CASE REPORTS

Optic Perineuritis Distinguishing Arteritic Ischaemic from Amiodarone-Associated Optic Neuropathy

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ABSTRACT

Giant cell arteritis (GCA) is a common medium to large vessel vasculitis of the elderly that can lead to permanent vision loss. Neuroimaging in GCA may reveal optic nerve sheath enhancement, which is a cardinal finding of optic perineuritis (OPN). The clinical manifestations of GCA can mimic that of other ocular disorders including amiodarone-associated optic neuropathy (AAON). We report a case of biopsy-proven GCA in a patient initially suspected to have AAON. This patient presented with bilateral optic disc oedema in conjunction with subacute predominately monocular vision loss and enhancement of the corresponding optic nerve sheath on neuroimaging. Clinicians should recognise that clinical and neuroimaging findings of GCA can mimic a variety of ocular and orbital pathologies including idiopathic OPN and AAON.

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Introduction

Optic perineuritis (OPN) is a rare orbital inflammatory disorder affecting the optic nerve sheath that commonly presents with decreased visual acuity, pain on eye movement, and visual field defects.¹ OPN can rarely present with orbital signs of ptosis, ophthalmoplegia, and proptosis and is a distinct entity necessitating a longer treatment with corticosteroids as compared to typical optic neuritis.^{1–3} A diagnosis of OPN requires a combination of clinical and imaging findings, specifically optic nerve sheath enhancement on magnetic resonance imaging (MRI).³ OPN can be idiopathic or occur secondary to a variety of systemic diseases including giant cell arteritis (GCA), a systemic vasculitis of elderly patients which affects large and medium-sized vessels.¹ We review the current literature and report an unusual case where optic nerve sheath enhancement on neuroimaging helped to distinguish GCA from the

alternative diagnosis of amiodarone-associated optic neuropathy (AAON).

Case

A 72-year-old White Caucasian male presented with painless bilateral subacute sequential central visual acuity loss in the left eye (OS) followed by the right eye (OD) over 3 months. His past medical history was significant for an aortic aneurysm, aortic valve repair and a 1-year history of amiodarone-controlled cardiac arrhythmia. The patient denied headache, pulsatile tinnitus, fever, weight loss, scalp tenderness, jaw claudication, or symptoms of polymyalgia rheumatica. His visual acuity was in the count fingers range OD and 20/30 OS. His pupils measured 4 mm in the dark and 2 mm in the light with a right relative afferent pupillary defect (RAPD). Humphrey visual field testing showed a dense central scotoma with break out to an inferior altitudinal defect OD and a relatively mild central scotoma with break out to the inferior field OS.

On funduscopy, bilateral Frisén grade III–IV optic disc oedema was noted.

His serum erythrocyte sedimentation rate (ESR) was 7 mm/hr (normal < 20 mm/hr), C reactive protein (CRP) was < 0.3 mg/dL (normal 0–0.5 mg/dL) and platelet count was $197 \times 10^9/L$ (normal $150\text{--}400 \times 10^9/L$). A non-contrast computed tomography scan of the brain was normal. MRI of the brain and orbits demonstrated enhancement of the intraorbital right optic nerve sheath without pathological enhancement of the optic nerve itself. (Figure 1). Serological studies for angiotensin converting enzyme levels, anti-nuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (ANCA), aquaporin-4 antibodies (NMO), and myelin oligodendrocyte glycoprotein antibodies (MOG) were negative. A lumbar puncture revealed a borderline elevated opening pressure of 24 cm of cerebrospinal fluid (CSF) (normal < 20 cmCSF). CSF analysis showed an elevated CSF protein of 83 mg/dL (normal 15–45 mg/dL) and

glucose 91 mg/dL (normal 40–70 mg/dL). CSF testing for cytomegalovirus, herpes simplex virus (HSV), varicella zoster virus (VZV) and serum testing for *Borrelia burgdorferi*, hepatitis C virus, hepatitis B virus, human immunodeficiency virus (HIV), and syphilis were negative.

Empirical treatment with 1 g/day intravenous methylprednisolone (IVMP) for 5 days followed by an oral prednisone taper and tocilizumab was initiated. Given the patient's negative symptomatology for GCA, AAON was considered as a possible cause of his vision loss and amiodarone was discontinued in consultation with cardiology.

A subsequent right temporal artery biopsy (TAB) revealed transmural histiocytic inflammatory infiltrate with numerous histiocytes at the level of internal elastic lamina, consistent with GCA (Figure 2). His visual acuity has remained stable throughout the six-months post-discharge follow-up with complete resolution of the bilateral optic disc oedema. Remarkably, the inflammatory

Figure 1. Gadolinium-enhanced fat-suppressed T1-weighted coronal (left) and axial (right) MRIs showing intraorbital right optic nerve sheath enhancement (yellow arrow).

Figure 2. Movat pentachrome stain (x40) of the right temporal artery biopsy demonstrating marked fibrointimal proliferation with luminal narrowing. Although the internal elastic lamina (black arrow) is intact, there is medial fibrosis (highlighted in green) (Figure 2a). CD163 immunoperoxidase staining (x40) highlights a transmural histiocytic inflammatory infiltrate with numerous histiocytic aggregates in the media and at the level of the internal elastic lamina (black arrows, Figure 2b). High-power view of CD163 immunohistochemical staining (x200) exhibiting several histiocytes at the level of the refractile internal elastic lamina (black arrow, Figure 2 C).

markers ESR and CRP remained within normal limits throughout the treatment course, with the ESR being 2 mm/hr and CRP <.3 mg/dL at six-month follow-up.

Discussion

GCA is the most common vasculitis of medium and large vessels in the elderly with an incidence rate of 18.8 (95% CI 15.9–21.6) per 100,000 in one 50-year population-based study from the US.⁴ Permanent vision loss is a devastating consequence of GCA and was found to afflict 8.2% of GCA sufferers in a retrospective population-based cohort-study, although others have reported much higher rates of irreversible vision loss.^{5,6} Other ocular pathologies may present similarly to GCA. One such pathology, AAON, develops in approximately 1–2% of patients within the first year of starting amiodarone therapy.⁷ AAON, a diagnosis of exclusion, is characterised by progressive monocular or binocular vision loss and bilateral optic disc swelling.⁸ Visual field defects in AAON are varied, ranging from central scotomas to inferior or superior altitudinal defects.⁹ The temporal relationship of amiodarone initiation to our patient's subacute vision loss, coupled with his bilateral optic disc oedema and visual field defects, was initially suggestive for AAON.

While the vision loss in AAON arises from a direct retinotoxic effects of amiodarone, vision loss in GCA is primarily due to the arteritic type of anterior ischaemic optic neuropathy (A-AION) which results from inflammation of the short posterior ciliary arteries supplying the optic nerve head.⁵ Inflammation and occlusion of the central retinal artery, ophthalmic artery, and cilioretinal artery have also been reported in GCA.^{5,6,10} Arteritis of the ophthalmic and posterior ciliary artery-derived penetrating pial branches, which supply the optic nerve sheath, is also speculated to cause the optic nerve sheath enhancement seen on neuroimaging,¹¹ a finding rarely evaluated for in GCA. In the twelve previously reported cases of GCA with optic nerve sheath enhancement

on neuroimaging, radiological enhancement was restricted solely to the optic nerve sheath and orbital fat (Table 1).^{2,12–21} In contrast, optic nerve sheath enhancement is not a recognised feature of AAON, which has poorly studied neuroradiological findings.

Emerging data suggest that optic nerve sheath enhancement is an under-recognised sign of GCA. In one 2016 retrospective case-series of GCA-associated MRI findings, optic nerve sheath enhancement was seen in eight out of fourteen (57%) cases with optic nerve enhancement seen in only five out of the fourteen cases (36%).^{3,11} A more recent analysis of GCA-associated MRI findings from a tertiary-referral centre found optic nerve sheath enhancement in five out of seven (71%) TAB proven-GCA cases.²² Another 2018 study found bilateral enhancement 'aside the optic nerve' in 14 out of 18 (78%) cases from TAB-prove GCA.²³ The latter two studies did not report radiological abnormalities of the optic nerve itself. Identifying instances where OPN occurs secondary to GCA has important clinical implications, as initiating an insufficient corticosteroid dose or too rapid a steroid taper might lead to relapse and recurrent visual loss.^{15,19} To this end, serum ESR, CRP, and a TAB should be considered in every case of OPN in the elderly.

Cases of GCA-associated OPN may often be missed or overlooked as neuroimaging is not generally recommended for diagnosis of arteritic (i.e., GCA) or non-arteritic AION.^{6,24} Additionally, in patients undergoing emergency room neuroimaging for headache, a non-contrast computed tomography scan is typically the initial imaging study of choice and is usually unremarkable in GCA. Likewise, in elderly patients admitted for stroke evaluation (e.g. acute monocular or bilateral visual loss) a non-contrast MRI of the head with diffusion weighted imaging (DWI) is the next neuroimaging study in the stroke work up.^{25,26} Unfortunately, the distinctive radiological finding of OPN is unlikely to be seen on a non-contrast, non-fat suppressed orbital MRI. When neuroimaging does show OPN, in the correct clinical context, clinicians should consider GCA in the differential diagnosis. In our case, both clinical and radiological data were needed to make the correct diagnosis and distinguish it from other causes like AAON, highlighting the importance of the clinical-radiological

Table 1. Summary of previous GCA cases with optic nerve sheath enhancement on MRI.

Author(s)	Age (years)	Sex	Visual Symptoms at Presentation	Imaging Finding(s)	Treatment	Outcome
Nassani et al., 1995 ²¹	69	F	Photophobia, diplopia to the right, bilateral retroorbital pain and exophthalmos	Thickening of bilateral optic nerve sheaths	Oral prednisone (50 mg/day)	Improvement of diplopia and exophthalmos. Regression of optic nerve sheath thickening
Lee et al., 2001 ²	69	M	Acute binocular vertical diplopia, proptosis, bilateral conjunctival injection, and chemosis	Enhancement of the left extra-ocular muscles, left anterior optic nerve sheath, and right posterior optic nerve sheath	Oral prednisone (100 mg/day)	Resolution of proptosis and diplopia. Resolved optic nerve sheath enhancement on MRI
Morgenstern et al., 2003 ¹⁴	83	M	Vision loss OU	Bilateral optic nerve sheath enhancement	IVMP followed by oral prednisone taper	Visual function stabilised
Morotti et al., 2013 ¹⁵	74	M	Fluctuating diplopia, subacute blurred vision OD, and central scotoma OS	Bilateral optic nerve sheath enhancement	IVMP (1 g/day) followed by oral prednisone taper	Complete blindness with no improvement
Reddi & Vollbrach, 2013 ¹⁷	83	F	Acute vision loss to hand motion range OU	Left optic nerve sheath enhancement with extension to the surrounding retrobulbar fat	IV solumedrol followed by oral prednisone taper	Some improvement of visual function. Resolved optic nerve sheath enhancement on MRI
Liu & Chestnutt, 2013 ¹⁸	83	F	Vision loss to hand motion range OD	Bilateral perineural enhancement of optic nerves	IVMP followed by oral prednisone taper	Deterioration of visual acuity to NLP OU
Liu & Chestnutt, 2013 ¹⁸	68	F	Acute blurred vision OS	Perineural enhancement of left optic nerve	IVMP followed by oral prednisone taper	Visual function stabilised
Liu & Miller, 2015 ¹⁹	67	M	Superior and central visual field loss OS, photopsia	Bilateral optic nerve sheath enhancement	IVMP followed by oral prednisone taper	Visual acuity stable OD, but declined to 20/400 OS
Emami et al., 2019 ¹²	60	M	Acute blurred vision OD with inferior field defect OD	Bilateral optic nerve sheath enhancement with mild orbital fat stranding	IVMP (1 g/day) followed by oral prednisone taper and methotrexate	Visual function stabilised
Pappolla et al., 2019 ¹⁶	76	F	Inferior visual field defect OS	Left greater than right optic nerve sheath enhancement	IVMP followed by oral prednisone taper	Residual peripheral visual field defect OS with preservation of central vision. Resolution of optic nerve sheath enhancement on MRI
Gold et al., 2020 ¹³	71	M	Subacute vision loss OS and inferonasal field defect OS	Left greater than right optic nerve sheath enhancement with fat stranding	IVMP followed by oral prednisone taper	Resolution of visual field defect and acuity to 20/20 OU. Resolved optic nerve sheath enhancement on MRI
Nguyen et., 2020 ²⁰	83	F	Transient diplopia and subacute vision OS	Left greater than right optic nerve sheath enhancement	IVMP followed by oral prednisone taper	Visual function stabilised
Our Patient	72	M	Subacute right greater than left vision loss	Right optic nerve sheath enhancement	IVMP followed by oral prednisone taper and tocilizumab	Visual function stabilised

IVMP: intravenous methylprednisolone, MRI: magnetic resonance imaging, NLP: no light perception, OD: right eye, OS: left eye, OU: both eyes.

correlation in diagnostic medicine and neuro-ophthalmology.^{3,27} Ultimately, an orbital MRI could be performed to adjudicate equivocal cases of GCA in the acute setting.

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Declaration of interest statement

The authors report no conflict of interest

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