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The crucial role of gadolinium-enhanced MRI in a case of amaurosis fugax – a case report and literature review

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Abstract: Optic perineuritis is the inflammation of the optic nerve sheath. This affliction can lead to visual field impairment and other signs and symptoms related to the orbital space, such as pain, disc edema, ophthalmoplegia, proptosis. However, not all patients present with such suggestive symptoms, requiring a thorough assessment. We report the case of a young male admitted to our hospital for recurrent episodes of monocular blindness. Amaurosis fugax is a well-known presentation of transient ischemic attacks (TIA) and it was ruled out. Gadolinium-enhanced MRI revealed a typical aspect of optic perineuritis. It was mandatory to consider all possible causes of secondary optic perineuritis as they all represent serious clinical conditions~~,~~ even if the idiopathic form is more frequent. The clinical and paraclinical evaluation of the patient excluded an underlying disease and primary optic perineuritis was diagnosed. Corticosteroid therapy is usually curative and a course of methylprednisolone was initiated for our patient with good outcome. However, response to treatment is not diagnostic as both primary and secondary optic perineuritis are normally responsive, hence thorough differential diagnosis is necessary.

Keywords: optic perineuritis; amaurosis fugax; monocular blindness; optic perineuritis differential diagnosis; TIA differential diagnosis.

What is new? What is important?

Monocular blindness is a common presentation of transient ischemic attacks and computer tomography is usually normal in such cases. Transient ischemic attacks represent an emergency and immediate treatment is needed. However, when history of the patient is unsignificant in terms of cardiovascular burden, a local cause involving the orbit should be evaluated and gadolinium-enhanced MRI is mandatory. Optic perineuritis displays typical features on gadolinium-enhanced MRI, although there is no difference between primary and secondary optic perineuritis in terms of imaging and usual response to treatment, thus underlying causes should always be thoroughly investigated.

INTRODUCTION

Optic perineuritis (OPN) is an inflammatory disease which affects the optic nerve sheath, without extension to the optic nerve itself, that usually presents with ipsilateral visual field impairment, pain, especially on eye movement, and sometimes disc edema [1–3]. These clinical features can be found in optic neuritis (ON) as well, hence a differential diagnosis between these two disorders is necessary, as management and prognosis usually differ. Older age at onset and visual field defects sparing central vision are more likely to suggest OPN [2,3]. Other clinical manifestations that may be present in OPN and may differentiate it from ON are ptosis, ophthalmoplegia and proptosis [2,4], which suggest an underlying orbital involvement. Gadolinium-enhanced MRI plays a crucial role in distinguishing OPN from ON, as it shows a circumferential enhancement of the optic nerve sheath without optic nerve enhancement. This aspect produces the "tram-track" sign on axial imaging and the "doughnut" sign on coronal imaging [1]. OPN is usually idiopathic, but infections, autoimmune diseases, neoplasia or drugs can cause secondary OPN [1,5,6]. Treatment consists in steroid therapy in high doses with rapid improvement of the clinical features [1], though spontaneous resolution of the disease has been reported [7,8]. Refractory cases to steroid therapy were successfully treated

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with radiation therapy, indomethacin, azathioprine or tocilizumab [1,3,8,9]. Nerve biopsy can be considered when OPN is resistant to treatment or an underlying cause is suspected [1]. We report the case of a patient diagnosed with OPN who had an atypical initial presentation and required thorough assessment and differential diagnosis.

MATERIALS AND METHODS

A 50-year-old man presented to the emergency department of our hospital in February of 2019, with episodes of abrupt loss of vision in the right eye, that lasted from 5 to 7 minutes. The patient had no significant medical history and his neurological exam showed no abnormalities apart from transient monocular blindness (amaurosis fugax) in the right eye, without retroocular pain, that lasted for few minutes. During the hospitalization, the amaurosis fugax was recurrent, with no variation in character and with similar duration of less than 10 minutes.

RESULTS

Blood pressure (BP) and heart rate (HR) were within normal parameters (HR = 61 bpm, BP = 140/80mmHg) and sinus rhythm was present on electrocardiography. The $ABCD^2$ (age, blood pressure, clinical features, duration of symptoms, diabetes) score was 0/7. Non-contrast cerebral computed tomography showed no lesions or structural anomalies. It did not show any ocular tumors, hemorrhages or ischemic lesions in the territory of the carotid artery (Figure 1. a, b). Carotid and vertebral arteries ultrasound proved to be normal, without artery stenoses. Transthoracic echocardiography was unremarkable. Laboratory results were within normal parameters, with the exception of a slightly elevated C reactive protein level 7.36 mg/L (0–5 mg/L). Given the absence of cardiovascular risk factors and the normal results of paraclinical tests, a transient ischemic attack was excluded.

Gadolinium-enhanced MRI of the brain was performed and it revealed a right optic perineuritis with enhancement around the intraorbital optic nerve, involving the nerve sheath and the surrounding fat tissue (Figure 2 a, b, c). and MRI angiography revealed no arterial occlusion (Figure 3). Ophthalmologic exam was normal with no papilledema.

Right optic perineuritis was the most likely diagnosis for this patient, causing compression on the optic nerve fibers that led to episodic visual field impairment. However, the underlying etiology of the perineuritis was unknown, requiring further tests.

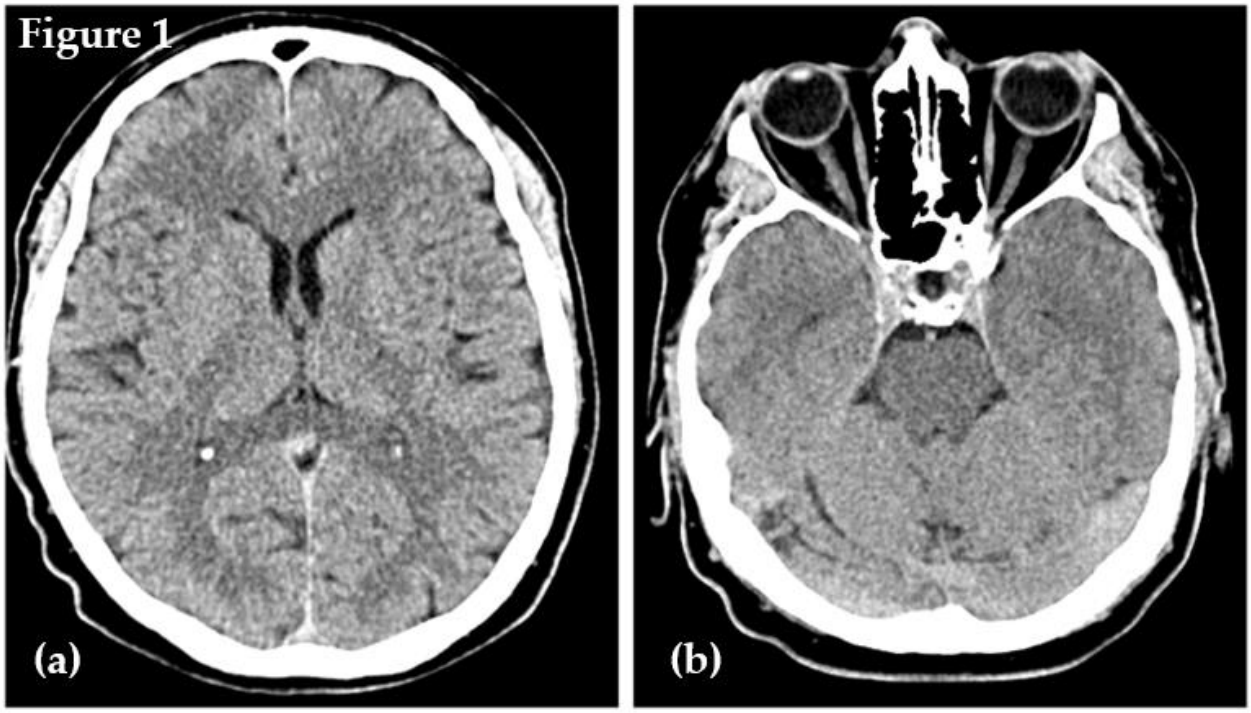


Figure 1. Non contrast cerebral computed tomography **(a), (b)** without hemorrhages, ischemic lesions in the territory of the carotid artery or masses involving the orbit.

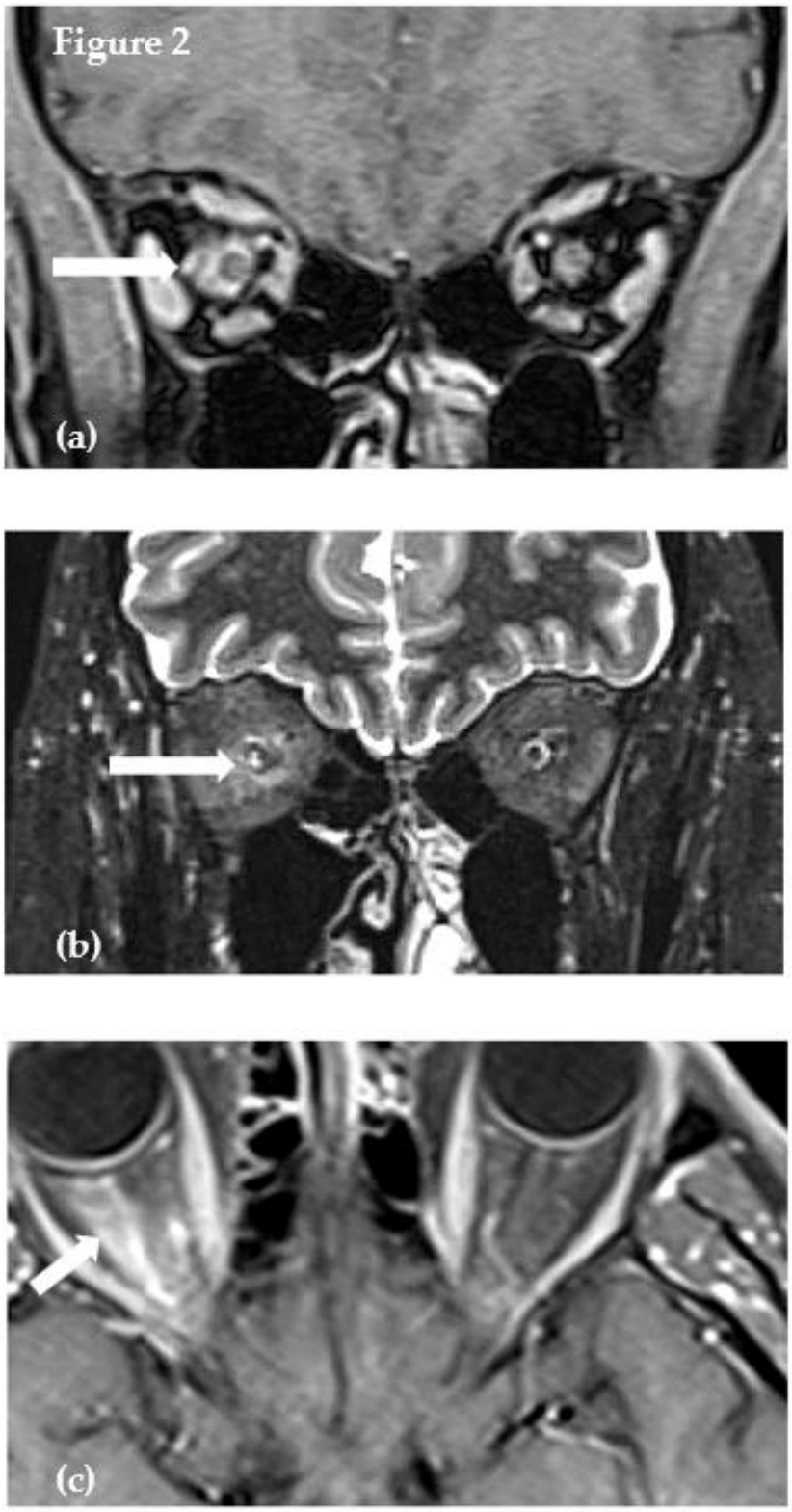


Figure 2. Magnetic resonance imaging.

(a) **Gadolinium-enhanced, fat saturated T1 VIBE MRI, coronal section of the orbit.** Right optic nerve sheath enhancement without involvement of the right optic nerve sheath and the surrounding fat tissue. (b) **STIR T2 MRI, coronal section of the orbit.** Hyperintense appearance of the right optic nerve sheath (edema) and the surrounding intraorbital fat tissue. Normal intensity of the right optic nerve. (c) **Fat saturated T1SE (spin echo) MRI, transversal section of the orbit.** Enhancement of the tissue around the right optic nerve, including the surrounding infraorbital fat.



Figure 3. 3D images reconstructed by maximum intensity projection (MIP) of time of flight angiography revealed no arterial occlusion.

An infectious etiology was excluded by performing serological tests for human immunodeficiency virus (HIV), syphilis, mycoplasma pneumoniae, herpes simplex or herpes zoster, all with negative results. Giant cell arteritis leading to amaurosis fugax in patients with normal clinical exam and normal lab results was reported before [10]. However, this diagnosis was unlikely due to the normal clinical exam; also, there were no abnormalities of the temporal artery at the ultrasound exam. The patient did not report jaw claudication or polymyalgia. Furthermore, very mildly elevated inflammatory markers could not sustain this diagnosis.

Other paraclinical tests were performed as part of the differential diagnosis. Antineutrophil cytoplasmic antibodies (C-ANCA) levels were normal, thus excluding the onset of granulomatosis with polyangiitis (formerly known as Wegener's granulomatosis). Serum angiotensin-converting enzyme (ACE) levels were within normal parameters and chest X-ray revealed no hilar or mediastinal nodal enlargement, leading to the exclusion of sarcoidosis as a possible diagnosis. Normal chest X-ray made tuberculosis improbable as well. Antibodies for systemic lupus erythematosus were measured and the results were within parameters. Anti-myelin oligodendrocyte glycoprotein (MOG) antibodies were negative. Moreover, orbital inflammation as a feature of a thyroid disease was taken into consideration, but was excluded as well, due to normal levels of (thyroid stimulating hormone) TSH and thyroid hormones.

DISCUSSION

Considering all of the above, the final diagnosis of the patient was idiopathic optic perineuritis. A course of corticosteroids was initiated. Oral methylprednisolone of 1mg/kg body-weight/day was prescribed for 3 weeks. The patient was instructed to keep an appropriate diet and to monitor his blood pressure during the corticosteroid therapy.

Treatment with methylprednisolone proved to be successful, as there were no other episodes of amaurosis fugax during the therapy. Eventually,

methylprednisolone was tapered in accordance to the clinical and neurological evaluation.

The presentation of the patient was atypical and the clinical picture didn't suggest a possible OPN. On the one hand, OPN is more frequently diagnosed in older female cohorts [1,2]. However, our patient was a young male, with no previous medical conditions. Since the patient did not follow any treatment at home, a drug-induced amaurosis fugax, which has been reported in literature [4,11], was excluded. Moreover, our patient did not present with elements suggesting ON – there was no pain upon eye movement, no subacute progression, nor was there any dyschromatopsia. However, ON must be considered in the differential diagnosis of patients with transient monocular blindness, as it may herald the presence of demyelinating or systemic diseases. Given that vision loss is typically progressive in ON, reaching nadir in days or weeks [12], a transitory presentation runs the risk of a misdiagnosis – as TIA is strikingly the first diagnostic possibility to come to mind [13]. While indeed rare, cases of ON presenting with amaurosis fugax have been reported [14], therefore, a thorough clinical and imaging evaluation is necessary. The transient monocular blindness was the only clinical feature and it naturally raised concern of a possible transient ischemic attack (TIA). The diagnosis of a TIA is clinical and it is of great importance, as TIA is considered the warning event of a stroke. Nevertheless, cerebral imaging studies must always be performed if TIA is suspected. TIA is usually characterized by "negative" symptoms and signs [15] – transient paralysis, aphasia, visual field defects etc. and amaurosis fugax is often reported. A study performed on 2938 patients with suspected TIA reported that transient monocular blindness was the most frequent visual disturbance experienced in the study group [16].

The loss of function without pain, the abrupt onset and the duration of the event suggested a possible TIA [15], but the patient's history was not suitable for this diagnosis, as there were no cardiovascular risk factors for ischemic events. Furthermore, the $ABCD^2$ score was 0/7, indicating a low risk for subsequent stroke. In spite of that, this score has become more controversial over the last years, as it cannot accurately predict the risk of stroke [17], with TIA mimics giving high scores, as well as certain cardiovascular risks not being accounted for. As a consequence, other scores were created to facilitate the diagnosis of a TIA, such as the Dawson Score and the Diagnosis of TIA (DOT) Score [15]. Interestingly, the Dawson score doesn't include amaurosis fugax as a predictive variable in detecting TIAs [18] and other variables were absent for our patient; similarly, by using the DOT score, where monocular vision loss is taken into consideration [19], our patient did not meet any other criteria. A similar presentation was reported in 2022 [20], where a male presented with episodes of transient visual loss associated with pain, fever and other orbital features. Amaurosis fugax as a sign of TIA was suspected as well and antiplatelet therapy was the treatment of choice. Eventually, MRI was suggestive for optic perineuritis that was considered related to SARS-CoV-2 exposure. This case was challenging as well due to the fact that clinical presentation suggested an orbital involvement, yet the patient was older and multiple cardiovascular risk factors were present.

hen trying to appropriately differentiate between perioptic and optic contrast enhancement, CT provides a level of detail that is below the standard set by MRI. Aside from spatial resolution, specific techniques have been developed for MRI to further assist diagnosis in such cases, such as fat suppression [3]. Nowadays, there are several imaging techniques that can be used to better visualize the eye in humans or other vertebrate species [21,22]. Clinicians can investigate the structure of the retina and the choroid by using optical coherence tomography (OCT) and scanning laser ophthalmoscopy (SLO) or even the function with optical coherence tomography angiography (OCTA). Despite the great information provided by these studies, the orbit and the optic nerve sheath cannot be visualized, thus optic perineuritis cannot be diagnosed. However, as optic perineuritis can lead to the impairment of the optic nerve, OCT might be used as a complementary tool to assess the damage of the optic fibers [23]. Furthermore, eye and orbit ultrasound is a widely accessible tool, safe and non-invasive, but it cannot show the whole sheath of the optic nerve. Nevertheless, when contraindications for MRI are present, it could be useful for OPN diagnosis [24].

When OPN was eventually diagnosed based on gadolinium-enhanced MRI, another important aspect was to determine whether the OPN is idiopathic or there is an underlying condition causing it. Even if OPN is frequently encountered as a primary disorder, a study published in 2021 included 44 cases of OPN, where only one patient had idiopathic OPN and the other 43 patients were found to have an underlying cause [5]. These results should raise concern in terms of further

management of OPN, as most cases (primary and secondary OPN) respond rapidly to steroid therapy [2,5,8], but a serious systemic condition may go unnoticed and lead to subsequent complications.

The etiology for secondary OPN includes inflammatory, autoimmune and connective tissue diseases (giant cell arteritis, Graves' disease, immunoglobulin G4-related disease, granulomatosis with polyangiitis, systemic lupus erythematosus, sarcoidosis, rheumatoid arthritis, Sjogren's syndrome, scleroderma, Behcet's disease, gout, Crohn's disease [2,5,25,26]), infections (syphilis, tuberculosis, mycoplasma pneumoniae, ocular toxoplasmosis, bacterial or fungal meningitis, sparganosis, cytomegalovirus, herpes zoster, COVID-19 [1,5,20,27]) or neoplasia (acute leukemia, primary or metastatic malignancies [1,25]). Furthermore, OPN after post-influenza vaccination [28] or induced by checkpoint inhibitors used for non-small cell lung cancer [6] was reported. It is important to mention that there are some reports that describe OPN cases associated with anti-myelin oligodendrocyte glycoprotein (MOG) antibodies [5,29,30]. It is not established yet whether there is a connection between the disease and the MOG antibodies or not. Further studies should be performed to investigate this association, since MOG antibodies target specific glycoproteins exclusively found in the myelin sheath formed by oligodendrocytes and cause demyelination, whereas the optic nerve is encased within all three meningeal layers~~,~~ which do not express these glycoproteins [31]. All these underlying causes have been excluded by the patient's history and the clinical and paraclinical examinations.

The strengths of our study consist in revealing a case of OPN with atypical presentation and in the demonstration of a mainly benign disorder that could mimic a TIA.

CONCLUSION

Optic perineuritis is an inflammatory disorder of the meningeal sheath that surrounds the optic nerve which can cause compression on the nerve fibers leading to visual field defects. Visual impairment in the absence of other symptoms requires a thorough assessment, and imaging studies play a crucial role for the diagnosis of optic perineuritis. Moreover, underlying causes should always be ruled out, as they can consist of severe systemic conditions that may present the typical gadolinium enhancement of optic perineuritis.

Perinevrita optică reprezintă o inflamație a tecii nervului optic. Această afecțiune poate duce la afectarea câmpului vizual și la alte semne și simptome legate de spațiul orbital, cum ar fi durerea, edem papilat, oftalmoplegia sau proptoza. Cu toate acestea, nu toți pacienții prezintă astfel de simptome sugestive, necesitând o evaluare aprofundată. Raportăm cazul unui tânăr de sex masculin internat pentru episoade recurente de orbire monoculară. Amaurosis fugax, o prezentare bine cunoscută a atacurilor ischemice tranzitorii (AIT) a fost exclusă, examenul RMN-ul evidențiind un aspect tipic al perinevritei optice. A fost obligatoriu să se ia în considerare toate cauzele posibile ale perinevritei optice secundare, deoarece toate reprezintă afecțiuni clinice grave, chiar dacă forma idiopatică este mai frecventă. Evaluarea clinică și paraclinică a pacientului a exclus o boală subiacentă și a fost diagnosticată perinevrita optică primară. Terapia cu corticosteroizi este de obicei curativă și a fost inițiată, obținându-se rezultate bune. Cu toate acestea, răspunsul la tratament nu este diagnostic, deoarece atât perinevrita optică primară, cât și cea secundară sunt în mod normal responsive, prin urmare este necesar un diagnostic diferențial important.

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REFERENCES

1. GUPTA S, SETHI P, DUVESH R, SETHI HS, NAIK M, RAI HK. *Optic perineur*itis. BMJ Open Ophthalmol. 2021;6:e000745.
2. HICKMAN SJ. *Optic Perineuritis*. Curr Neurol Neurosci Rep. 2016;16:16.
3. PURVIN V. *Optic Perineuritis: Clinical and Radiographic Features*. Arch Ophthalmol. 2001;119:1299.
4. TSENG AM, HARISH BINDIGANAVILE S, BHAT N, DIVATIA MK, LEE AG. *Optic Perineuritis Distinguishing Arteritic Ischaemic from Amiodarone-Associated Optic Neuropathy.* Neuro-Ophthalmol. 2021;45:329–33.
5. LI H, ZHOU H, SUN J, WANG H, WANG Y, WANG Z, *et al. Optic Perineuritis and Its Association With Autoimmune Diseases*. Front Neurol. 2021;11:627077.
6. TAKADA K, FUJIWARA K, ANDO E, ONISHI K, KURIBAYASHI T, MITSUMUNE S, *et al. Optic Perineuritis Associated with Nivolumab Treatment for Non-Small Cell Lung Cancer.* Case Rep Oncol. 2021;14:792–6.
7. TUNG C, HASHEMI N, LEE AG. *Spontaneous Resolution of Optic Perineuritis.* J Neuroophthalmol. 2013;33:93–5.
8. BERGMAN O, ANDERSSON T, ZETTERBERG M. *Optic perineuritis: a retrospective case series.* Int Med Case Rep J. 2017;Volume 10:181–8.
9. MALEKI A, RAMEZANI K, COLOMBO A, FOSTER CS. *Intravenous tocilizumab in the treatment of resistant optic perineuritis*. Can J Ophthalmol. 2021;S0008418221003628.
10. MANEA MM, DRAGOȘ D, ARSENE D, TUȚĂ S. *Bilateral simultaneous amaurosis as onset and unique symptom in giant cell arteritis.* Acta Neurol Belg. 2018;118:321–2.
11. KUBO K, KIMURA N, WATANABE R, HIGASHINO M, TSUDA M, KATO M. *Oxaliplatin-Associated Amaurosis Fugax*. Case Rep Oncol. 2021;14:832–7.
12. TOOSY AT, MASON DF, MILLER DH. *Optic neuritis.* Lancet Neurol. 2014;13:83–99.
13. FISHER CM. "*Transient monocular blindness" versus "amaurosis fugax."* Neurology. 1989;39:1622–1622.
14. AWAD AM, ESTEPHAN B, WARNACK W, STÜVE O. *Optic neuritis presenting with amaurosis fugax*. J Neurol. 2009;256:2100–3.
15. FITZPATRICK T, GOCAN S, WANG CQ, HAMEL C, BOURGOIN A, DOWLATSHAHI D, *et al. How do neurologists diagnose transient ischemic attack: A systematic review*. Int J Stroke. 2019;14:115–24.
16. LAVALLÉE PC, CABREJO L, LABREUCHE J, MAZIGHI M, MESEGUER E, GUIDOUX C, *et al. Spectrum of Transient Visual Symptoms in a Transient Ischemic Attack Cohort.* Stroke. 2013;44:3312–7.
17. EDLOW JA. *Managing Patients With Transient Ischemic Attack.* Ann Emerg Med. 2018;71:409–15.
18. DAWSON J, LAMB KE, QUINN TJ, LEES KR, HORVERS M, VERRIJTH MJ, *et al. A recognition tool for transient ischaemic attack.* QJM. 2009;102:43–9.
19. DUTTA D. *Diagnosis of TIA (DOT) score – design and validation of a new clinical diagnostic tool for transient ischaemic attack.* BMC Neurol. 2016;16:20.
20. DINKIN M, FEINBERG E, OLIVEIRA C, TSAI J. *Orbital Inflammation With Optic Perineuritis in Association With COVID-19.* J Neuroophthalmol. 2022;42:e300–1.
21. MELEPPAT RK, FORTENBACH CR, JIAN Y, MARTINEZ ES, WAGNER K, MODJTAHEDI BS, *et al. In Vivo Imaging of Retinal and Choroidal Morphology and Vascular Plexuses of Vertebrates Using Swept-Source Optical Coherence Tomography*. Transl Vis Sci Technol. 2022;11:11.
22. DELORI F, GREENBERG JP, WOODS RL, FISCHER J, DUNCKER T, SPARROW J, *et al. Quantitative Measurements of Autofluorescence with the Scanning Laser Ophthalmoscope.* Investig Opthalmology Vis Sci. 2011;52:9379.
23. BYON IS, JUNG JH, CHOI J-H, SEO JH, LEE JE, CHOI H-Y. *Evaluation of Retinal Nerve Fiber Layer in Patients with Idiopathic Optic Perineuritis using Optical Coherence Tomography.* Neuro-Ophthalmol. 2015;39:34–8.
24. EDO A, HARADA Y, KIUCHI Y. *Usefulness of B-scan ocular ultrasound images for diagnosis of optic perineuritis.* Am J Ophthalmol Case Rep. 2018;12:45–8.
25. GROSSO S, CORNACCHIONE S, ROMANO D, BERTRANDO S, FRANCESCHINI R, BALESTRI P. *Optic perineuritis: A further cause of visual loss and disc edema in children.* Brain Dev. 2014;36:932–5.
26. JULIANA EMY TOLACHINSKI O, JULIA GOMES LEITE DE S, VITÓRIA CAROLINE CARDOSO F, PAULO ROBERTO W, LAURA FIUZA P, MARCUS VINÍCIUS MAGNO G. *Optic Perineuritis Secondary to Sjogreen's Syndrome: Case Report.* Int J Brain Disord Treat. 2019;5.
27. YATES WB, NOTHLING S, LAWLOR M. *Optic Perineuritis Due to Tuberculosis*. J Neuroophthalmol. 2019;39:257–9.
28. VILAIN S, WATERSCHOOT MP, MAVROUDAKIS N. *Encephalomyelitis and bilateral optic perineuritis after influenza vaccination.* Bull Soc Belge Ophtalmol. 2000;71–3.
29. YANAGIDAIRA M, HATTORI T, EMOTO H, KIYOSAWA M, YOKOTA T. *Optic perineuritis with anti-myelin oligodendrocyte glycoprotein antibody.* Mult Scler Relat Disord. 2020;38:101444.
30. LOPEZ-CHIRIBOGA AS, VAN STAVERN G, FLANAGAN EP, PITTOCK SJ, FRYER J, BHATTI MT, *et al. Myelin Oligodendrocyte Glycoprotein Antibody (MOG-IgG)-Positive Optic Perineuritis*. Neuro-Ophthalmol. 2020;44:1–4.
31. JOHNS TG, BERNARD CCA. *The Structure and Function of Myelin Oligodendrocyte Glycoprotein.* J Neurochem. 1999;72:1–9.

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