighted imaging (DWI) restriction on magnetic resonance imaging (MRI) can occur in acute ischemic infarction and can be seen in the optic nerve in NAION.

DWI may be diagnostic and prognostic in cases of NAION secondary to papilledema especially in fulminant IIH. There is significant overlap in the visual loss of NAION and fulminant IIH especially when associated with systemic hypertension. We review a case of NAION in IIH and discuss the similarities and differences in clinical and radiographic presentation for this scenario. In addition to our case report, the PubMed, Google Scholar and Embase databases, most recently in December 2023 were filtered using the search terms "diffusion restriction" and "ischemic optic neuropathy". This search was limited to human studies and included publications obtained from our initial review. The search revealed 289 articles and was narrowed to 108 publications on the topic of restriction diffusion and ischemic optic neuropathy. Studies then excluded noted diffusion restriction with giant cell arteritis and posterior ischemic optic neuropathy or those that did not distinguish management by individual cases. Seven published articles were selected for further review based on inclusion of demographic information regarding gender, age, etiology of ischemic optic neuropathy, laterality, MRI findings and ADC values.

2. Case report

A 46-year-old female presented with sudden loss of vision in the right eye (OD) and transient right hemiparesis. The blood pressure measured 180/100 mm Hg. Her body mass index was 28.32. Past medical history was significant for chronic hypertension, congenital kidney disease, right parietal development venous anomaly, migraines, microcytic anemia, hyperlipidemia. Social history included prior cocaine use.

After her acute transient ischemic attack (TIA) she received tissue plasminogen activator (tPA) with resolution of the hemiparesis but persistence of the visual loss OD. Family and surgical histories were noncontributory. The urine drug screen at admission was positive for cocaine.

On neuro-ophthalmology examination, the visual acuity was 20/200 OD and 20/50 in the left eye (OS). The pupils measured 5 mm–3 mm in the dark with a relative afferent pupillary defect OD. Intraocular pressure measurements, motility examination, and slit lamp biomicroscope of the anterior segment were normal in both eyes (OU). Confrontational visual field demonstrated a nerve fiber layer nasal and temporal arcuate defect with central loss OD and a normal visual field OS. Ishihara color plate testing showed only 2 out of 14 correct plates OD and 9 out of 11 OS. Ophthalmoscopy showed Frisen grade 4 papilledema OU.

Computed tomography (CT) of the head without contrast was normal. Magnetic resonance imaging (MRI) brain showed a partial empty sellae (Fig. 1A) and flattening of the globes OU (Fig. 1B) consistent with the radiographic findings of increased ICP. DWI (Fig. 2A) and ADC (Fig. 2B) sequence showed restricted diffusion in the optic nerve head OD. No optical coherence tomography (OCT) or automated perimetry was available during the hospitalization.

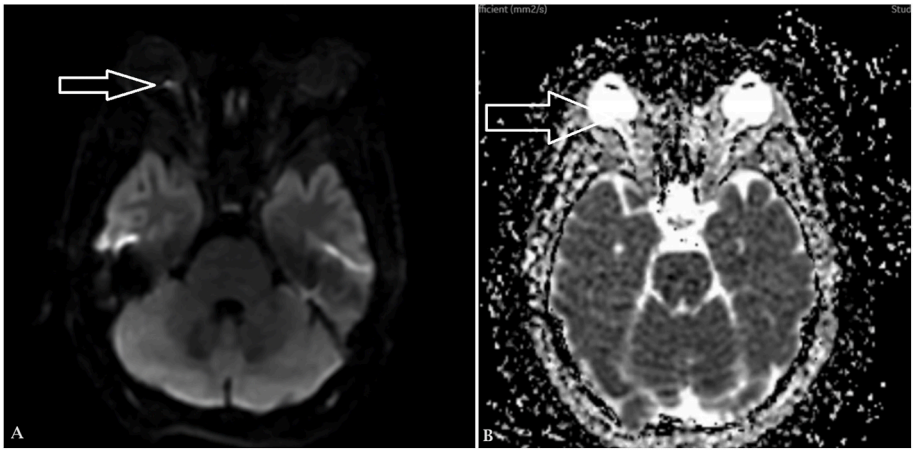

Fig. 2. (A, B): Diffusion restriction of the optic nerve head is indicated by A) MRI DWI axial scan demonstrating focal diffusion restriction in the right optic nerve head. B) ADC demonstrating hypo-intensity near the right optic nerve head.

Table 1
Cases Reported in the Literature of NAION with elevated ICP.

Study	Patient Presentation	Neuro-Ophthalmic Findings on Imaging	Risk Factors
Pirouzmand et al. (2022)[3]	A 48-year-old man with blurry vision and bilateral papilledema	Severe flattening of the posterior sclera and enhancement of optic nerve head DWI restricted diffusion within the optic nerve head on MRI orbits.	Liver transplant, chronic kidney disease
Ma et al. (2020)[2]	A 29-year-old obese woman presented to the emergency room with horizontal binocular diplopia, new headaches, and transient visual obscurations.	Magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) showed signs of raised intracranial pressure. Superior altitudinal visual field defect on Humphrey 24-2.	Obesity and elevated hypertension
Amit Kumar Deb (2021)[4]	A 28-year-old female presented to us with a history of sudden onset painless diminution of vision in both eyes associated with headache and vomiting for one day.	Fundus examination showed bilateral diffuse pale disc edema and peri-papillary superficial splinter hemorrhages. Fundus fluorescein angiography showed bilateral optic disc filling delay in the early phases and disc staining in the late phases	Acute severe anemia and hypotension
Green et al. (1980)[5]	A 41-year-old woman was admitted to the hospital for evaluation of papilledema, band like headaches.	Enlarged blind spot in the right eye. Early arterial phase of the fluorescein angiogram with hypo-fluorescence in the peripapillary choroid from the 1- to the 3-o'clock position	Chronic Hypertension
Lamirel et al. (2010)[5]	A 20-year-old white woman complained of severe headaches with nausea, photophobia, and pulsatile tinnitus.	Bilateral severe optic nerve head edema with peripapillary hemorrhages and white nerve fiber layer infarctions. Humphrey and Goldmann visual fields showed bilateral constriction with an inferior nasal defect and enlarged blind spot in the right eye and an inferior altitudinal defect in the left eye.	Overweight

MR angiography (MRA) and MR venography (MRV) were normal. The lumbar puncture showed normal CSF contents but an elevated opening pressure of 34.8 cm H_2O. Acetazolamide (Diamox) 1000 mg twice a day was initiated. Surgical treatment of papilledema was not performed. The blood pressure was treated medically, and the patient was discharged but did not return for follow up.

3. Discussion

We believe that our patient had NAION in the setting of IIH related papilledema. Table 1 summarizes the cases reported in the English language ophthalmic literature of presumed NAION secondary to papilledema.[1–5] There is significant overlap between the clinical presentation of NAION and papilledema related visual loss. The nerve fiber layer and central patterns of visual field do not differentiate NAION from fulminant IIH related papilledema (Table 2).

Table 2
Comparing characteristics of NAION with Papilledema and fulminant IIH.

Characteristics	NAION with Papilledema	Fulminant IIH
Age	>50 years old	25–45 years old
Gender	Male = Female	Female > male
Ethnicity	Caucasians	All races, but African Americans may have worse presentations.
Ophthalmic Findings	Hyperemic, unilateral disc optic disc edema Isolated painless, vision loss, usually unilateral with nerve fiber layer defect	Bilateral and symmetric papilledema. Bilateral, dilated retinal veins, peripapillary hemorrhages, and cotton wool spots. Vision field loss, often bilateral with enlarged blind spots.
Associated Symptoms	Painless, mild, or no headache Other systemic vascular risk factors	Diplopia from non-localizing sixth nerve palsy Headache May have nausea and vomiting
Visual Field	Inferior Altitudinal defect Nasal sector loss Central depression	Enlarged blind spot Glaucomatous-like field defects (nasal step, arcuate defect, constricted field) May have a central loss in fulminant cases
Treatment	Treatment of underlying vasculopathic risk factors Management of risk factors Monitoring and follow-up	Urgent medical intervention to lower ICP (Lumbar Puncture) and preserve vision Weight management Surgical intervention (optic nerve sheath fenestration, venous stent, CSF shunt)

Raised ICP in IIH produces papilledema which may predispose to the development of NAION (a "structural disc at risk" which is crowded from papilledema). Prior vasculopathic risk factors including drug use (e.g., cocaine in our patient) can be both predisposing and precipitating factors for NAION. Although optic disc edema is the hallmark of acute NAION, papilledema from IIH may also lead to impairment of optic nerve functions (e.g., visual acuity, dyschromatopsia, visual field) and both NAION and papilledema can be unilateral or asymmetric may produce a relative afferent pupillary defect (RAPD).

Among the main differentiating factors between vision loss due to fulminant IIH (FIH) and NAION is the course of vision loss. The visual loss FIH tends to be subacute (within days to weeks) versus the vision loss from NAION which is acute.

The structural risk factor for "garden variety" typical NAION is a small and crowded optic nerve (i.e., the structural "disc at risk"). The proposed mechanism is a vicious cycle of edema causing decreased blood flow and ischemic damage and further edema leading to further

Table 3
Characteristics of NAION versus IIH.

Characteristics	NAION	IIH
Timing	Acute onset of vision loss	Subacute or chronic in IIH
Laterality	Usually, unilateral	Bilateral but may be asymmetric
Features	Restriction diffusion-limited to the affected optic nerve head, inferiorly Commonly, post-contrast enhancement or positive DWI signal along optic disc nerve	Edema usually involves both optic disc heads DWI signals the greatest temporally Post-contrast enhancement of the optic nerve head alone. Optic nerve tortuosity distended optic nerve sheath, optic nerve head protrusion.
White Matter Abnormalities	Normal or chronic white matter ischemia	No white matter lesions

Table 4
Demographics of patients with MRI diffusion restriction and ischemic optic neuropathy.

Feature	Value
Number of Patients	10
Age (Mean, SD)	47.69 ± 12.63
Gender	Male (90%) Female (10%)
Ischemic Optic Neuropathy Etiology	Anterior Ischemic Optic Neuropathy (40%) Lymphomatous Ischemic Optic Neuropathy (10%) Embolic Ischemic Optic Neuropathy (10%) Hemorrhagic Ischemic Optic Neuropathy (10%) Shock-Induced Ischemic Optic Neuropathy (10%) Uremic Optic Neuropathy (10%)
Unilaterality	Bilateral (90%) Unilateral (10%)
MRI Findings	Reduced ADC (90%) High Intensity DWI Signal (100%)
Mean ADC Value (10^{-3} cm^2/s)	0.59

ischemia. Fulminant IIH (FIH) is a severe and rapidly progressive form of IIH, affecting roughly 3% of patients with IIH.[6] If left untreated, severe visual loss may occur in FIH. Many authors recommend urgent admission to the hospital in FIH including placement of a temporizing lumbar drain and aggressive medical and definitive surgical intervention (e.g., optic nerve sheath fenestration, CSF diversion procedure, or venous sinus stenting).[7]

Modabber et al. reports time to treatment was critical. Patients who ended with legal blindness at final follow-up had a mean surgical delay of 6.5 days, whereas patients with a better visual outcome only had a median delay of 2 days.[8] The mechanism of permanent vision loss in FIH may be superimposed NAION.[1,2] Table 3 compares characteristics of both NAION with papilledema and fulminant IIH. Unfortunately, both NAION and FIH can produce acute visual loss, nerve fiber layer and central visual field loss, and optic disc edema in one or both eyes. Optical coherence tomography (OCT) likewise may help define disc edema but cannot definitively and reliably differentiate the underlying etiology based upon retinal nerve fiber layer thickening alone. Unfortunately, both formal automated perimetry and OCT are not usually available in most hospitals on the in-patient side.[9] Our patient had neither formal visual fields nor OCT during their hospitalization because they are not available in the hospital. Fundus fluorescein angiography may show delayed filling of the disc or choroidal segment in NAION but typically shows disc hyperfluorescence from leakage bilaterally in papilledema but like OCT and automated perimetry, FFA is often not available during hospitalizations.[5]

3.1. *Diffuse weighted imaging in NAION and IIH*

Diffusion-weighted imaging (DWI) is an MRI technique that measures the diffusion of water molecules in tissues. DWI is helpful in establishing the presence of hyperacute/acute ischemia and cytotoxic edema. Table 4 summarizes the radiographic findings on MRI in NAION and IIH.[3,10–15] Post-contrast enhancement was seen in up to 2/5th of patients with NAION in one study and up to 1/5th had DWI abnormalities.[16,17] The radiographic findings of IIH (e.g., empty sella, fluid in the sheath, venous sinus stenosis) are not present in NAION.

Our case demonstrated MRI features of increased ICP and a potentially differentiating finding of unilateral restricted diffusion of the optic disc head consistent with NAION. Limited visualization of the optic nerve head, localized field distortion, and artifacts however limit the clinical utility of DWI in typical IIH. Unilateral involvement of optic nerve head DWI restriction is suggestive of ischemia (e.g., NAION) but is neither 100% specific nor 100% sensitive.[18] Patients with papilledema in FIH have also been reported to have bilateral DWI restriction but the precise correlation with final visual acuity and potential correlation with cytotoxic edema histopathologically remains controversial and ill defined. Table 4 summarizes the demographic variables of the previous cases of ischemic optic neuropathy with diffusion restriction on MRI. Anecdotally, diffusion restriction on MRI is more indicative of "stroke of the nerve" rather than papilledema on MRI.

The imaging finding of restricted diffusion may reflect a similar pathogenesis to posterior reversible encephalopathy syndrome (PRES)[19] and may not reflect cytotoxic edema (restricted diffusion) from vasogenic edema (no restriction diffusion).[20] The absence of DWI restriction suggests a better prognosis for recovery in PRES (i.e., reversibility), but may not have the same radiographic significance in fulminant IIH or NAION related to papilledema.[21]

4. Conclusion

Clinicians should be aware of the overlap in presentation in NAION secondary to IIH and FIH. Visual loss in both conditions can be acute and severe. Papilledema related visual loss in FIH however requires aggressive medical (Diamox, lumbar puncture) and surgical intervention for elevated ICP. The presence of diffusion restriction on MRI with reduced ADC values however may suggest NAION with or without papilledema related visual loss in IIH. This information may be of both diagnostic and prognostic value in such cases, especially in FIH related papilledema. The absence of unilateral or bilateral DWI restriction on MRI in FIH should not be used as the sole determinant of surgical intervention but might be helping in providing prognosis for the patient and might inform final decision making.

Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

CRediT authorship contribution statement

Ryung Lee: Writing – review & editing, Writing – original draft, Investigation. **Saif Aldeen Alryalat:** Writing – review & editing, Validation, Data curation. **Osama Al Deyabat:** Writing – review & editing, Validation. **Noor Laylani:** Data curation, Conceptualization. **Peter Mortensen:** Data curation, Conceptualization, Methodology. **Andrew G. Lee:** Investigation, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors have no conflict of interest.

Acknowledgements

None.

References

1. Lamirel C, Bruce BB, Newman N, Biousse V. Choroidal infarction in fulminant idiopathic intracranial hypertension. *J Neuro Ophthalmol*. 2010;30(2):167. https://doi.org/10.1097/WNO.0B013E3181C25581.
2. Ma J, Micieli JA. Anterior ischemic optic neuropathy in a patient with papilledema from idiopathic intracranial hypertension. *Am J Ophthalmol Case Rep*. 2020;17. https://doi.org/10.1016/J.AJOC.2020.100593.
3. Pirouzmand N, Micieli JA. Optic disc restricted diffusion in papilledema-related anterior ischemic optic neuropathy. *Can J Neurol Sci*. 2023;50(3):464–465. https://doi.org/10.1017/cjn.2022.39.
4. Deb AK, Ghag G, Gera P, Kasturi N, Sarkar S. Bilateral non-arteritic anterior ischemic optic neuropathy with idiopathic intracranial hypertension secondary to attempted abortion related hemorrhage: a rare case report. *Indian Journal of Ophthalmology - Case Reports*. 2021;1(1):137. https://doi.org/10.4103/IJO.IJO_383_20.
5. Green GJ, Lessell S, Loewenstein JI. Ischemic optic neuropathy in chronic papilledema. *Arch Ophthalmol*. 1980;98(3):502–504. https://doi.org/10.1001/ARCHOPHT.1980.01020030498013.
6. Bouffard MA. Fulminant idiopathic intracranial hypertension. *Curr Neurol Neurosci Rep*. 2020;20(4):1–9. https://doi.org/10.1007/S11910-020-1026-8/FIGURES/1.
7. Abbasi HN, Brady AJ, Cooper SA. Fulminant idiopathic intracranial hypertension with malignant systemic hypertension - a case report. *Neuro Ophthalmol*. 2013;37(3):120–123. https://doi.org/10.3109/01658107.2013.785573.
8. Modabber M, Gupta V, Rodriguez AR. A 24-year-old woman with rapidly progressing vision loss. *Digit J Ophthalmol*. 2017;23(1):36. https://doi.org/10.5693/DJO.03.2016.10.001.
9. Miller JW, Wang JK, Thurtell M, Kardon RH, Garvin MK. Differentiation between papilledema and nonarteritic anterior ischemic optic neuropathy using retinal layer shape and regional volume features in spectral-domain optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2018;59(9), 2196-2196.
10. Bender B, Heine C, Danz S, et al. Diffusion restriction of the optic nerve in patients with acute visual deficit. *J Magn Reson Imag*. 2014;40(2):334–340. https://doi.org/10.1002/jmri.24367.
11. Lakhani DA, Balar AB, Tarabishy AR, Hogg JP, Khan M. Acute ischemic optic neuropathy in a case of heroin overdose. *Radiol Case Rep*. 2022;17(10):3950–3954. https://doi.org/10.1016/j.radcr.2022.07.100.
12. Vicente M, Serrano AR, Falgàs N, et al. Diffusion restriction in the optic nerve and retina in patients with carotid occlusion. *Neurol*. 2017;22(3):77–79. https://doi.org/10.1097/NRL.0000000000000113.
13. Sudhakar P, Rodriguez FR, Trobe JD. MRI restricted diffusion in lymphomatous optic neuropathy. *J Neuro Ophthalmol*. 2011;31(4):306–309. https://doi.org/10.1097/WNO.0b013e31821ee581.
14. Al Othman BA, Naser M, Kini AT, Lee AG. Restricted diffusion in the optic nerve head after shock-induced anterior ischemic optic neuropathy. *J Neuro Ophthalmol*. 2021;41(1):E114–E115. https://doi.org/10.1097/WNO.0000000000000897.
15. Greenberg JH, Guttha S, Pullano A, Warren FA. A Rare Case of Uremic Optic Neuropathy Without Optic Disc Edema and With a Unique Imaging Correlate: Bilateral Diffusion Restriction of the Optic Nerves. *J Neuroophthalmol*. Published online December 12, 2023. doi:10.1097/WNO.0000000000002049.
16. Rizzo JF, Andreoli CM, Rabinov JD. Use of magnetic resonance imaging to differentiate optic neuritis and nonarteritic anterior ischemic optic neuropathy. *Ophthalmology*. 2002;109(9):1679–1684. https://doi.org/10.1016/S0161-6420(02)01148-X.
17. Adesina O ofe O, Scott McNally J, Salzman KL, et al. Diffusion-weighted imaging and post-contrast enhancement in differentiating optic neuritis and non-arteritic anterior optic neuropathy. *Neuro Ophthalmol*. 2018;42(2):90. https://doi.org/10.1080/01658107.2017.1356856.
18. Golden E, Krivochenitser R, Mathews N, et al. Contrast-enhanced 3D-FLAIR imaging of the optic nerve and optic nerve head: novel neuroimaging findings of idiopathic intracranial hypertension. *Am J Neuroradiol*. 2019;40(2):334–339. https://doi.org/10.3174/AJNR.A5937.
19. Marrone LCP, Martins WA, Ramos SWMI, et al. Posterior reversible encephalopathy syndrome (PRES): is DWI a prognosis factor? *J Clin Neurosci*. 2020;72:357–359. https://doi.org/10.1016/j.jocn.2019.12.023.
20. Ho ML, Rojas R, Eisenberg RL. Cerebral edema. *Am J Roentgenol*. 2012;199(3). https://doi.org/10.2214/AJR.11.8081/ASSET/IMAGES/09_11_8081_17B.JPEG.
21. Campeau DJ, Covarrubias PH, Luetmer NG, Covarrubias DJ, Luetmer PH, Campeau NG. Diffusion-Weighted MR Images Syndrome: Prognostic Utility of Quantitative Posterior Reversible Encephalopathy Posterior Reversible Encephalopathy Syndrome: Prognostic Utility of Quantitative Diffusion-Weighted MR Images Vol vol. 23.; 2023. http://www.ajnr.org/content/23/6/1038.