Ocular ischemic syndrome: recent trends in medical management
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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 cause 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, paresis, 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 result of secondary elevation of intraocular pressure due to chronic hypoperfusion of the eye.
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 fragile 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

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**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 hyperfusion 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 (pp. 000–000).

This study involving 39 patients (41 eyes) demonstrated that intravitreal bevacizumab represents a tolerable and effective therapy in the treatment of ocular complications of ischemic retinal diseases.