The eye in cardiac and cardiovascular disease

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There is an extensive range of cardiac and cardiovascular disease that can have ophthalmic manifestations and only the most commonly occurring examples are discussed below. The eye in diabetes is discussed in a separate article in this series.

HISTORY AND EXAMINATION

Cardiovascular disease can be responsible for a wide-ranging spectrum of ophthalmic symptoms and signs, ranging from sudden loss of vision to asymptomatic changes in the retinal vasculature. Assessment of visual acuity, assessment of pupillary responses, visual field testing and fundoscopy provide a starting point for assessing retinal and optic nerve function. Dilated fundoscopy, paying particular attention to the retinal vasculature, often reveals the ophthalmic diagnosis.

INVESTIGATIONS

Common initial investigations include arterial blood pressure and blood glucose levels, with more specialized investigations being directed by the patient's presenting symptoms and signs. Visual fields can be helpful in identifying characteristic defects, such as the altitudinal defect present in anterior ischaemic optic neuropathy (AION). If giant cell arteritis (GCA) is suspected, then an erythrocyte sedimentation rate (ESR) needs to be obtained urgently and a temporal artery biopsy may need to be arranged to confirm the diagnosis. Embolic processes require follow-up cardiovascular investigations including carotid Doppler ultrasound and echocardiography to locate the source of the emboli.

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HYPERTENSION, ATHEROSCLEROSIS AND RETINAL VASCULAR OCCLUSION

Retinal vessels narrow in response to systemic hypertension and this is the earliest sign of hypertensive retinopathy. Hypertensive retinopathy can be subdivided into four grades describing general arteriolar attenuation (grade 1), arteriovenous crossing changes (grade 2), flame-shaped retinal haemorrhages, exudates and cotton-wool spots (grade 3) and optic disc swelling (grade 4). As the retinopathy becomes more serious, the patient's risk of having underlying cardiac and renal dysfunction increases, as does the risk of stroke. Grade 4 retinopathy is synonymous with accelerated phase (malignant) hypertension and carries a poor prognosis; optic disc swelling is diagnostic of this condition (McGregor et al, 1986). Hypertension is also a risk factor for acceleration of diabetic retinopathy (UK Prospective Diabetes Study Group, 1998).

Arteriosclerotic retinal changes are normally seen in association with hypertensive retinopathy, but can be seen in the elderly without evidence of hypertension. They are similarly graded from grade 1 to 4, starting with broadening of the arteriolar light reflex (grade 1), through arteriovenous crossing changes to 'copper-wiring' and eventually 'silver-wiring' (grade 4), by which time vein occlusions are common.

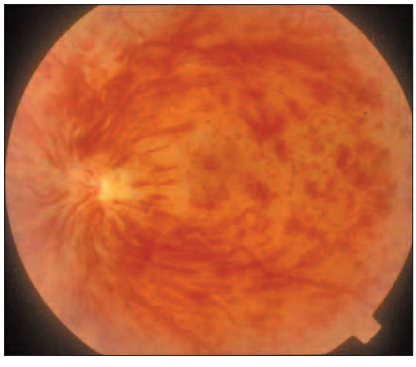
Retinal vein occlusions are more common than retinal arterial occlusions, and are divided into central retinal vein occlusions and branch retinal vein occlusions depending on whether the blockage is posterior or anterior to the cribriform plate. Retinal examination reveals dilated, tortuous retinal veins associated with flame-shaped haemorrhages, retinal oedema, cotton-wool spots and optic disc swelling (*Figure 1*). When the optic nerve or macula are involved (either by oedema, haemorrhage or ischaemia) vision is reduced and an afferent pupillary defect may be present. The most common cause is external pressure on the vessel wall as a result of hypertension. This increases pressure on the veins at the points where they share an adventitial sheath with their corresponding retinal artery, i.e. at arteriovenous crossing points for branch veins or just posterior to the lamina cribrosa for the central retinal vein.

Retinal vein occlusions can also be caused by vessel wall disease, such as that which occurs in diabetes. Vein occlusion as a result of increased blood viscosity is rare, but can result from chronic leukaemia, polycythaemia, myeloma and Waldenström's macroglobulinaemia; 'slow-flow retinopathy' with tortuous veins but without frank vein occlusion is more common in such conditions.

EMBOLIC SYNDROMES

Retinal arteriolar emboli can be found in approximately 1% of adults over 40 years of age (Wong and Klein, 2002). They are associated with the presence of carotid artery plaques and stenosis, hypertension, cigarette smoking and diabetes. Studies show that patients with retinal emboli, with or without overt retinal artery occlusion, are at a higher risk of stroke and mortality from cardiovascular disease (Klein et al, 1999). Arterial occlusion is most

Figure 1. A central retinal vein occlusion, showing widespread haemorrhages.

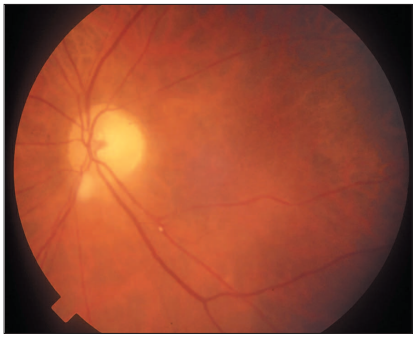


commonly caused by retinal emboli of cardiac or carotid origin. If emboli are visible on fundoscopy, their appearance can help in distinguishing these causes:

- Calcific emboli are single, large and white. Owing to their size, they are often impacted onto the wall of an arteriole near the disc, causing extensive retinal ischaemia. They usually originate from a calcified aortic valve in the heart, from the ascending aorta or from a calcified atheromatous plaque in the carotid arteries.
- Cholesterol emboli (Hollenhorst plaques) are multiple, small and yellowish (*Figure 2*). They are often seen at retinal arteriolar bifurcations, and may move and disperse with ocular massage. They usually originate from an atheromatous plaque within the carotid arteries that has ulcerated, releasing its contents.
- Fibrinoplatelet emboli are only usually visible during an attack of amaurosis fugax and are small and white. They tend to pass rapidly through the retinal vessels.

In retinal artery occlusion, either the central retinal artery or a branch retinal artery is involved. Onset is acute, with profound visual loss in central artery occlusion, and development of a field defect and variable visual loss in branch artery occlusion. Fundoscopy reveals pale, swollen retina in the area supplied by the affected artery and an embolus may or may not be visible; in central retinal artery occlusion, the whole fundus can appear pale, with a classic cherry-red spot at the macula and an afferent pupillary defect (*Figure 3*). With time, arteriolar attenuation and optic atrophy with concomitant pallor develop. Patients with a cilioretinal artery may retain central vision as the macula may be spared (*Figure 4*).

Figure 2. A typical Hollenhorst plaque (cholesterol embolus).



Patients with retinal emboli should undergo thorough cardiovascular and cerebrovascular risk assessment. Investigation of embolic retinal artery occlusion should include assessment of the cardiac system and carotid arteries as a source of emboli, involving clinical examination, electrocardiogram, echocardiogram and Doppler ultrasound of the carotid arteries. Myxomatous material shed by an atrial myxoma is a rare source of cardiac emboli; atrial fibrillation is a common, important risk factor.

Retinal artery occlusion can also be caused by the vasculitides, particularly GCA in the form of temporal arteritis, and this vaso-obliterative cause needs to be excluded in elderly patients, particularly in the case of central retinal artery occlusion. Apart from GCA, other vasculitic causes include systemic lupus erythematosus, polyarteritis nodosa, Wegener's granulomatosis, scleroderma, dermatomyositis and syphilis.

Localized retinal artery atheroma can also cause vaso-obliteration and subsequent arterial occlusion, so systemic atherosclerosis, hypertension and hyperlipidaemia may also be relevant. Central retinal artery occlusion has also been reported following cardiac catheterization (Nakata et al, 2002).

Figure 3. A central retinal artery occlusion, showing the classical cherry-red spot at the macula.

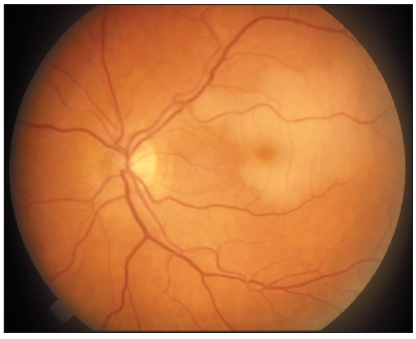
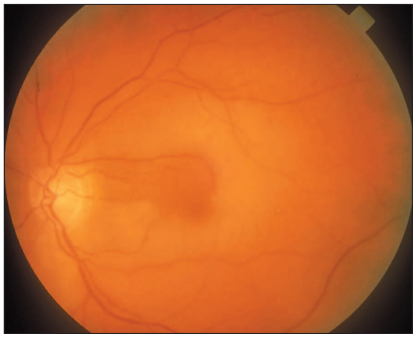


Figure 4. A central retinal artery occlusion in the presence of a spared cilioretinal artery, allowing continued perfusion of the macula.



GIANT CELL ARTERITIS

GCA is an important cause of central retinal artery occlusion that needs to be identified quickly and treated with high-dose systemic corticosteroids to avoid further ophthalmic or systemic complications (Bhatti and Tabandeh, 2001). It is an idiopathic granulomatous vasculitis that affects medium-calibre arteries in elderly patients, giving it a predilection for the ophthalmic vasculature. Visual symptoms are therefore often the presenting feature of the disease.

Ocular manifestations include retinal artery occlusion and AION. The latter presents as a unilateral loss of vision associated with an altitudinal visual field defect. Examination typically reveals a pale and swollen optic nerve head with small splinter haemorrhages. AION can occur in the absence of GCA (said to be non-arteritic); this is caused by a microvasculopathy, typically in association with hypertension or diabetes. Other specific symptoms of GCA include headache, scalp tenderness and jaw claudication. GCA is associated with a high ESR of >60 mm/hr, although this may be normal in some cases. Immediate treatment with high-dose corticosteroids is started, based on laboratory results or clinical suspicion, with further investigations, e.g. temporal artery biopsy, arranged as soon as is practicable (Riordan-Eva et al, 2001).

BACTERIAL ENDOCARDITIS

Bacterial endocarditis can cause a number of different ocular syndromes. Valvular vegetations can release emboli and lead to episodes of amaurosis fugax or retinal artery occlusion. Infected emboli can cause a metastatic endophthalmitis with a severely inflamed eye and visual loss (*Figure 5*). Roth spots are retinal haemorrhages with a pale or white centre. They are usually caused by blood disorders, particularly anaemia and leukaemia, but occur in about 5% of cases of subacute bacterial endocarditis.

SYSTEMIC SYNDROMES

A large number of genetic conditions involve both the cardiovascular and ocular systems to varying extents. Some of the commonest are described below.

Marfan syndrome is a widespread connective tissue disorder characterized by dystrophia mesodermalis hypoplasia. Classical features include skeletal abnormalities, cardiovascular abnormalities and ocular features, of which the most important are lens dislocation (which occurs in 80% and tends to be bilateral, symmetrical and upwards), glaucoma, and retinal detachment. Cardiovascular problems include aortic dilatation with or without dissecting aneurysms of the ascending aorta, aortic regurgitation and mitral valve prolapse.

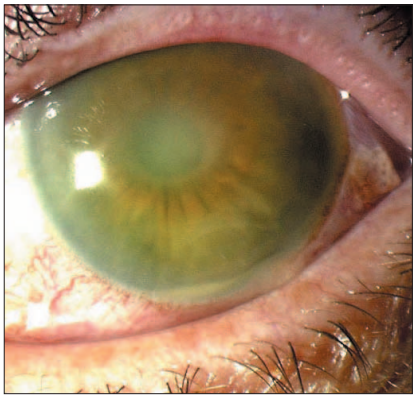
Homocysteinuria is another cause of lens subluxation, although in this case it is usually downwards. This disorder is also associated with an increased incidence of arterial and venous thrombosis.

Down's syndrome (trisomy 21) is linked to a number of ocular findings. Apart from the characteristic upward slanting of the palpebral fissure and epicanthal folds, common ocular findings include refractive errors, cataracts and keratoconus. Myopia and myopic astigmatism have been reported to be more common in patients with cardiac abnormalities (da Cunha and Moreira, 1996), typically septal defects.

Kearns–Sayre syndrome is a form of ocular myopathy characterized by the development of chronic progressive external ophthalmoplegia and a pigmentary retinopathy. It is associated with cardiac conduction defects, which can lead to heart block and death.

Myotonic dystrophy is a generalized, autosomal dominant condition that typically presents with myotonic features and bilateral ptosis. Cardiac conduction problems and cardiomyopathy also occur.

Figure 5. Endophthalmitis, demonstrating a hypopyon (an inferior layer of white cells in the anterior chamber) and generalized inflammatory haze.



DRUGS

Amiodarone

Corneal verticellata (whorls of faint grey pigment within the lower cornea) may form in patients taking amiodarone, usually at a dose in excess of 400 mg/day. The extent of the corneal keratopathy is proportional to the drug dose and is reversible on cessation; its absence may indicate a compliance problem. Amiodarone may also cause visual disturbances, lens opacities and has been inconclusively linked to causing a toxic optic neuropathy.

Digoxin

This is a cardiac glycoside used to treat cardiac arrhythmias and heart failure. It is known to cause dyschromatopsia, visual disturbances, and visual-field defects, especially at a serum digoxin level of > 2 μg/litre. Digoxin serum levels and toxicity risks increase with the addition of amiodarone.

Sildenafil citrate (Viagra)

This is a phosphodiesterase (PDE) inhibitor used to treat erectile dysfunction that has been extensively investigated to detect potential ocular side effects. There are few clinical as opposed to experimental reports of problems, but it has been linked to the development of a non-arteritic AION in the absence of other vascular risk factors (Laties and Zrenner, 2002). In addition, the perception of flashing lights has been reported, probably because of the effect of PDE inhibition on the phototransduction cascade.

Warfarin and aspirin

Both of these anticoagulant drugs are widely prescribed for cardiac or vascular indications. They have been linked to the development of extensive vitreous haemorrhage in proliferative diabetic retinopathy and exudative age-related macular degeneration (Tilanus et al, 2000).

Ophthalmic drugs

Many commonly used topical glaucoma medications have systemic cardiovascular effects. Beta-blockers such as timolol can cause bradycardia and hypotension, in addition to their well-known respiratory complications; brimonidine, an alpha-2-adrenergic agonist, can also elicit hypotension, although this tends to be less serious than that caused by beta-blockers.

Cardiovascular drugs

Aggressive treatment of hypertension, especially in the elderly, may cause periods of hypotension when the patient is supine. This can further compromise the circulation of the optic nerve head in some glaucoma patients, leading to progressive visual field loss (Graham and Drance, 1999).

CARDIAC TRANSPLANTATION

Cytomegalovirus retinitis has been reported following cardiac transplantation (Fishburne et al, 1998). HM

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