CLINICAL CASE REPORT

Hyperbaric oxygen therapy for perioperative posterior ischemic optic neuropathy: a case report

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ABSTRACT

Purpose: To report the successful treatment of post-operative posterior ischemic optic neuropathy (PION) with hyperbaric oxygen therapy and to review the current literature on the pathogenesis and treatment of PION.

Observations: During an angiographic procedure at a community hospital, an elderly woman had a transient drop in blood pressure after receiving an intravenous dose of hydralazine. During recovery, the patient experienced bilateral vision loss. She was transferred to our specialty referral center for treatment with hyperbaric oxygen. We followed Table 5 in the U.S. Navy Diving Manual, the protocol for decompression sickness. Our patient's vision improved markedly immediately after the first session and continued to improve throughout the course of treatment to its completion. Follow-up ophthalmology visits found the patient's vision to be close to baseline.

Conclusions and importance: PION is a rare condition. It has been difficult to determine a successful therapeutic approach because of the lack of large case-controlled studies. Hyperbaric oxygen has been used to treat other ischemic ophthalmic conditions, but there are only few reports of its use in patients with PION. Systemic steroids and antiplatelet therapy have also been used, with mixed success. In our patient, the combination of hyperbaric oxygen therapy and steroids was successful in restoring vision after postoperative PION.

KEYWORDS: case reports; hyperbaric medicine; hyperbaric oxygen therapy; ischemic optic neuropathies; ophthalmology; optic neuropathy,; post operative visual loss; posterior ischemic optic neuropathy; retinal artery occlusion; vision; visual loss

INTRODUCTION

Ischemic optic neuropathies (IONs) can be divided anatomically into anterior ischemic optic neuropathy (AION) and posterior ischemic optic neuropathy (PION) [1]. Postoperative ION is almost universally a non-arteritic ischemic optic neuropathy (NAION) caused by hemodynamic and vascular factors, as opposed to arteritic ischemic optic neuropathy, a manifestation of giant cell arteritis, a generalized inflammatory disease.

In this article we focus on postoperative NAION. Its estimated overall incidence is 2.3 to 10.2 cases per 100,000 persons older than 50 years of age [2]. PION accounts for less than 10% of all non-post-surgical ION cases [3] but for 67% of cases of postoperative visual loss (POVL) caused by ischemic neuropathies, according to a report by the American Society of Anesthesiologists [4].

Understanding the anatomy of the optic nerve helps in understanding the pathophysiology of the disease. The anterior part of the optic nerve, at the optic disc, is supplied by branches of the posterior ciliary arteries, forming the circle of Zinn-Haller [5]. The posterior part of the nerve is supplied mainly by collaterals from the ophthalmic artery, and by small branches from surrounding arteries – the anterior superior hypophyseal, the anterior cerebral, the anterior communicating, and the anterior ophthalmic arteries [6], receiving no axial supply from the central retinal artery (CRA) that runs in the center of the nerve [7, 8]. Lack of axial supply creates a watershed area in the central part of the posterior optic nerve [7, 8]. This is thought to be the reason why the most common pattern of visual field defects in PION is central, either alone or in combination with other areas of the peripheral visual field [7, 8]. Histopathologic studies have confirmed wide variation in the

the distribution of ischemia when studying cross sections of posterior optic nerves at different distances from the globe [8].

In general, NAION typically presents as acute, painless visual loss of varying degrees. Bilateral loss is more common in postoperative NAION [2]. Physical examination reveals decreased color vision, an altitudinal visual field defect, and a relative afferent pupillary defect (APD), which might be absent in bilateral PION [5]. Optic disc edema is seen only in AION (it is absent in PION). In AION, a congenitally anomalous "crowded" optic nerve is usually present in the unaffected eye, whereas both optic nerves may appear normal in PION. While AION presents with a classic altitudinal visual field defect, a central visual field defect can often be seen in PION.

Perioperative ION presents within several hours to a few days after non-ophthalmic surgery [9,10]. It has been documented most frequently after spinal surgery, radical dissections of the neck, and cardiac procedures [1,4,11]. General risk factors for NAION include hypercholesterolemia, sleep apnea syndrome, atherosclerosis, cardiovascular disease, history of stroke, tobacco use, and use of phosphodiesterase inhibitors such as sildenafil (Viagra) [5, 12]. Procedure-specific risk factors include hypovolemia, hypotensive episodes, and prone positioning [2].

Data regarding the treatment of PION and IONs, in general, are sparse and mainly come from case reports. We found no randomized control trials about the treatment of PION. The most important steps in its treatment are preventive measures and hemodynamic optimization [7, 8]. Prophylactic measures include avoiding hypotension, avoiding hemodilution, minimizing physical pressure on the eyeball, decreasing time of surgery, and limiting time of prone positioning. A few authors have suggested the use of corticosteroids for AION [3,13] but a beneficial effect of steroids for PION has not been documented. Hyperbaric oxygen (HBO_2) therapy has been found to be effective in treating non-arteritic ischemia in central retinal artery occlusion (CRAO) [14,15]. Because of the similarity in the underlying pathophysiology of CRAO and PION, hyperbaric oxygen seems to be a reasonable consideration in the therapeutic strategy for NAION. Bojić described two patients with AION who were treated with HBO_2, suggesting a beneficial outcome [16], but Arnold could see no advantage to HBO_2 treatment for his patient with that type of neuropathy [3]. We found no reports of the use of HBO_2 for the treatment of PION.

Prognosis of PION varies, with different reports predicting poor outcome of this rare disease. However, few papers predicted that early and aggressive treatment with oxygen and steroids could prevent disease progression and deterioration of vision and in some cases restoration of vision if treated early and promptly [2,7].

CASE REPORT

An 82-year-old woman with a history of hypertension, hyperlipidemia, lupus erythematosus, peripheral vein disease (PVD), and subclavian stenosis plus an ocular history of cataract excision was admitted to a community hospital to undergo angiography for the evaluation and treatment of left subclavian stenosis. The vascular surgeon at the transferring hospital reported that the patient experienced a transient drop in blood pressure during the procedure, from a systolic level of 170 to 190 mmHg to 100 mmHg. This change was attributed to administration of a single intravenous dose of hydralazine. A systolic pressure of 100 mmHg does not constitute hypotension, but we believe the drop to this level from our patient's high baseline pressure could have caused decreased perfusion and subsequent hypoxia. Immediately after the procedure, in the recovery unit, the patient complained of profound bilateral vision loss. Her visual acuity was found to be hand motion in both eyes (OU). She had no other focal findings except mild confusion. Emergent consultations from the ophthalmology and neurology teams were obtained. The patient's funduscopic exam was normal. Immediate computed tomography (CT) and magnetic resonance imaging (MRI) studies showed no signs of infarction, hemorrhage, or mass. CT angiography of her head and neck showed patent carotids, with less than 50% occlusion, and normal posterior circulation of the brain. An emergent echocardiogram obtained at the transferring hospital showed an ejection fraction of 60%, with grade 1 diastolic dysfunction. The diagnosis of exclusion was PION. After a phone consultation with the on-call hyperbaric medicine physician, the patient was accepted for transfer to our specialty referral center for emergent HBO_2 therapy.

After we examined the patient, we chose to follow our institutional protocol for CRAO, acknowledging that the mechanism of injury and the rationale for the use of hyperbaric oxygen for that condition and PION are different [15]. The specific treatment table was selected at the bedside based on clinical judgment in an attempt to maximize salvage of the patient's vision. For compression, we followed the algorithm in Table 5 of the U.S.

Navy Diving Manual [17], designed to treat decompression illness. In this algorithm, patients are compressed at a rate of no more than 20 feet/minute until they reach a depth of 2.8 atmospheres absolute (ATA). Upon reaching that depth patients begin two 20-minute intervals of breathing 100% oxygen, with a five-minute air break between them. Patients are then decompressed slowly at a maximum rate of 1 foot/minute until they reach 2.0 ATA. Once they reach that depth, they take a five-minute air break before breathing 100% oxygen for an additional 20 minutes. This is followed by a five-minute air break and then ascend to surface. Total treatment time is 135 minutes.

When the patient arrived at our facility, her examination findings were similar to those stated above, with a visual acuity of hand motion OU (Table 1). It was difficult to perform a full slit-lamp examination (SLE) or a direct funduscopic examination because of the patient's altered mental status. After obtaining consent from the family, the patient was taken for an initial HBO_2 treatment. Concurrently, she was started on intravenous (IV) methylprednisolone, 1 g/day, with the hope of achieving a synergistic effect with HBO_2 therapy, as has been reported for optic nerve injuries [1].

After the first treatment the patient's vision showed immediate improvement, with visual acuity reaching 20/40 OU. Unfortunately, VA exam after the first dive was not documented. Another HBO_2 treatment was administered on the morning of the second day (2.0 ATA for 120 minutes). Repeat ophthalmological examination (Table 1) performed by an attending ophthalmology physician revealed the following in visual acuity :

- right eye (oculus dexter/OD) 20/40;
- left eye (oculus sinister/OS) 20/40+2, showing no improvement with pinhole.

Her pupils were briskly reactive without APD. Maculas were flat, with mild retinal pigment mottling, but no cherry-red spot or edema. Retinal vessels were attenuated in both eyes.

The patient's third and final hyperbaric oxygen session was administered later on the second day of admission. It lasted for 120 minutes at 2.4 ATA. The patient's vision continued to improve after the second and third sessions and approximated her baseline acuity (Table 1). A final ophthalmologic evaluation revealed visual acuity of 20/20 in both eyes, briskly reactive pupils without APD, improvement on Ishihara color plate detection (now 7 of 11 images identified with both eyes), and no color desaturation.

Because of the marked improvement in the patient's vision, HBO_2 was stopped after the third session and she was discharged home, with a scheduled follow-up appointment at a neuro-ophthalmology clinic. At follow-up one week after discharge, examination showed an improvement in visual acuity (Table I). At a second follow-up appointment within a month after discharge the patient's visual acuity was 20/40+2 in her right eye and 20/30 on the left, with no new findings. Her vision returned to levels comparable to baseline and remained there one month after completion of treatment.

DISCUSSION

Treatment of PION is not well studied and documented, mainly because of the low incidence of the disease. To know what treatment options are beneficial we need to understand its underlying pathophysiology. The posterior part of the optic nerve has a very complex system of blood supply, with collaterals from multiple major arteries (Figure 1). Because of this intricate blood supply, the posterior segment is hypothesized to contain watershed areas, making the posterior segment of the optic nerve prone to hypoperfusion and ischemia [7, 8].

A variety of factors can affect optic nerve perfusion: arterial autoregulation; venous stasis; increased intraocular pressure during surgery, caused by orbital edema or mechanical pressure on the eye; and decreased arterial perfusion related to transient hypotension, hemodilution, or blood loss [1, 11, 18]. Because of the lack of adequate histopathologic evidence, it is difficult to determine if perioperative PION is caused mainly by an arterial or a venous insult [11]. In either case, the underlying pathophysiology of PION is thought to be ischemic in nature [2] and would naturally follow the ischemia and reperfusion (IR) injury pattern.

The first recommended line of treatment of PION is the identification of risk factors and the prevention of intraoperative events that might lead to this condition. Those events include any drop in blood pressure during surgery, hypovolemia, and prolonged surgeries that might cause edema to the optic nerve, especially in the prone position. In our case, we suspect that the drop in blood pressure from the patient's baseline level to 100 mmHg, although considered normal for other patients, led to a decrease in blood flow to the posterior optic nerve area.

Once loss of vision has occurred and is detected, immediate treatment with high-flow oxygen is warranted, given that the differential diagnosis for sudden-onset visual loss includes vision-threatening disorders such

Table 1. Summary of ophthalmologic exam findings during the treatment course

	Initial Exam	**After Second HBO_2 Treatment**	**After Third HBO_2 Treatment**	**One Week After discharge**	**One Month** After Discharge
Visual acuity	Hand motion OU	OD: 20/40, no improvement with pinhole OS: 20/40+2, no improvement with pinhole	20/20 OU OS: 20/30	20/25 OU	OD: 20/40+2
Extraocular movement		Full OU	Full OU	Full OU	Full OU Full OU
Alignment	–	Ortho in primary gaze	Ortho in primary gaze	Ortho in primary gaze	Ortho in primary gaze
Pupils	–	2.5 to 1.5 and brisk OU	3 to 2 and and brisk OU	Equally round, reactive to light	Equally round, reactive to light
Afferent pupillary defect	–	Not present OU	Not present OU	Not present OU	Not present OU
Tonometry	–	–	–	20 OU	OD 20 OS 21
Ishihara test	–	OD: 5/11 OS: 1/11	7/11 OU	–	-
Color desaturation	–	OD: 50%	None	–	-
SLIT LAMP/PENLIGHT EXAM					
External/lids	-	Lashes dry Periorbital skin OU Poliosis OU	Lashes dry Periorbital skin OU Poliosis OU	Brow ptosis OU Dermatochalasis of upper lids	Normal OU
Conjunctiva/sclera	–	White and quiet OU	White and quiet OU	Injected OU	White and quiet OU
Cornea	–	Clear/arcus OU	Clear/arcus OU	Clear OU	Clear OU
Anterior chamber	–	Deep and quiet OU	Deep and quiet OU	Deep and quiet OU	Deep and quiet OU
Iris	–	Regular, round, reactive OU	Regular, round, reactive OU	Regular, round, reactive OU	Regular, round, reactive OU
Lens	–	Posterior chamber intraocular lens OU	Posterior chamber intraocular lens OU	Posterior chamber intraocular lens OU	Posterior chamber intraocular lens OU
Vitreous	–	–	–	Clear OU	-
DILATED FUNDUS EXAM					
Disc	–	Sharp margins OU Mild PPA OS>OD No pallor or disc edema OU	-	Disc without pallor OU	-
Cup/desk ratio	–	–	–	0.35 without pallor OU	-
Macula	–	Flat/pigmentary mottling OU	–	Decreased foveal reflex OU	-
Vessels	–	Attenuated OU	–	Arterial attenuation OU	-
Periphery	–	No holes/tears/intra-retinal hemorrhage/CWS OU	–	No holes or tears OU	-

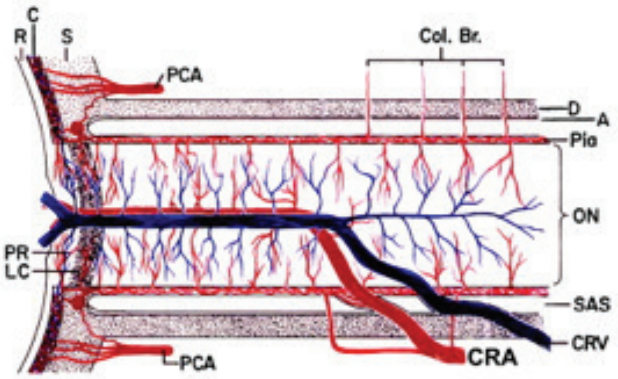

Figure 1: Optic nerve blood supply.
A, arachnoid; C, choroid; CRA, central retinal artery; Col. Br., collateral branches; CRV, central retinal vein; D, dura; LC, lamina cribrosa; ON, optic nerve; P, pia; PCA, posterior ciliary artery; PR, prelaminar region; R, retina; S, sclera; SAS, subarachnoid space. (Used with permission from Hayreh 2009 [8]).

as CRAO. Whenever CRAO is suspected, it is standard to treat patients immediately with normobaric oxygen. Murphy-Lavoie and colleagues [15] recommended treating suspected CRAO patients immediately with high-flow oxygen while waiting for HBO_2 therapy. Butler and associates [21] also suggested that, due to the time sensitivity of this disease and its sequelae, any patient presenting with sudden vision loss and suspected CRAO should be started immediately on high-flow oxygen and then HBO_2 if the symptoms do not resolve. They found that the response to treatment was best when treatment was started within 24 hours after the onset of symptoms. They categorized PION as one of the entities that can benefit from HBO_2 due to the similarities in the pathophysiologic processes of PION and CRAO.

HBO_2 for CRAO is part of the treatment recommended by the Hyperbaric Committee of the Undersea and Hyperbaric Medical Society (UHMS) [21]. In some studies, it was effective therapy for CRAO when initiated early [15, 22-25]. Due to its importance, HBO_2 was considered by the American Heart Association to be effective therapy, with a level IIb evidence for efficacy [15]. In a retrospective chart review, HBO_2 was most beneficial when initiated within eight hours after the onset of CRAO symptoms and showed varying degrees of success when initiated later than eight hours after onset [22]. Nonetheless, patients should be considered for HBO_2 if they present within 24 hours after symptom onset, as some reports showed some benefit when treated within this period [15].

No large-scale studies have been conducted to test the true effect of HBO_2 on the resolution of PION, especially when it is treated early, and we found no reports of hyperbaric oxygen used specifically as a treatment for postoperative PION. Case reports on the use of HBO_2 for other NAIONs vary in their results. Bojić, et al. [16] concluded that HBO_2 was successful in the resolution of AION in two patients who did not respond to prednisone therapy alone. Beran and colleagues suggested that treatment of ION consist of early detection and reversal of causes but did not mention hyperbaric oxygen as a treatment; however, they did recommend it as a treatment for CRAO [26]. Kitaba and colleagues [18] suggested HBO_2 for perioperative PION. Grover and coworkers [10] suggested HBO_2 therapy for IONs but commented that its efficacy is not proven. Arnold, et al. [3], on the other hand, saw no benefit of the treatment. However, it is important to mention that timing is essential for therapy. Butler and associates [21] suggested that the unfavorable result in Arnold's observation might have been due to delay in treatment and that earlier treatment (within 72 hours after onset) would give more favorable results. Several clinical review articles expressed skepticism toward the use of hyperbaric oxygen for ocular ischemic events based on its lack of sustainable effect [3, 12, 15]. Most patients improve while being actively treated but then revert to their initial visual loss immediately afterward. Those articles, however, did not address the importance of early initiation of treatment and follow-up care.

On a molecular level ischemia triggers a complex cascade on the cellular level. Its main effect is adhesion of polymorphonuclear cells (PMNs) to the surrounding endothelial cells (ECs) through activation of cell adhesion molecules (CAMs) and other factors [19]. CAMs also cause PMNs to migrate distally along the vascular wall through diapedesis [19]. On a nuclear level ischemia affects injured cells directly and their adjacent cells indirectly by promoting apoptosis through the regulation of gene expression. Cell injury has a direct effect on the proapoptotic protein bax. Upregulation of bax leads to an increase in the expression of caspase-3 and other caspases, resulting in full activation of the apoptosis cascade and, eventually, cell death. This pattern has been found in retinal ganglionic cell layers after IR injury in humans and rats [20].

It has been proposed that hyperbaric oxygen reduces the adhesion of PMNs to injured endothelium by increasing the partial oxygen pressure and decreasing the PMN adhesion process by enhancing the release of nitric oxide (NO) [19]. Subsequently, NO prevents PMN adhesion to ECs by suppressing the intracellular expression of P-selectin and other CAMs [19]. On the other hand, HBO_2 is significantly related to the downregulation of proapoptosis proteins (bax and Caspase-3) and upregulation of anti-apoptotic proteins (bcl-2 and bcl-xL) in ischemic tissues, making it a candidate for treatment of diseases such as CRAO and ION [27].

Given the similarities in the pathophysiologic process between CRAO and ION and the evidence of success in treatment of CRAO with hyperbaric oxygen both clinically and on the cellular and nuclear levels, we presume that the hyperbaric oxygen protocol used for CRAO will have beneficial effects on patients with ION. This approach is supported by Butler and colleagues in their extensive review of the use of HBO_2 therapy in perioperative visual loss cases [21]. They recommend early oxygen administration and HBO_2 for patients with acute visual loss, in whom CRAO and IONs are part of the differential diagnosis. In our patient, application of the CRAO protocol in conjunction with intravenous administration of steroids was effective in the treatment of PION, resulting in a clinically significant and sustained recovery of vision. This successful outcome suggests that treatment protocols should be reconsidered to achieve more consistent responses.

CONCLUSIONS

Initiation of HBO_2 therapy within a few hours after the onset of PION symptoms could be beneficial in saving patients' vision. Medical treatment might be necessary to produce a sustained effect. Additional studies should be conducted to test this approach.

Conflict of interest statement
The authors have declared that no conflict of interest exists with this submission.

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