Ocular ischemic syndrome: recent trends in medical management

Ribhi Hazin[a], Yassine J. Daoud[b] and Faisal Khan[c]

[a]Harvard University, Faculty of Arts & Sciences, Cambridge, Massachusetts, USA, [b]Duke University Eye Center and [c]Division of Neurology, Duke University Medical Center, Durham, North Carolina, USA

Correspondence to Faisal Khan, MD, Neurodiagnostic and Sleep Center, Gulf Coast Medical Center, 10119 US 59 Road, Wharton, TX 77488-7224, USA
e-mail: fskhan786@gmail.com

Current Opinion in Ophthalmology 2009, 20:000–000

Purpose of review

To summarize general concepts of ocular ischemic syndrome (OIS), and present current scientific developments in delineating the pathogenesis and treatment of this disorder.

Recent findings

Recent studies suggest that OIS is associated with a significant risk of cerebrovascular, ocular, and systemic morbidity.

Summary

OIS is a serious blinding condition that occurs in the setting of carotid artery occlusion. Restoration of arterial perfusion and early diagnosis are critical for preserving visual function and reducing the risk of devastating ocular complications.

Keywords

carotid artery occlusion, neovascularization, ocular ischemic syndrome, retina cerebrovascular disease

Curr Opin Ophthalmol 20:000–000

1040-8738

Introduction

Ocular ischemic syndrome (OIS) is a potentially blinding disorder that arises in the setting of arterial hypoperfusion of the eye [1]. OIS most commonly results from hemodynamically significant internal carotid artery occlusion [1,2]. The ophthalmic artery is the first branch of the carotid artery and the primary arterial source of the eye. Therefore, any occlusion of the carotid artery via stenosis or obstruction can catalyze ocular hypoperfusion and, as a result, OIS [1,3,4]. Fortunately, if recognized early the effects of OIS may be reversible. Notwithstanding, this condition is highly underdiagnosed. Given the association with serious systemic diseases, failure to promptly recognize and appropriately treat OIS can result in serious consequences for those afflicted with the disease [5–8].

Complications of OIS are as follows (modified from [4,8]):

(1) Neovascular glaucoma
(2) Corneal decompensation
(3) Ocular hypotony
(4) Maculopathy
(5) Cataract formation.

Recent studies demonstrate a 5-year mortality as high as 40% in patients diagnosed with OIS [5]. The most common causes of death in patients with OIS are cardiac disease and stroke [5]. Carotid artery dissection has also been reported as a cause of mortality in OIS patients [1,6]. Ocular sequelae in patients with OIS, although not life-threatening, represent important sources of morbidity and may cause severe vision loss [2,5,7].

Clinical manifestations

Patients with OIS often present with eye pain and decreased visual acuity [1,3]. Most patients complain of gradual loss of vision, however, sudden blindness can occur in severe cases [3,8]. Patients may also complain of recent episodes of transient visual loss (amaurosis fugax) or symptoms associated with transient ischemic attacks such as loss of consciousness, paresthesias, temporary aphasia, or weakness [8,9]. Rarely, OIS may arise in the setting of giant cell arteritis but this association remains rare [10,11].

Common retinal findings in OIS are as follows (modified from [3,8,9]):

(1) Mid-peripheral dot and blot hemorrhages
(2) Cotton-wool spots
(3) Microaneurysms
(4) Neovascularizations
(5) Exudates
(6) Macular edema
(7) Dilatation of retinal veins.

Chronic involvement of associated arterial vessels may also yield serious deformation of ocular structures in the form of cataracts, macular edema, dilatation of retinal veins, dot hemorrhages, neovascularization of the retina, cotton wool spots, and exudates [2,3,10,12]. Furthermore, intractable glaucoma may ensue in patients with OIS as a

 DOI:10.1097/ICU.0b013e3283313d38

result of increased intraocular pressure (IOP) secondary to obstruction of aqueous humor flow that can occur with neovascularization of the iris [8,13,14]. This form of glaucoma, referred to as neovascular glaucoma (NVG), can be a source of both morbidity and irreversible visual loss in patients with OIS [14]. NVG may account for the eye pain that commonly accompanies OIS, however, the widespread ischemia and inflammation that characterizes the disease may also account for this finding in some cases [3,14]. In addition, patients with chronic OIS are also at increased risk of developing central retinal artery occlusion (CRAO) that may significantly undermine visual processes [15].

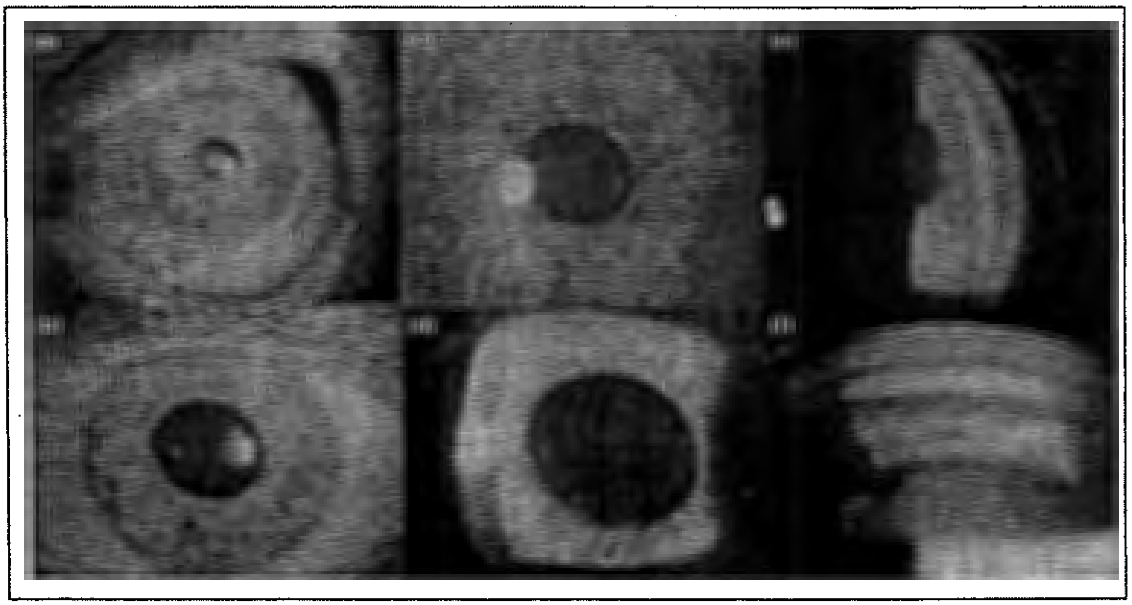
In instances of OIS in which severe hypoperfusion of vital ocular structures such as the ciliary body occurs, ocular hypotony can arise [6,9]. Critically low IOPs can exacerbate OIS symptoms insofar as the low pressures accelerate cataract formation and maculopathy [9,16]. Further, patients with ocular hypotony are at increased risk of developing corneal decompensation, which is associated with persistent disturbances in vision and may lead to near blindness [17]. Although asymptomatic OIS has been reported, the preponderance of cases present with one or more of the aforementioned clinical findings [3,8,9].

On examination of patients with OIS, typical findings include unilateral or bilateral decrease in visual acuity [18]. Slit-lamp and ophthalmoscopic examination may also reveal conjunctival hyperemia, prominent conjunctival vessels, and anterior chamber inflammation. Fundus exam may reveal cotton-wool spots, retinal hemorrhages, microaneurysms, mid-peripheral dot and blot hemorrhages, as well as posterior segment neovascularization (Fig. 1) [2,3,10,12]. A recent study found that 80% of OIS patients demonstrate retinal hemorrhages, whereas only 37% reveal signs of neovascularization [5]. It has been suggested that the hemorrhages seen in OIS are secondary to microaneurysms and neovascularization [5]. The new vessels that arise via neovascularization and microaneurysms tend to be increasingly friable and prone to hemorrhage [7]. Fluorescein angiography in affected eyes of patients with OIS commonly reveals delayed retinal and choroidal filling [7]. Ophthalmodynamometry may reveal decreased central retinal artery perfusion pressure and electroretinography may demonstrate decreased amplitude of both '*a*' and '*b*' waves [7].

Epidemiology

OIS most commonly afflicts the elderly with a mean age of approximately 64 years [7]. OIS has a predilection for men in whom the disorder occurs twice as commonly as in women [7]. Incidentally, most patients with OIS have a history of hypertension, diabetes, ischemic heart disease, or other known systemic diseases [1,5]. A recent study

Figure 1 Ocular features of OIS



Pictures of OIS before (a,c,e) and after (b,d,e) one intraocular injection of avastin (bevacizumab), an anti-vascular endothelial growth factor (VEGF) agent. Hallmarks of OIS include conjunctival injection (a) neovascularization of the iris; (c) secondary to ischemia and increased production of VEGF. On gonioscopy, occlusion and neovascularization of the angle is evident. After one intraocular injection of bevacizumab and pan-retinal laser photocoagulation, resolution of conjunctival injection and regression of neovascularization of the iris can be observed (b and d). On gonioscopy, regression of the neovascularization with remaining peripheral synechiae is noted.

Conclusion

OIS is an underdiagnosed cause of visual loss and blindness among elderly populations. It is also a significant cause of vision morbidity in the elderly population. The predominant cause is occlusive disease affecting the internal carotid artery. Serious vision-threatening complications associated with OIS include cataract formation, maculopathy, corneal decompensation, neovascularization, and NVG. The leading cause of death is cardiac disease and stroke. Therapeutic intervention should involve appropriately addressing underlying arterial hypoperfusion with concomitant treatment of ophthalmic lesions.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

1 Takaki Y, Nagata M, Shinoda K, *et al.* Severe acute ocular ischemia associated with spontaneous internal carotid artery dissection. Int Ophthalmol 2008; 28:447–449.

2 Foncea Beti N, Mateo I, Diaz La Calle V, *et al.* The ocular ischemic syndrome. Clin Neurol Neurosurg 2003; 106:60–62.

3 Amselem L, Montero J, Diaz-Llopis M, *et al.* Intravitreal bevacizumab (Avastin) injection in ocular ischemic syndrome. Am J Ophthalmol 2007; 144:122–124.

4 Chen CS, Miller NR. Ocular ischemic syndrome: review of clinical presentations, etiology, investigation, and management. Compr Ophthalmol Update 2007; 8:17–28.

5 Sivalingam A, Brown GC, Magargal LE, Menduke H. The ocular ischemic syndrome II. Mortality and systemic morbidity. Int Ophthalmol 1989; 13:187–191.

6 Furino C, Guerriero S, Boscia F, *et al.* In vivo evidence of hypotrophic ciliary body in ocular ischemic syndrome by ultrasound biomicroscopy. Ophthalmic Surg Lasers Imaging 2007; 38:505–507.

7 Takaki Y, Nagata M, Shinoda K, *et al.* Severe acute ocular ischemia associated with spontaneous internal carotid artery dissection. Int Ophthalmol 2008; 28:447–449.

8 Ros MA, Magargal LE, Hedges TR Jr, Simeone FA. Ocular ischemic syndrome: long-term ocular complications. Ann Ophthalmol 1987; 19:270–272.

9 Winterkorn JM, Beckman RL. Recovery from ocular ischemic syndrome after treatment with verapamil. J Neuroophthalmol 1995; 15:209–211.

10 Koz OG, Ates A, Numan Alp M, *et al.* Bilateral ocular ischemic syndrome as an initial manifestation of Takayasu's arteritis associated with carotid steal syndrome. Rheumatol Int 2007; 27:299–302.

11 Casson RJ, Fleming FK, Shaikh A, James B. Bilateral ocular ischemic syndrome secondary to giant cell arteritis. Arch Ophthalmol 2001; 119:306–307.

12 Schmidt D. The mystery of cotton-wool spots: a review of recent and historical descriptions. Eur J Med Res 2008; 13:231–266.

13 Mizener JB, Podhajsky P, Hayreh SS. Ocular ischemic syndrome. Ophthalmology 1997; 104:859–864.

14 Hayreh SS. Neovascular glaucoma. Prog Retin Eye Res 2007; 26:470–485.

15 Hazin R, Dixon JA, Bhatti MT. Thrombolytic therapy in central retinal artery occlusion: cutting edge therapy, standard of care therapy, or impractical therapy? Curr Opin Ophthalmol 2009; 20:210–218.

16 Gupta OP, Weichel ED, Regillo CD, *et al.* Postoperative complications associated with 25-gauge pars plana vitrectomy. Ophthalmic Surg Lasers Imaging 2007; 38:270–275.

17 Ehlers N, Hjortdal J. Riboflavin-ultraviolet light induced cross-linking in endothelial decompensation. Acta Ophthalmol 2008; 86:549–551.

18 Morales J, Corona J, Langford JD, *et al.* Bilateral decreased vision and cotton-wool spots in a 42-year-old man. Surv Ophthalmol 2002; 47:257–262.

19 Kawaguchi S, Sakaki T, Iwahashi H, *et al.* Effect of carotid artery stenting on ocular circulation and chronic ocular ischemic syndrome. Cerebrovasc Dis 2006; 22:402–408.

20 Alizai AM, Trobe JD, Thompson BG, *et al.* Ocular ischemic syndrome after occlusion of both external carotid arteries. J Neuroophthalmol 2005; 25:268–272.

21 Lavinsky D, Artemi NS, Achaval M, Netto CA. Chronic bilateral common carotid artery occlusion: a model for ocular ischemic syndrome in the rat. Graefes Arch Clin Exp Ophthalmol 2006; 244:199–204.

22 Marx JL, Hreib K, Choi IS, *et al.* Percutaneous carotid artery angioplasty and stenting for ocular ischemic syndrome. Ophthalmology 2004; 111:2284–2291.

23 Josifova T, Schneider U, Henrich PB, Schrader W. Eye disorders in diabetes: potential drug targets. Infect Disord Drug Targets 2008; 8:70–75.

24 Pokhrel PK, Loftus SA. Ocular emergencies. Am Fam Physician 2007; 76:829–836.

25 • Wakabayashi T, Oshima Y, Sakaguchi H, *et al.* Intravitreal bevacizumab to treat iris neovascularization and neovascular glaucoma secondary to ischemic retinal diseases in 41 consecutive cases. Ophthalmology 2008; 115:1571–1580; 1580.e1-3.

This study involving 30 patients (41 eyes) demonstrated that intravitreal bevacizumab represents a tolerable and effective therapy in the treatment of ocular complications of ischemic retinal diseases.

26 Rassam SM, Patel V, Kohner EM. The effect of acetazolamide on the retinal circulation. Eye 1993; 7:697–702.

27 Mazlumzadeh M, Hunder GG, Easley KA, *et al.* Treatment of giant cell arteritis using induction therapy with high-dose glucocorticoids: a double-blind, placebo-controlled, randomized prospective clinical trial. Arthritis Rheum 2006; 54:3310–3318.

28 Batioğlu F, Astam N, Ozmert E. Rapid improvement of retinal and iris neovascularization after a single intravitreal bevacizumab injection in a patient with central retinal vein occlusion and neovascular glaucoma. Int Ophthalmol 2008; 28:59–61.

29 McIntosh RL, Mohamed Q, Saw SM, Wong TY. Interventions for branch retinal vein occlusion: an evidence-based systematic review. Ophthalmology 2007; 114:835–854.

30 Gheith ME, Siam GA, de Barros DS, *et al.* Role of intravitreal bevacizumab in neovascular glaucoma. J Ocul Pharmacol Ther 2007; 23:487–491.