ORIGINAL ARTICLE

A Stereotyped Syndrome with Retro-Ocular Pain, Photophobia, and Visual Disturbance Masquerading as Optic Neuritis: Case Series

Joanna M. Jefferis^a, Revelle Littlewood^a, Irene M. Pepper^a, and Simon J. Hickman^b

^aDepartment of Ophthalmology, Royal Hallamshire Hospital, Sheffield, UK; ^bDepartment of Neurology, Royal Hallamshire Hospital, Sheffield, UK

ABSTRACT

We describe here a case series of six patients referred to the Neuro-ophthalmology service in Sheffield, UK with possible acute unilateral optic neuritis. Each patient had a triad of unilateral photophobia, ipsilateral retro-ocular pain, and ipsilateral loss of vision. All patients had normal ocular examinations and investigation findings with no objective structural or functional abnormalities identified. Patients were treated by weaning-off regular analgesia and, where appropriate, commencing migraine prophylaxis. In the three patients with complete recovery of pain, there was also complete recovery of vision. We propose that this is a migraine syndrome and that the decreased visual acuity is a functional consequence of the pain and photophobia.

ARTICLE HISTORY

Received 18 January 2018
Accepted 4 February 2018

KEYWORDS

Photophobia; migraine; headache; functional vision loss

Introduction

Photophobia is defined as pain (in the eye or head) secondary to light exposure.¹ It is a common feature of migraine, reported in up to 80% of migraineurs,² and is a feature of both classical migraine and migraine without aura.³ The neural pathways accounting for photophobia have been proposed to include non-image-forming photosensitive retinal ganglion cells containing melanopsin^{4–6}; and even light responsive pathways independent of the retina and optic nerve.^{7,8} These light responsive pathways enable light to modulate the trigemino-vascular pathway such that bright light increases sensitivity to trigeminal stimuli.^{9,10} Migraineurs seem to have a particular susceptibility to photophobia and this heightened susceptibility persists following a migraine attack and results in a drop in pain perception thresholds following light stimulation.^{10,11} Photophobia forms part of the diagnostic criteria for migraine headache in the international headache classification³ and is increasingly being recognised to have a complex, multi-factorial neural circuitry.^{1,9}

Patients with retro-ocular pain and ipsilateral visual loss are frequently referred to Neuro-ophthalmology clinics with a suspicion of acute unilateral optic neuritis. However, photophobia is

not a symptom of optic neuritis, in which light sensitivity is decreased.¹² In our Neuro-ophthalmology practice in Sheffield (UK), we have become aware of a subset of suspected optic neuritis patients who have a stereotyped set of symptoms and clinical findings, which includes unilateral photophobia, retro-ocular pain, and visual loss with no objective evidence to suggest optic neuritis. The aim of this article is to describe the syndrome, as well as possible treatments, and to explain why we believe that this is likely to represent a migraine type syndrome.

Materials and methods

We carried out a retrospective case-note review of six patients referred to the Neuro-ophthalmology service in Sheffield, UK between 2008 and 2016 who were referred as possible acute unilateral optic neuritis and who presented with unilateral photophobia, ipsilateral retro-ocular pain, and ipsilateral loss of vision. All patients had normal ocular examinations and investigation findings with no objective structural or functional abnormalities identified. Data were collected using a standardised pro-forma.

Results

The mean age for the six patients was 22 (range 16–32) and 5/6 were female. The clinical features are shown in [Tables 1](#) and [2](#). All the patients described their headaches as severe.

None of the patients had any signs of dry eye or ocular inflammation and they had a normal tear film height. They all had a normal cranial nerve examination and no evidence of ptosis or limitation in eye movements. There was no evidence of optic nerve head swelling in any of the patients. Assessment of a relative afferent pupillary defect (RAPD) was usually difficult and unpleasant for the patient due to the photophobia elicited by the swinging light test.

In terms of investigations, five patients had a B-scan to exclude posterior scleritis; four patients underwent neuroimaging (CT, MRI, or MRI/MRV); three patients had an OCT scan (of macula and optic nerve head); and one patient underwent electrodiagnostic testing. None of these investigations provided an explanation for the patients' symptoms and signs.

An attempt was made to wean all the patients off any regular analgesics. Five out of the six patients were treated with migraine prophylaxis. [Table 3](#) describes the recovery of pain and vision seen for the six patients. Pain and vision tended to improve in tandem with each other. Patients 2, 3, and 4 all had full recovery of their pain and vision with varying time courses (see [Table 3](#)). Patient 4 was already on amitriptyline and gabapentin, so the doses of these were increased to treat her headache. Patient 1 had a reduction in headaches to once per week instead of three times per week; her vision remained reduced and it was felt that this may in part be due to amblyopia (she had a significant amount of astigmatic error in this eye ($-1.0, -2.5 \times 13$), with no refractive error in the fellow eye). Patient 5 had an improvement in her symptoms such that she just had occasional pain on eye movements and an improvement of her vision to 6/9, which was close to the 6/7.5 vision recorded by her own optician two years previously. Patient 6 did not experience any improvement of symptoms with amitriptyline. It was therefore decided to wean this off and begin topiramate,

Table 1. Symptoms at presentation.

Pt	Unilateral retro-ocular pain	Ipsilateral photophobia	Ipsilateral loss of vision	Quality of pain	Pain on eye movement	Presence of Nausea	Time-course of headache	Past history of migraine	Symptoms of dry eye/watering/nasal congestion
1	Yes	Yes	Yes	Throbbing	Yes	Yes	6 hours per day, 3 days per week, building up to a constant headache	No	No
2	Yes	Yes	Yes	Throbbing	Yes	Yes	12 hours on 3 days of one week	Yes	No
3	Yes	Yes	Yes	Throbbing	Yes	Yes	6 hours building in intensity and then settling over 72 hours	Yes	No
4	Yes	Yes	Yes	Sharp	No	No	Intermittent headaches on most days lasting for a period of 3–4 hours	Yes	No
5	Yes	Yes	Yes	Sharp	Yes	No	Intense headache for 1 week, improving gradually over a period of months	No	No
6	Yes	Yes	Yes	Sharp	Yes	No	Constant pain	Yes	No

Table 2. Examination findings (VA: visual acuity; ND: not documented; RAPD: relative afferent pupillary defect).

Pt	Presenting best VA symptomatic eye	Presenting VA asymptomatic eye	Ishihara score symptomatic eye	Ishihara score asymptomatic eye	RAPD	External ocular examination
1	6/18	6/6	11/14	ND	No	Normal
2	6/36	6/5	0/21	21/21	No	Normal
3	6/9	6/5	8/17	16/17	No	Normal
4	6/18	6/6	0/14	12/14	No	Normal
5	6/18	6/9	11/11	11/11	No	Normal
6	6/60	6/4	1/17	17/17	No	Normal

Table 3. Follow up, treatment, and recovery.

Pt	Length of follow-up (days)	Migraine prophylaxis given	Recovery of pain	Recovery of vision	Final visual acuity symptomatic eye	Time at which pain and vision both recorded as recovered
1	448	Propranolol/amitriptyline/pizotofen	Partial	No	6/18	
2	40	Amitriptyline	Yes	Yes	6/6–1	28 days
3	21	Amitriptyline	Yes	Yes	6/5	19 days
4	283	Amitriptyline/gabapentin	Yes	Yes	6/6	9 months
5	91	Nil	Partial	Incomplete	6/9	
6	364	Amitriptyline/topiramate	No	No	6/36	

but unfortunately he did not attend for further follow-up after this change in medication. Patient 2 had a further admission with recurrence of her symptoms during pregnancy. The episode followed a similar pattern to her first presentation.

Discussion

We have described a case series of six patients with a stereotyped syndrome of unilateral, retro-ocular pain, and photophobia with associated vision loss but no identifiable ocular or neurological cause. Most patients experienced at least partial recovery of their pain and vision and visual recovery mirrored resolution of pain: patients experiencing full recovery of pain also experienced full recovery of vision.

The prominent photophobia in our patients makes this syndrome symptomatically distinct from optic neuritis, in which light sensitivity is decreased.¹² Furthermore, none of the patients in this series had an RAPD. The syndrome we describe is also distinct from the trigeminal autonomic cephalgias (TACs). These include cluster headache, paroxysmal hemicranias, and hemicrania continua, and whilst patients suffering from the TACs often have prominent photophobia, they also have autonomic dysfunction which manifests as lacrimation, nasal congestion, conjunctival injection, or ptosis.¹³ No patients in this series had any of these autonomic symptoms or signs. Another important negative is that none of our patients here had dry eye symptoms, foreign body sensation, or blepharospasm. This also makes it clinically distinct from photo-oculodysnia syndrome, which is a category of chronic eye pain accompanied by exquisite light sensitivity but without any signs of ocular inflammation.¹⁴

The time course of the headaches varied in this series; but with the exception of patient 6, the headaches lasted between three hours and one week. There was a recurring nature to the headaches in patients 1, 2, and 4. All of the headaches had a unilateral location; three had a pulsating quality and all were severe in intensity. In addition to photophobia, three patients had nausea associated with their headache. These features all point towards a migraine-type headache.³ Digre and Brennan¹ offer a useful diagnostic algorithm for photophobia. In this, after considering neurological, corneal, ocular inflammatory or retinal causes and blepharospasm; migraine should be considered as the cause for the photophobia.

Photophobia is known to be associated with non-organic vision loss.¹⁵ All of the patients in this series had symptoms of visual blurring and presented with reduced visual acuity. We think that this loss of acuity is likely a functional consequence of the headache and photophobia. This is supported by the absence of any RAPD or other subjective structural or functional abnormalities. Furthermore, where the headache and photophobia improved, vision also improved. Patients can be reassured that as the headache improves the vision can also be expected to improve.

The treatment strategy that we used for these patients was to wean off any regular analgesics and then, where appropriate to introduce a preventative headache treatment. Preventative headache treatments included propranolol, amitriptyline, and topiramate.¹⁶

In summary, we describe a triad of photophobia, pain, and visual disturbance that we believe represents a subtype of migraine. Patients should be reassured that their visual acuity should improve with the headache and preventative headache treatments should be considered.

Conflicts of interest

None

Funding

None

References

1. Digre KB, Brennan KC. Shedding light on photophobia. *J Neuroophthalmol.* 2012;32(1):68–81. doi:10.1097/WNO.0b013e3182474548.
2. Choi JY, Oh K, Kim BJ, Chung CS, Koh SB, Park KW. Usefulness of a photophobia questionnaire in patients with migraine. *Cephalalgia.* 2009;29(9):953–959. doi:10.1111/j.1468-2982.2008.01822.x.
3. Headache Classification Committee of the International Headache S. The international classification of headache disorders, 3rd edition (beta version). *Cephalalgia.* 2013;33(9):629–808. doi:10.1177/0333102413485658.
4. Nosedá R, Kainz V, Jakubowski M, et al. A neural mechanism for exacerbation of headache by light. *Nat Neurosci.* 2010;13(2):239–245. doi:10.1038/nn.2475.
5. Nosedá R, Bernstein CA, Nir RR, et al. Migraine photophobia originating in cone-driven retinal pathways. *Brain.* 2016;139(Pt 7):1971–1986. doi:10.1093/brain/aww119.
6. Okamoto K, Tashiro A, Chang Z, Bereiter DA. Bright light activates a trigeminal nociceptive pathway. *Pain.* 2010;149(2):235–242. doi:10.1016/j.pain.2010.02.004.
7. Matynia A, Nguyen E, Sun X, et al. Peripheral sensory neurons expressing melanopsin respond to light. *Front Neural Circuit.* 2016;10:60. doi:10.3389/fncir.2016.00060.
8. Dolgonos S, Ayyala H, Evinger C. Light-induced trigeminal sensitization without central visual pathways: another mechanism for photophobia. *Invest Ophthalm Vis Sci.* 2011;52(11):7852–7858. doi:10.1167/iovs.11-7604.
9. Nosedá R, Burstein R. Advances in understanding the mechanisms of migraine-type photophobia. *Curr Opin Neurol.* 2011;24(3):197–202. doi:10.1097/WCO.0b013e3283466c8e.
10. Kowacs PA, Piovesan EJ, Werneck LC, et al. Influence of intense light stimulation on trigeminal and cervical pain perception thresholds. *Cephalalgia.* 2001;21(3):184–188. doi:10.1046/j.1468-2982.2001.00178.x.
11. Vanagaite J, Pareja JA, Storen O, White LR, Sand T, Stovner LJ. Light-induced discomfort and pain in migraine. *Cephalalgia.* 1997;17(7):733–741. doi:10.1046/j.1468-2982.1997.1707733.x.
12. Barbur JL, Moro S, Harlow JA, Lam BL, Liu M. Comparison of pupil responses to luminance and colour in severe optic neuritis. *Clin Neurophysiol.* 2004;115(11):2650–2658. doi:10.1016/j.clinph.2004.05.022.
13. Irimia P, Cittadini E, Paemeleire K, Cohen AS, Goadsby PJ. Unilateral photophobia or phonophobia in migraine compared with trigeminal autonomic cephalalgias. *Cephalalgia.* 2008;28(6):626–630. doi:10.1111/j.1468-2982.2008.01565.x.
14. Fine PG, Digre KB. A controlled trial of regional sympatholysis in the treatment of photo-oculodysnia syndrome. *J Neuroophthalmol.* 1995;15:90–94.
15. Bengtzen R, Woodward M, Lynn MJ, Newman NJ, Bioussé V. The “sunglasses sign” predicts nonorganic visual loss in neuro-ophthalmologic practice. *Neurology.* 2008;70(3):218–221. doi:10.1212/01.wnl.0000287090.98555.56.
16. Weatherall MW. The diagnosis and treatment of chronic migraine. *Ther Adv Chronic Dis.* 2015;6(3):115–123. doi:10.1177/2040622315579627.