

## Ocular ischaemic syndrome

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Ocular ischaemic syndrome is a rare condition. It often results in blindness and is linked to serious systemic morbidity. Its presentation is usually subtle and it can be misdiagnosed due to its diverse signs and symptoms. A case of ocular ischaemic syndrome is presented and current diagnostic procedures and treatment described. Recognition by the clinician is important because of the severe ocular and potential systemic sequelae. (*Clin Exp Optom* 2000; 83: 4: 212–221)

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Ocular ischaemic syndrome (OIS) is an uncommonly reported, serious blinding condition, first described by Knox in 1965.<sup>1</sup> It is often misdiagnosed because of its diverse and sometimes subtle presentation.<sup>2</sup> Sturrock and Miller<sup>3</sup> estimated the incidence to be 7.5 cases per million persons per year, based on only six cases over a two-year period in a large hospital setting. However, the exact frequency is unknown and previous reports may underestimate the incidence, when one considers the various ocular disorders that have similar presentations.

### CASE REPORT

A 71-year-old Caucasian male presented for optometric examination, complaining of sore, dry eyes and a gradual reduction

in distance and near acuity. He had no other presenting complaints. His previous eye examination had been two years earlier. He had a history of head trauma 30 years earlier, which is believed to have resulted in static right optic atrophy. He suffered from severe occlusive carotid artery disease (OCAD) with previous endarterectomy of the right internal carotid artery (ICA) two months before the present examination. The left ICA was reported to be completely blocked and inoperable. There was no history of diabetes.

Visual acuities were R 6/24 with +1.25/-0.75x75 and L 6/12 with +1.25/0.25x110. There was no improvement with pinhole (NIPH). A +3.00 D near addition enabled N5 print to be read at 33 cm. At optometric examinations two and four years previously, visual acuities were recorded as

R 6/15 = (NIPH) and L 6/4.8. Previous automated visual fields demonstrated a dense temporal defect of the right eye (Figure 1). There was also a right relative afferent pupillary defect. Slitlamp examination revealed moderate signs of dry eye with a reduced tear break-up time and inferior and diffuse sodium-fluorescein and Rose Bengal staining. Non-preserved tear supplements were suggested. The ocular media were clear, but trace left iris neovascularisation was noted. Dilated ocular fundus examination revealed a pale and atrophic right optic disc. In the left posterior pole, focal and general arteriole attenuation was noted. Scattered small blot retinal haemorrhages were also noted in all four quadrants (Figure 2). Intraocular pressures (IOP) were R 9 mmHg and L 9 mmHg measured with Perkins

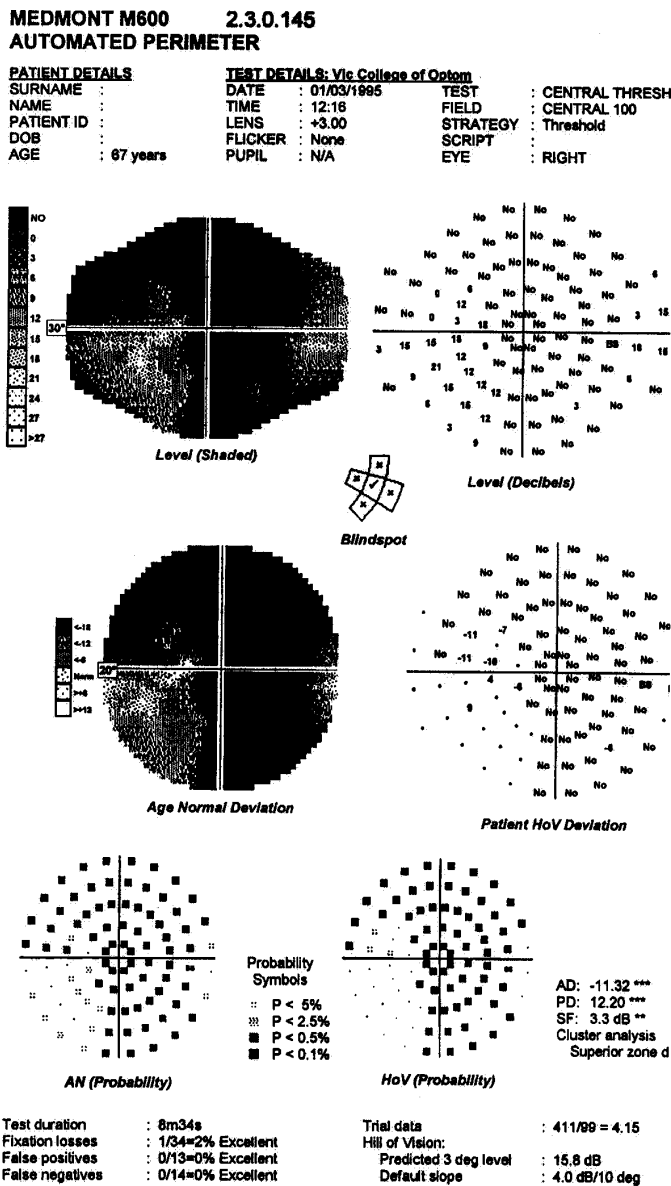


Figure 1. Right visual field as a result of optic atrophy

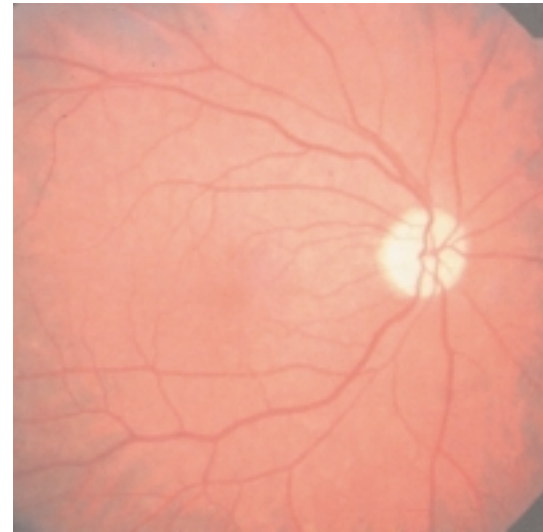


Figure 2a. Right fundus with pale atrophic disc

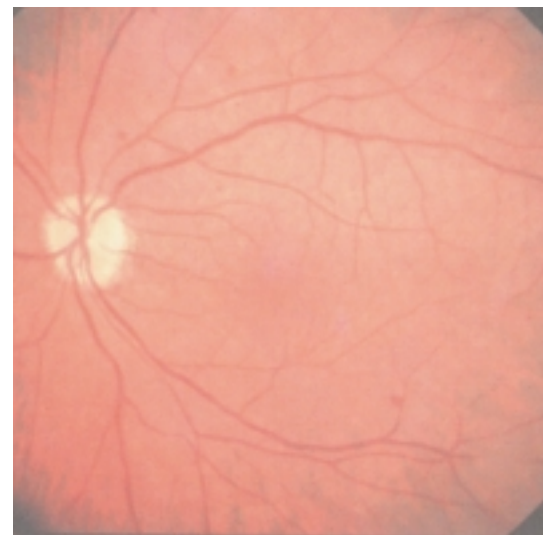


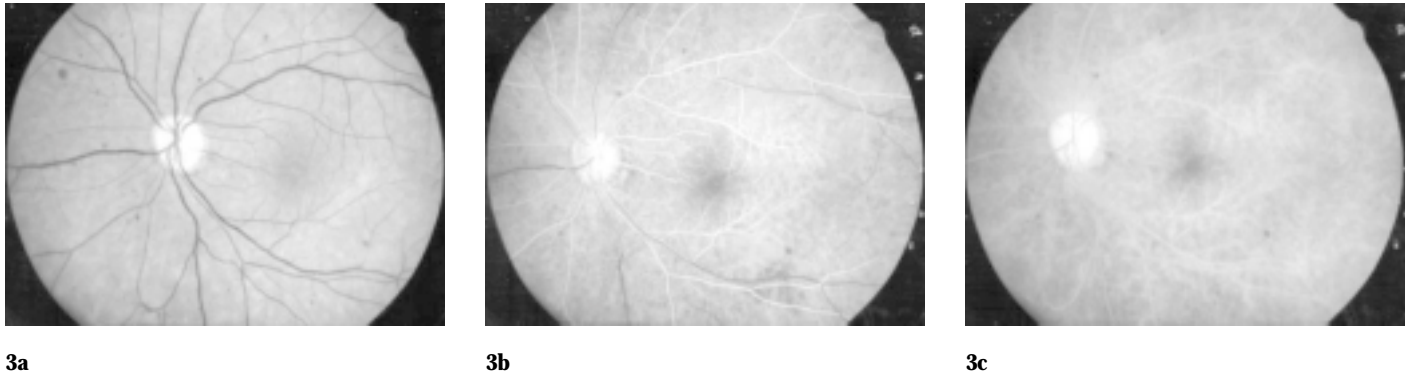
Figure 2b. Left fundus with blot intraretinal haemorrhages in the mid-periphery

tonometry. Ophthalmological referral confirmed OIS. Fluorescein angiography (FA) indicated a pathologically delayed circulation time for the left eye, suggestive of OIS. Dye arrival in the left eye was at 28 seconds post-injection and the photoprint (Figure 3) was from 50 seconds, at which time there was still incomplete filling of the retinal veins and the choroid. Normal arterio-venous transit

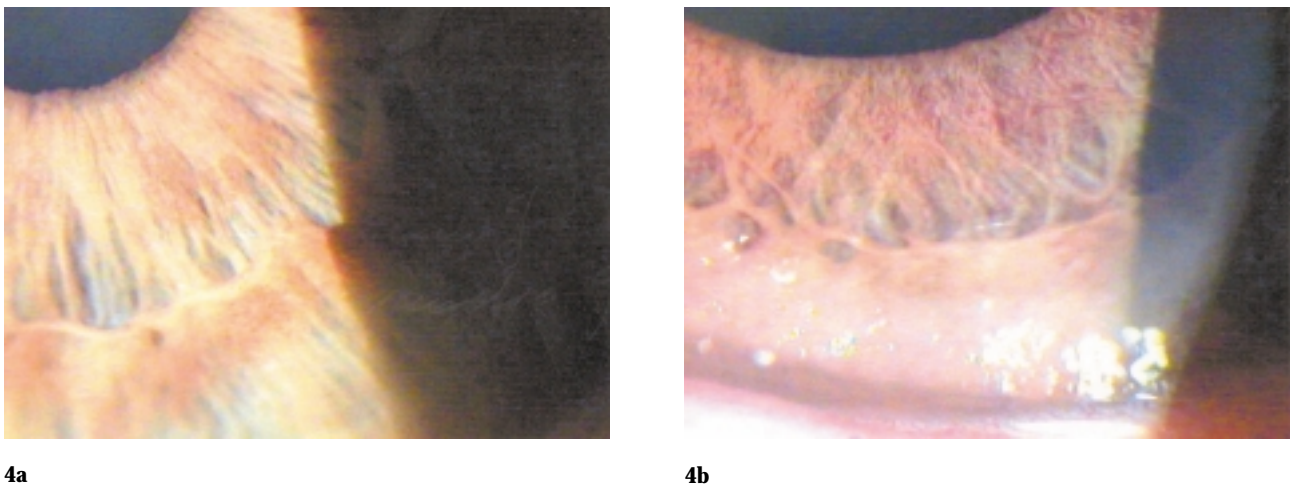
time is approximately 11 seconds.<sup>4</sup> In the late photographs, there was leakage from retinal arterioles in the left eye and some optic disc staining. The right eye appeared comparatively normal. The patient subsequently underwent panretinal photocoagulation (PRP) in the left eye.

The patient returned three months after the initial examination with broken spectacles. At review, visual acuities were

R 6/12 = (NIPH) with +1.00/-1.00x75 and L hand movements at one metre. A +6.00 D near addition enabled N6 print to be read at 16 cm in focal light. Contrast sensitivity was markedly reduced to nine decibels with the Melbourne Edge Test. Slitlamp examination revealed marked left iris neovascularisation (Figure 4), conjunctival hyperaemia and chemosis. The recent deterioration in the



**Figure 3. Fluorescein angiography of the left fundus. Dye arrival in the left eye was at 28 seconds and the photo print was from 50 seconds (b), at which time there was still incomplete filling of the retinal veins and the choroid. In the late photograph (c) there was leakage from retinal arterioles and some optic disc staining.**



**Figure 4. A comparison of the right iris (a) and the left iris with iris neovascularisation (b)**

left visual status of the patient described in this case may relate to further compromise of collateral circulation derived via the external carotid branches. IOPs at review were R 11 mmHg and L 24 mmHg measured with Perkins tonometry. The patient was receiving continuing ophthalmological care and undergoing further PRP. After referral to a low vision clinic, the patient reported receiving multidis-

ciplinary support with occupational therapy, orthoptist support and orientation and mobility instruction.

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## DISCUSSION

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### Presentation

The average age of OIS presentation has been reported to be approximately 64

years, with a range of 50 to 80 years.<sup>4</sup> However, OIS has been reported in a child as young as 19 months with moyamoya disease. This condition is characterised by cerebral ischaemia due to occlusion of arteries within the circle of Willis, resulting in neurological disability and neurofibromatosis.<sup>5</sup> The majority of cases (80 per cent) are unilateral,<sup>6</sup> with a higher incidence (67 to 71 per cent) reported in

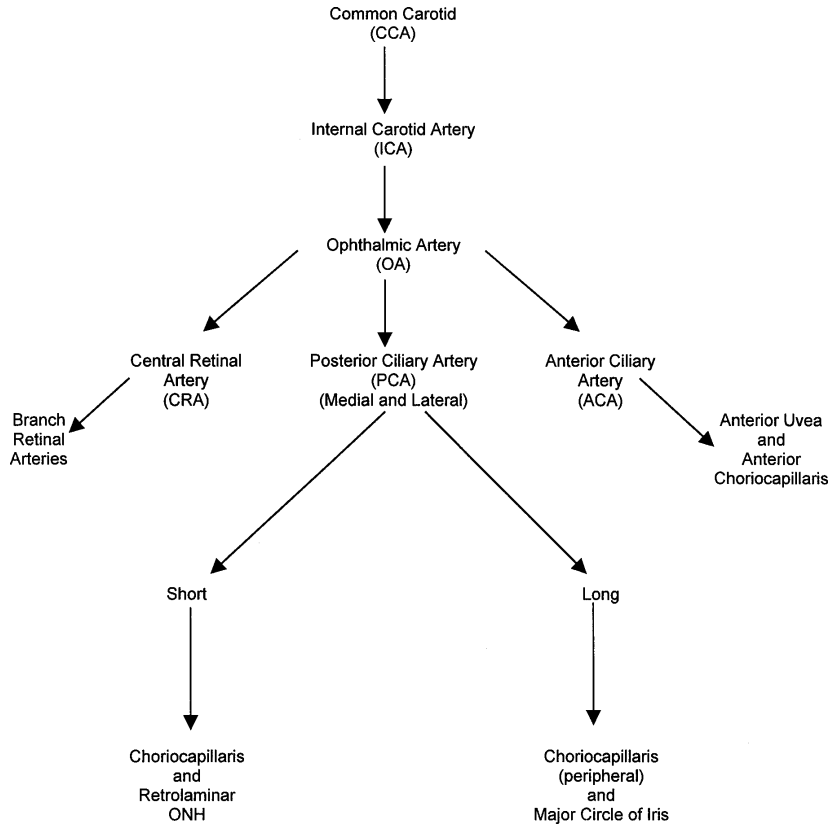
Associated systemic condition	Frequency %
Systemic arterial hypertension	50-73
Diabetes mellitus	44-56
Ischaemic heart disease	48
Cerebrovascular accident	24
Peripheral vascular disease	19

**Table 1. The principle systemic associations of OIS** <sup>2,4,7</sup>

males.<sup>4,6,7</sup> No racial predilection has been identified.<sup>6</sup>

Systemic diseases associated with OIS are detailed in Table 1. One study found that the incidence of diabetes was greater in their sample of OIS patients relative to the general population, suggesting that small vessel disease in the presence of large vessel disease may increase the risk of OIS.<sup>2</sup> To a lesser extent, OIS may manifest as a result of giant cell arteritis.<sup>8</sup> OIS has also been reported in patients with Eisenmenger's syndrome,<sup>9</sup> which consists of pulmonary hypertension due to long-standing congenital heart disease.

Angiographic evaluation of the carotid system typically discloses a 90 per cent or greater obstruction of the ipsilateral ICA or common carotid artery (CCA) in persons with OIS.<sup>4</sup> One study showed that almost 50 per cent of patients with OIS had evidence of ischaemic heart disease, while approximately another 25 per cent had a history of a cardiovascular accident (CVA) at presentation.<sup>7</sup> However, despite the presence of severe OCAD, the primary cause of death in persons with the OIS appears to be cardiac disease (63 per cent), followed by CVA (19 per cent). The five-year mortality rate in persons with OIS has been reported to be 40 per cent as compared to 11 per cent for age-matched normals.<sup>7</sup> The severe atherosclerosis is often generalised and the ischaemic damage additionally affects other major organs such as the heart, brain and kidneys, accounting for the high mortality rate.<sup>7</sup>



**Figure 5. Normal ocular blood supply**

**Aetiology**

The normal ocular blood supply is shown in Figure 5. The most common causes of OIS include stenosis, thromboembolism and vasculitis of the carotid artery or ophthalmic artery (OA).<sup>10</sup> A dissecting aneurysm of the carotid artery has also been reported as a cause.<sup>11</sup> Atherosclerotic degenerative changes are the primary aetiology of carotid disease, with the bifurcation of the CCA into the ICA and external carotid artery (ECA) being particularly prone to build-up of fibrofatty atheromatous plaques.<sup>12</sup> The subsequent neurologic manifestations may be embolic in nature, or caused by a haemodynamic insufficiency from progressive stenosis of the vessel lumen.<sup>13</sup> As the OA is one of the first branches of the ICA in the neck, ocular symptoms are often the first indication of vascular insufficiency.<sup>13</sup> Predicting the

risk of ocular ischaemic complications from carotid disease is difficult, in part because the collateral system between the ECA and ICA is complex. It has been shown that with ICA obstruction, flow may occur to the ipsilateral brain via retrograde flow from the ECA.<sup>14</sup>

Between four and 18 per cent of patients with ICA occlusion develop ocular ischaemia.<sup>3</sup> The time course is highly variable.<sup>15</sup> In one study, the minimal ICA or CCA obstruction was 80 per cent in unilateral cases.<sup>4</sup> In addition, it has been shown that 80 to 90 per cent stenosis of the ipsilateral ICA is necessary for marked lowering of the retinal arterial perfusion pressure to become apparent. It is estimated that 90 per cent stenosis of the ICA reduces the CRA pressure by at least 50 per cent.<sup>16</sup> Between five and nine per cent of patients with severe bilateral carotid stenosis are

diagnosed with OIS.<sup>4</sup> In the bilateral cases, a complete ICA obstruction is usually present on one side, whereas on the contralateral side the corresponding obstruction may be as low as 50 per cent.<sup>4,17</sup>

Acute manifestation of OCAD may present as an embolism to the retinal circulation and can result in transitory visual loss (amaurosis fugax),<sup>14</sup> partial or complete irreversible loss of vision from OA occlusion, central retinal artery occlusion (CRAO) or branch retinal artery occlusion (BRAO) and OIS.<sup>13,14,18</sup> It is estimated between 53 per cent and 98 per cent of patients with amaurosis fugax, between 35 per cent and 76 per cent of patients with CRAO and between 43 per cent and 67 per cent of patients with BRAO have OCAD.<sup>18</sup> Patients with severe OCAD show haemodynamic changes that suggest reduced retrobulbar blood flow.<sup>18</sup> Although OIS may result from prolonged ocular hypoperfusion caused by either high grade stenosis or complete occlusion of the extracranial ICA or CCA,<sup>13</sup> OA disease alone, unassociated with ICA stenosis or arteritis, may also lead to ocular ischaemia.<sup>19</sup> This hypoperfusion of the globe may produce anterior or posterior ischaemia or both. The resulting chronic hypoxia elicits the production of angiogenesis factors capable of inducing ocular neovascularisation.<sup>20</sup>

OIS may result from collateral vessels creating a 'steal syndrome', shunting blood towards the brain and away from the eye.<sup>4,21,22</sup> Alternatively, the development of collateral vessels in response to ischaemia in patients with severe stenosis may protect the eye against OIS, offering an explanation for the question of why relatively few patients with carotid stenosis develop OIS.<sup>13</sup> Although studies have not found a correlation between blood flow in the OA and the severity of clinical signs,<sup>15,23</sup> it is possible that decreased blood flow to the eye results from both the blocked ICA and the induced ophthalmic 'steal' effect.<sup>20</sup>

Reversal of flow in the OA is a well-recognised feature of ICA occlusion as a result of development of collateral circulation from branches of the ECA to the circle of Willis via the OA.<sup>15,24</sup> As the demand for the intracranial circulation is

Diabetic retinopathy
Hypertensive retinopathy
Venous stasis retinopathy (non-ischaemic CRVO)
AION
CRAO
Radiation retinopathy
HIV retinopathy
Retinopathy of blood dyscrasias (e.g. anaemia, leukaemia, polycythaemia)
Sarcoidosis
Giant cell arteritis
Systemic lupus erythematosus

**Table 2. Differential diagnosis of hypoperfusion retinopathy**<sup>8,13,29,30</sup>

large, this may isolate the eye and diminish perfusion pressure in the distal OA and central retinal artery.<sup>24</sup> However, OA flow reversal may be found in mild cases of OIS, without rubeosis iridis.<sup>15</sup> Patients with severe (greater than 70 per cent stenosis) bilateral OCAD, high grade carotid stenosis, and reverse OA flow may have a greater chance of developing OIS. The factors that influence the progression and severity of ocular ischaemia are still unclear.<sup>15,18</sup> One study suggested that posterior ciliary artery (PCA) hypoperfusion correlates with poor vision.<sup>23</sup> Subsequently, optic nerve, choroid and outer retina ischaemia may represent primary determinants of visual loss.<sup>13</sup>

### Differential diagnosis

As OIS can be associated with potentially life-threatening cerebral ischaemia, it is a diagnosis which is important not to miss or confuse with other more common conditions such as central retinal vein occlusion (CRVO) or diabetic retinopathy.<sup>7,25</sup> OIS may be distinguished from CRVO where the veins are generally tortuous,<sup>4</sup> the optic disc is swollen and generally more haemorrhages are present.<sup>6,25</sup> Although diabetic patients present special diagnostic difficulty, an important distinguishing factor is marked asymmetry of the retinopathy. In OIS, venous beading

is not usually of the same extent as that observed in diabetic retinopathy. In addition, the observation of rubeosis in a non-diabetic patient, without venous obstruction is suggestive of ocular ischaemia.<sup>4</sup>

Although retinopathy associated with OCAD has been termed 'venous stasis retinopathy',<sup>26,27</sup> the term 'hypoperfusion retinopathy' is preferred.<sup>28</sup> The term venous stasis retinopathy may be considered confusing and a misnomer, as the mechanism does not involve decreased venous outflow, but rather decreased arterial outflow. In addition, the term has been used to describe the non-ischaemic form of CRVO.<sup>13</sup> Further differential diagnoses of hypoperfusion retinopathy are outlined in Table 2. Successful management may depend on expeditious identification and referral of these patients.

### Symptoms

The symptoms of OIS (Table 3) include decreased vision that can range from 6/6 to no light perception. A reduction in visual acuity occurs in about 90 per cent of cases and is usually gradual over weeks or months.<sup>4,6</sup> However, in about 12 per cent, the visual loss is abrupt and may occur within seconds, minutes or on awakening.<sup>4</sup> The majority of patients who present with abrupt visual loss also present with a 'cherry red spot' at the macula,

<b>SYMPTOMS</b>	
<b>Visual disturbance</b>	
Reduced acuity	
Amaurosis fugax	
Light induced amaurosis	
Teichopsia	
<b>Pain</b>	
<b>COMMON SIGNS</b>	
<b>Posterior segment</b>	<b>Anterior segment</b>
Hypoperfusion retinopathy	iris neovascularisation
Mid peripheral haemorrhages (dot, blot)	neovascular glaucoma
Microaneurysms	uveitis
Dilated (non-tortuous) retinal veins	asymmetric cataract
Macular 'cherry-red' spot	
Macular oedema	
Cotton wool patches	
Pale optic disc	
Optic disc and retinal neovascularisation	
<b>DIAGNOSTIC TESTS</b>	
<b>Fluorescein angiography</b>	
Delayed choroidal filling	
Prolonged arteriovenous transit time	
Retinal vessel staining	
<b>Electroretinography</b>	
Diminished/absent a- and b-wave	
<b>Colour Doppler imaging</b>	
Qualitative and quantitative assessment of blood flow in the OA, CRA and PCAs	
<b>Ophthalmodynamometry, oculoplethysmography and oculopneumoplethysmography</b>	
Measurements of relative OA pressure	

**Table 3. A summary of clinical signs and symptoms associated with OIS** <sup>2,4,6,13,14,17,20,24,36</sup>

indicating acute inner layer retinal ischaemia. Stabilisation or amelioration of vision occurs in about 25 per cent of eyes following endarterectomy.<sup>7</sup> The visual prognosis for patients with OIS is generally poor with approximately 60 per cent having visual acuity less than 1/60 within one year of diagnosis. Loss of light perception can occur with time,<sup>2,13</sup> particularly in the presence of neovascular glaucoma.<sup>4,17</sup> Generally, patients who present with visual acuity

of 6/48 or better are more likely to maintain this level of acuity.<sup>2</sup>

Pain in and around the eye (ocular angina) is experienced by about 40 per cent of patients and is described as a dull ache.<sup>4</sup> This may result from ischaemia to the globe, increased IOP in eyes with neovascular glaucoma, dural ischaemia or a combination of these factors. Although approximately 94 per cent of those who experience pain also have rubeosis iridis,

only 70 per cent have pressures exceeding 25 mmHg.<sup>4</sup> Others believe that the pain is mostly related to the ischaemia, rather than any increase in IOP.<sup>31</sup>

A transient ischaemic attack (TIA) involving the carotid system may give rise to temporary motor and sensory deficits contralateral to the causative lesion, aphasia and amaurosis fugax.<sup>13</sup> Amaurosis fugax is the most common ocular symptom of OCAD and occurs in approximately nine to 15 per cent of patients with OIS.<sup>2,4</sup> Approximately one-third of patients with amaurosis fugax have a concomitant carotid artery obstruction of 75 per cent or greater.<sup>6</sup> It is characterised by sudden, painless, monocular loss of vision lasting seconds to minutes that may be partial or complete.<sup>32</sup> It may be caused by emboli arising from lesions of the CCA, ICA or retina and/or choroidal hypoperfusion.<sup>33</sup> Exertion, increased facial temperature or a change in posture may precipitate the attack.<sup>21,34</sup> These factors decrease perfusion pressure, impeding ophthalmic blood flow by causing a diversion of blood from the eye and cause a reduction in systemic blood pressure or a rise in venous pressure or IOP.<sup>21</sup>

As many as one-third of patients untreated after a TIA will subsequently experience a stroke.<sup>13</sup> Approximately 30 per cent of patients with OIS have experienced a stroke or TIA.<sup>2</sup> A number of authors have described amaurosis fugax occurring in patients with severe carotid insufficiency after exposure to bright light.<sup>32,35</sup> Most patients report unilateral dimming or blurring of the entire visual field with only partial visual loss.<sup>32</sup> Furlan, Whisnaut and Kearns<sup>35</sup> suggest this phenomenon may be due to increased metabolic demand of the outer retina that is not met or a constriction of local retinal vasculature. Thus, chronic hypoperfusion of the eye probably induces a delay in the regeneration of visual pigments in the photoreceptor layer of the retina, resulting in blurred or absent vision that persists until regeneration of pigments is achieved.<sup>35</sup> Exposure of an ischaemic retina to bright lights may also stimulate positive after-images of varying shapes and colours, known as teichopsia.<sup>31</sup>

## Signs

### ANTERIOR SEGMENT

Diverse anterior segment signs (Table 3) may be present including conjunctival and episcleral injection, corneal oedema, uveitis, iris neovascularisation, neovascular glaucoma and asymmetric cataract.<sup>17,20,36</sup> Iris rubeosis indicates poor visual prognosis, suggesting a greater degree of ischaemia to the globe and increased ocular damage.<sup>13,17</sup> Huckman and Haas<sup>21</sup> suggest that iris neovascularisation is due to the OA 'steal' phenomenon whereby the iris becomes ischaemic because of the retrograde ophthalmic arterial flow, shunting blood from the iris. Neovascularisation may follow the release of vasoproliferative agents from the chronically ischaemic iris, choroid or retina.<sup>37</sup> Although rubeosis is found in approximately two-thirds of eyes with OIS, neovascular glaucoma has been reported to occur in only 35 per cent of cases.<sup>4</sup>

Lenticular opacities generally develop in the later stages.<sup>4</sup> At presentation, the patient's ocular media were clear. However, it is anticipated that he will develop cataract in the left eye. Pupils may be dilated, sluggish or non-reactive.<sup>5,31,38</sup> Although anterior chamber cells are found in only approximately one-fifth of eyes with OIS,<sup>4</sup> OIS should be considered in the differential diagnosis of new onset uveitis in a person over the age of 55 years.<sup>1</sup> Most eyes with anterior chamber flare also have iris neovascularisation, although a cellular response in the vitreous is usually absent.<sup>4</sup>

A fall in mean blood pressure, a rise in IOP or a combination of both reduces the perfusion pressure.<sup>2</sup> Increased IOP is found in only one-third of eyes with OIS.<sup>6</sup> It may be normal or even low, even in the presence of angle closure caused by a fibrovascular membrane, due to reduced ciliary body perfusion and aqueous production.<sup>4,10</sup>

### POSTERIOR POLE

The spectrum of signs in hypoperfusion retinopathy (Table 3) includes changes in retinal calibre (narrowed retinal arteries), dilated but non-tortuous retinal veins, retinal haemorrhages (dot and blot),

microaneurysms, optic disc and retinal neovascularisation and arterio-venous communications.<sup>20,31</sup> A macular 'cherry red spot' occurs in 12 per cent of cases, appearing if the IOP exceeds the perfusion pressure of the retinal artery.<sup>4</sup> This may result from emboli or increased IOP secondary to neovascular glaucoma.<sup>4,5,17,36</sup> Retinal haemorrhages are observed in about 80 per cent of eyes and usually occur in the mid-peripheral retina.<sup>4,31</sup> Numerous haemorrhages at the macula are rare. Microaneurysms are also common and generally appear in the mid-periphery.<sup>4</sup> Neovascularisation of the disc and retina occurs in about 35 per cent and eight per cent of eyes respectively. Dugan and Green<sup>38</sup> reported cobblestone degeneration resulting from outer retinal ischaemic atrophy, wedge-shaped areas of retinal pigment epithelial atrophy, diffuse inner retinal atrophy and dense proteinaceous material in the vitreous. Flaxel and Gregor<sup>39</sup> also reported an uncommon presentation of OIS associated with a choroidal neovascular membrane. Although uncommon, anterior ischaemic optic neuropathy (AION) may also occur.<sup>6</sup> It follows that hypotensive retinopathy may have contributed to the patient's right optic atrophy. Other uncommon posterior segment signs include vitreous haemorrhage, cotton wool patches (six per cent), spontaneous retinal arterial pulsations (four per cent) and Hollenhorst plaques (two per cent).<sup>4</sup>

### Diagnostic tests

A clinical diagnosis of chronic ocular ischaemia usually implies the presence of severe OCAD,<sup>20</sup> which requires a thorough and prompt investigation. Patients with suspected OCAD require evaluation of the extracranial carotid system to confirm the carotid lesion, to establish its cause (for example, atheroma or vasculitis), assess the severity of the lesion (percentage of stenosis and occlusion) and the ocular and cerebral tolerance (hypoperfusion of the ipsilateral eye and hemisphere).

Orbital ultrasound techniques (Table 3) allow a non-invasive method of examining flow velocities in the orbital vessels, particularly the OA.<sup>15</sup> Carotid duplex scan-

ning, a combination of B-mode ultrasound arterial imaging and pulsed Doppler analysis of blood flow velocity, will detect both haemodynamically significant lesions (high grade stenosis or occlusion) and haemodynamically insignificant lesions (small plaques and ulcers).<sup>31,36</sup> Duplex ultrasonography provides both an anatomic picture and a pulse Doppler ultrasound. This provides visualisation of vascular plaques and a quantitative assessment of peak systolic and end diastolic velocities.<sup>15,38</sup>

The orbital blood vessels, except for the superior ophthalmic vein, are rarely identified with grey scale B-mode ultrasound imaging.<sup>15</sup> Studies comparing duplex scanning and angiography have reported 95 per cent or greater agreement when there is stenosis greater than 50 per cent.<sup>36</sup> Due to its accuracy, duplex scanning is usually performed in the initial evaluation of the carotid system, but is not useful for lesions of the aortic arch, its proximal branches or the intracranial circulation.<sup>13</sup> The definitive test to detect obstruction of the extra and intracranial circulation is the arteriogram, involving the circulation of a dye typically introduced through the femoral artery. However, it is an invasive procedure,<sup>4,7,15,18,24,31</sup> does not provide sufficient resolution to analyse blood flow in OA branches, is expensive, time consuming and may harm the patient through adverse reactions to contrast agents, vascular spasms or high levels of irradiation if repeated angiograms are used to monitor disease progression.<sup>15,18</sup>

Orbital colour Doppler imaging (CDI) is an accurate, non-invasive, quick and reproducible technique that is an excellent alternative to invasive vascular studies such as angiography for the diagnosis and evaluation of chronic OIS.<sup>24</sup> CDI displays both anatomic and velocity data on blood flow in a colour-encoded, real-time format. It provides qualitative and quantitative assessment of blood flow through specific vessels, combining traditional B-mode ultrasound imaging with simultaneous real-time spectral Doppler analysis of blood flow.<sup>24</sup> CDI is also superior to conventional ultrasound in its ability to

demonstrate the direction of vascular flow and flow velocities of the OA, CRA and PCAs.<sup>14,24</sup> CDI can demonstrate evolving disease within the OA and secondary changes in its branches in patients with various presentations of ocular ischaemia.<sup>19</sup>

Fluorescein angiography (FA) can be used to demonstrate flow obstruction and structural abnormalities of the vasculature and also help determine the cause of iris neovascularisation. However, FA is considered difficult to quantify.<sup>15</sup> OIS may be indicated by delayed retinal arteriovenous transit time (greater than 11 seconds in 95 per cent of cases), areas of non-perfusion, patchy choroidal filling (60 per cent of cases), microaneurysms and venous beading, leakage from neovascularisation, leakage at bifurcations suggesting emboli damage, delayed arm-to-retina transit (95 per cent of cases) and retinal vessel staining secondary to hypoxic damage to the vascular endothelium (85 per cent of cases).<sup>4,6,7,38,40</sup> The last seems to be associated with complete CCA obstruction.<sup>20</sup>

Macular oedema is seen with FA in 14 per cent of cases.<sup>6</sup> This is probably due to endothelial damage within the smaller vessels leading to vascular incompetence, as well as leakage from microaneurysms. The retinal vessels in areas of retinal non-perfusion appear to be devoid of pericytes and endothelial cells.<sup>26</sup> The clinical thickening of the retina tends to be less pronounced than the FA appearance, possibly due to the low flow state from the carotid obstruction causing less extravasation of plasma than would be the case in an eye with macular oedema from diabetic retinopathy.<sup>6</sup>

Orbital flow may also be assessed to detect proximal obstruction of the cervical vasculature using ophthalmodynamometry, oculoplethysmography, oculopneumoplethysmography.<sup>31,38</sup> Ophthalmodynamometry and oculoplethysmography assess carotid artery patency by measurement of the OA pulse pressure. Ophthalmodynamometry measures systolic and diastolic pressure in the CRA.<sup>36</sup> Kearns, Siekert and Sundt<sup>41</sup> demonstrated that ophthalmodynamometry was able to detect pressure

reductions of the CRA only when ICA stenosis was above 90 per cent. It is generally considered insensitive and inaccurate.<sup>24</sup> Oculopneumoplethysmography allows the determination of reduced OA systolic pressure in patients with severe OCAD but also has limitations in diagnosing bilateral stenosis and low sensitivity in detecting carotid stenosis.<sup>18</sup>

The a- and b-waves may be absent or diminished in the electroretinogram (ERG). The a-wave represents photoreceptor activity, thereby indicating choroidal vascular compromise and resultant outer retinal layer ischaemia.<sup>4</sup> The b-wave corresponds to bipolar and Müller cell activity. Loss in this wave suggests retinal ischaemia.<sup>6</sup> However, similar results may be obtained in CRAO and the technique has been considered insensitive and inaccurate.<sup>4,24</sup>

If carotid insufficiency is suspected, palpation and auscultation of the carotids may be performed.<sup>13</sup> The presence of a carotid bruit correlates with a greater incidence of carotid lesions. However, the absence of carotid bruit does not rule out underlying OCAD. Moreover, in instances of complete carotid occlusion, a bruit is not likely to be heard.<sup>13</sup> Asymmetric carotid pulses indicate carotid stenosis on the side of the weaker pulse.<sup>36</sup> Auscultation of facial and orbital pulses allows retrograde flow into the external carotid system from the internal carotid to be heard. Retrograde flow may occur with significant ICA stenosis and is heard as an increased pulse on the side of the stenosis. Blood pressure in each arm may be recorded. Besides indicating hypertension, significant differences between the arms may be indicative of peripheral vascular disease.<sup>36</sup> Laboratory tests should be ordered to rule out diabetes, hyperlipidaemia and blood dyscrasias. An erythrocyte sedimentation rate (ESR) may be conducted to rule out giant cell arteritis. Given that patients with OIS have significant systemic disease and that cardiac infarction is the primary cause of mortality, patients should be under the care of a cardiologist for complete serology, electrocardiogram (ECG), cardiac evaluation and full carotid investigation.

## Treatment

Treatment of OIS remains difficult and controversial.<sup>29</sup> Surgical intervention depends on the patients' operative risk, degree of stenosis and symptoms. The ophthalmic management is primarily aimed at reducing the stimulus for ocular neovascularisation.<sup>13</sup> Winterkorn and Beckman<sup>10</sup> found that the calcium channel blocker verapamil was an effective treatment of OIS, where vasospasm appeared to be a contributing cause. Episodes of transient visual dimming ceased, visual acuity improved, rubeosis partially regressed and hypotony reversed. Aspirin may be used in young, low-risk patients to prevent cranial ischaemia of a non-cardiac origin.<sup>13</sup> Therapy for patients with ocular ischaemia secondary to carotid atherosclerosis includes identification and reduction of risk factors for further atherosclerosis, platelet anti-aggregants and carotid endarterectomy.<sup>24</sup> Although carotid endarterectomy attempts to prevent a subsequent stroke in severe atheromatous stenosis of the ICA, it may be employed to remove the carotid obstruction only if the carotid artery is less than 99 per cent blocked. If a carotid artery is completely obstructed, endarterectomy is ineffective as a thrombus often propagates distally to the next major vessel.<sup>6</sup> Although, carotid endarterectomy has been shown to significantly increase flow in the OA and CRA, the individual response has been shown to be variable and provides little visual benefit.<sup>17</sup> Complications such as neovascular glaucoma after carotid endarterectomy have been reported and probably relate to the acute reperfusion that occurs after surgery and the production of oxygen free radicals.<sup>6,14,29,42</sup> If the anterior chamber angle is closed due to fibrovascular tissue, a sudden reversal of stenosis results in improved ciliary body perfusion and increased aqueous production and therefore a severe rise in IOP.<sup>6</sup>

Panretinal photocoagulation (PRP) is the preferred treatment option for retinal hypoxia and neovascular glaucoma.<sup>13</sup> It may be performed when FA shows evidence of retinal ischaemia in the form of retinal capillary obliteration.<sup>29</sup> However, Hayreh and Baines<sup>43</sup> have demonstrated

experimentally that anterior segment neovascularisation can be produced by causing uveal ischaemia alone without any retinal ischaemia. This suggests that PRP may not be beneficial, when FA shows no signs of retinal ischaemia in the form of capillary obliteration.<sup>2</sup> Peripheral cryoablation represents an acceptable alternative if the media opacities prevent the use of PRP.<sup>13</sup> The efficacy of PRP in the treatment of OIS patients is difficult to assess due to variation in treatment methods and the lack of control groups. PRP and cyclocryotherapy do not appear to improve vision in patients with IOS. However, they reduce the incidence of neovascular glaucoma and ultimately improve the patients' ocular cosmesis and the possibility of retaining limited vision. Jacobs and Ridgway<sup>31</sup> found laser retinal photocoagulation to be ineffective in the treatment of disc neovascularisation.

Neovascular glaucoma may be treated with conventional ocular anti-hypertensive agents, topical steroids to control inflammation, filtration surgery in the presence of extensive peripheral synechiae or cycloablative therapy including cyclocryotherapy. Lowering IOP to improve ocular perfusion (eventually by cyclocryotherapy, if medical therapy is not effective) is essential.<sup>29</sup> Enucleation is the last resort for a painful, blind eye when previous treatment strategies have proved unsuccessful.<sup>13</sup> Cycloplegics may be used to decrease ciliary pain and prevent posterior synechiae.<sup>2</sup>

## CONCLUSION

Although OIS is uncommon, the syndrome manifests with a number of characteristic clinical, ERG, fundus fluorescein and carotid angiographic features. Despite the rather therapeutically resistant course of chronic ocular ischaemia, it remains important to recognise the condition for timely intervention and management of the severe ocular and potential systemic sequelae.<sup>2,24</sup> Early intervention may offer hope of a therapeutic effect.<sup>31</sup>

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