A patient with central retinal vein occlusion and neovascular glaucoma

Comments by:
Bob Dhillon, FRCS, Alvin K. H. Kwok, FRCS, FCOphthHK, Vincent W. H. Lee MD

Ophthalmic Forum is a new section introduced into the *Hong Kong Journal of Ophthalmology* by the editors to provide a platform for the ophthalmic colleagues in different countries to share their experiences and exchange their ideas. The editors will describe interesting and challenging cases and invite discussion from experts in related fields from Hong Kong and overseas. While the opinions expressed may not be the best or only ways to manage the cases, they provide useful insights and inspiration for readers when similar cases present in their clinics. The editors invite Fellows of the Hong Kong College of Ophthalmology to submit interesting cases for the editors to publish in Ophthalmic Forum.

Case history

A 48-year-old man has a history of non-insulin dependent diabetes mellitus for 10 years. Previous fundal examination showed non-proliferative diabetic retinopathy. Visual acuities were 6/9 in both eyes. The patient presented with blurring of vision in the right eye for the previous 2 days. Examination revealed central retinal vein occlusion (CRVO)

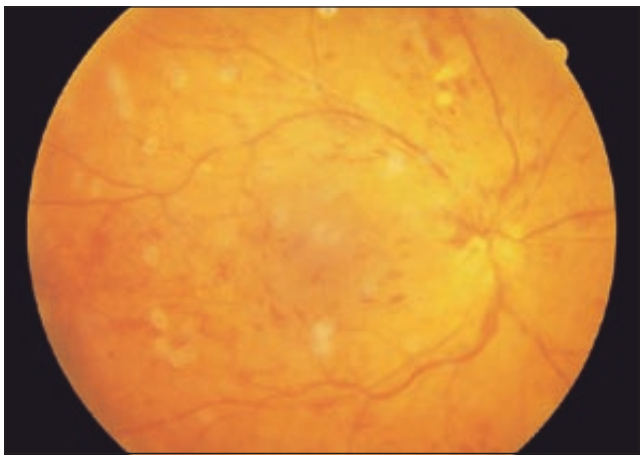

Figure 1. Central retinal vein occlusion with minimal ischemic change.

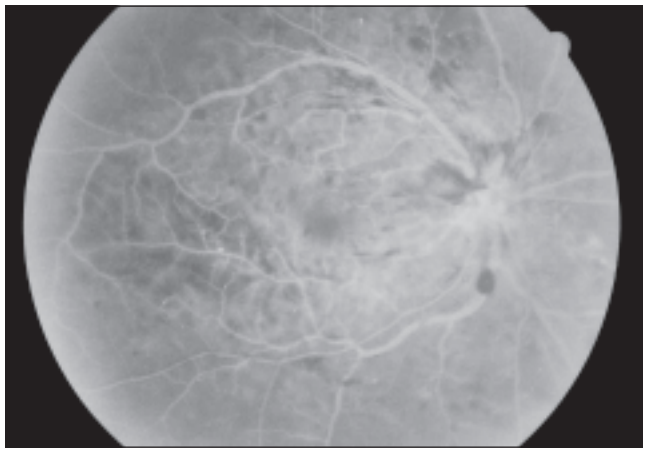

Figure 2. Non-ischemic central retinal vein occlusion shown by fluorescein angiogram.

in the right eye with minimal ischemic change (**Figure 1**). Visual acuity was 6/60 in the right eye and 6/9 in the left eye. No relative afferent pupillary defect was present. Fluorescein angiogram showed findings compatible with non-ischemic central retinal vein occlusion (**Figure 2**). The intraocular pressure (IOP) was normal. The patient was observed without specific treatment for the retinal vein occlusion.

At follow up 4 weeks later, the IOP was found to be 60 mm Hg in the right eye. Marked corneal edema was present and rubeosis iridis was detected. The patient was given intravenous mannitol infusion, diamox, slow potassium, 2% arteoptic (carteolol) twice daily, 0.1% propine twice daily and xalatan once daily. The IOP remained at approximately 50 mm Hg. Fundal details were not clear because of persistent corneal edema, which also precluded transpupillary laser treatment.

What are the pathogenesis, treatment plan, likely outcome, and prognosis? Are there any other comments or important issues in this case?

Comments

by Dr. Bob Dhillon, Consultant Ophthalmologist, Princess Alexandra Eye Pavilion, Edinburgh, UK

This report describes a 48-year-old male who presented with a central retinal vein occlusion in the right eye. The only risk factor described is non-insulin dependent diabetes mellitus. My thoughts on the evolution of rubeosis iridis and further management are described below.

Risk factors

Associated risk factors should be actively solicited at initial presentation including history of systemic hypertension, hyperlipidemia, thrombotic susceptibility (extraocular), and adequacy of diabetic control. The presence of one or more risk factors for rapid progression from a 'non-ischemic' picture to an 'ischemic' picture would modify ocular and non-ocular follow up and therapy.

Status of fellow eye

Under the circumstances, management will be largely aimed at preserving vision in the fellow eye. Therefore, fundus examination for evidence of diabetic retinopathy and/or hypertensive retinopathy should be performed. In addition, anterior chamber depth and the IOP level in the fellow eye, and optic nerve head appearance should be assessed.

Evaluation

Essential steps at initial examination should include checking for an afferent pupillary defect, gonioscopy/anterior chamber depth assessment, peripheral visual field testing (Goldman perimetry using a large central target for this patient), carotid assessment (simple stethoscope examination to check for bruits), and basic cardiovascular work-up including blood pressure, checking for atrial fibrillation or other arrhythmia, and drug history, specifically for anticoagulant therapy, is of value. Peripheral fundus examination for signs of ischemia, including deep, dark blotch hemorrhages adds to the simple clinical assessment for ischemia. Relying on fundus fluorescein angiogram and, more specifically, posterior retinal assessment using the fundus camera risks misdiagnosing ischemic fundi. The late fluorescein angiogram shows reasonable posterior retinal perfusion and no marked macular edema. However, the ischemic source is more likely to reside within and diffuse from the peripheral retina, anterior to the equator, which can only be assessed by binocular indirect ophthalmoscopy.

Evolution to rubeotic glaucoma

The diagnosis of well-perfused CRVO is usually made retrospectively following partial or full resolution of symptoms and signs. Clearly this is not the case for the individual presented here, who progressed rapidly to rubeosis iridis. Whilst attention to risk factors on further progression is of interest from the patient's perspective, the affected eye is managed based on the residual function and degree of comfort. If there is vision to be salvaged, then transcleral retinal destructive procedures including transcleral YAG or transcleral cryotherapy may be employed. In addition, glaucoma surgery in the form of augmented tube implantation with mitomycin C offers some hope for IOP control. However, unless the peripheral retina is adequately treated, the neovascular response is likely to close down any filter. Some new alternative modalities, including endoscopic ablation of the ciliary processes, may circumvent the problems of corneal edema and obscured fundus visualization using conventional transpupillary modes of therapy may be useful.

If there is no vision to be salvaged and the aim is to retain a comfortable eye, the range of therapy from the least to the most interventional include topical steroids and atropine, cyclodestructive procedures, including transcleral YAG or cyclocryoablation, retrobulbar alcohol, or as a last resort, removal of a painful blind eye.

Protection of the fellow eye

Clearly, the imperative is to protect the fellow eye, therefore systemic or thrombotic tendencies should be investigated by a thrombophilia screen, close attention to diabetic control, ocular perfusion assessment, including carotid evaluation, and prophylactic use of anticoagulation, probably low-dose aspirin, should all be considered. In my experience, two neglected areas include failure to detect and adequately manage systemic hypertension and failure to detect the early signs of glaucoma in the fellow eye, which can result in further vascular events occurring.

I think the main message of this forum should be to not rely on fundus fluorescein angiography alone in assessment and management of individuals with retinal vascular occlusive disease.

Comments

by Dr. Alvin K. H. Kwok, Associate Professor, Department of Ophthalmology & Visual Sciences, The Chinese University of Hong Kong, Hong Kong, China

Interesting points that I would like to discuss in this forum include ischemia versus non-ischemia, the natural history of CRVO, a young patient with CRVO, and a management plan.

Ischemic versus non-ischemic central retinal vein occlusion

It may be misleading if only the central fields are examined during fluorescein angiography (FFA). Additional information of the perfusion status of the peripheral retina would be desirable. Hayreh *et al* used four functional tests [visual acuity, visual fields, relative afferent pupillary defect (RAPD), electroretinography (ERG)] and two morphologic tests (ophthalmoscopy and FFA) in differentiating ischemic from non-ischemic CRVO.[1] Overall, the four functional tests proved to be far superior to the two morphologic tests: RAPD

was most reliable in uni-ocular CRVO (with a normal fellow eye), closely followed by ERG in all cases; perimetry was the next most reliable, followed by visual acuity. The two morphologic tests performed worst; FFA provided either no information at all of retinal capillary non-perfusion because of multiple limitations (at least one-third of eyes during the early, acute phase), or provided misleading information. Ophthalmoscopic appearance was the least reliable, most misleading parameter.

Natural history of central retinal vein occlusion

The outcome for visual acuity is largely dependent on the initial acuity.[2] Patients with intermediate initial acuity (20/50-20/200) show a variable outcome: 19% improve to better than 20/50, 44% stay in the intermediate group, and 37% have a final visual acuity worse than 20/200. Patients who have poor visual acuity at the first visit (< 20/200) have an 80% chance of a visual acuity of less than 20/200 at the final visit, whether perfused or non-perfused initially. In the first 4 months of follow-up, 15% of eyes with perfusion convert to ischemia. The development of non-perfusion or ischemia is most rapid in the first 4 months. Thus the follow-up schedule should be tailor-made to the individual.

Young patient with central retinal vein occlusion

This patient is relatively young at 48 years. Many biochemical and genetic studies could be performed (**Table1**), but the cost-benefit ratio should be considered. I would routinely do simple blood tests such as erythrocyte sedimentation rate and fluorescent treponemal antibody absorption test and refer the patient to an internist. The other tests could be withheld unless there is a history of thrombotic disease or a positive family history.

Table 1. Possible biochemical and genetic studies for central retinal vein occlusion

Full blood count	• Fasting lipid profile (cholesterol, triglyceride), fasting blood glucose
Inflammatory marker	• Erythrocyte sedimentation rate (ESR) • C-reactive protein • VDRL Fluorescent treponemal antibody absorption test • Antinuclear antibodies • Rheumatoid factor • Complement level • Antiphospholipid antibodies (anti-cardiolipin antibody, lupus anticoagulant)
Prothrombotic states	• Activated partial thromboplastin time/ prothrombin time • Protein C • Protein S • Antithrombin III • Factor XII Plasma viscosity (fibrinogen, ESR, hematocrit, α_1-globulin, α_2-globulin) • Heritable thrombophilia — activated protein C resistance (factor V leiden), methylenetetrahydrofolate reductase, prothrombin gene • Heritable hypofibrinolysis — lipoprotein (a), plasminogen activator inhibitor activity, PCR analysis of hypofibrinolytic 4G/5G polymorphism of the PAI1 gene • Homocysteine plasma endothelin-1

Management plan

After medically lowering the IOP, gonioscopy may be performed again to assess whether the angle is congested by rubeosis or closed by peripheral anterior synechiae. More aggressive retinal ablation should be considered for the former. Indirect diode laser retinopexy is my preferred technique, although some colleagues may prefer cryoretinopexy.

Ultrasound may be needed to assess the vitreoretinal status if the fundal view is poor. If there is no concomitant vitreoretinal problem, the patient should be referred to a glaucoma specialist. If there is a concomitant vitreoretinal problem such as vitreous hemorrhage, pars plana vitrectomy with endoretinopexy may be considered. This may be combined with endocyclophotocoagulation or a drainage implant through the pars plana if the patient is aphakic or pseudophakic. However, if the patient is phakic and the lens is relatively clear, then a conventional drainage implant may be required. Close co-operation between glaucoma and retinal specialists is needed to provide the best care for the patient.

References

1. *Hayreh SS, Klugman MR, Beri M, et al. Differentiation of ischemic from non-ischemic central retinal vein occlusion during the early acute phase. Graefes Arch Clin Exp Ophthalmol 1990;228:201-217.*
2. *Natural history and clinical management of central retinal vein occlusion. The Central Vein Occlusion Study Group. Arch Ophthalmol 1997;115:486-491.*

Comments

by Dr. Vincent W. H. Lee, Director of Eye Centre, Hong Kong Adventist Hospital and Honorary Associate Professor, Department of Anatomy, Faculty of Medicine, University of Hong Kong, Hong Kong, China

The findings of rubeosis iridis and markedly elevated IOP confirm the diagnosis of neovascular glaucoma — probably with total secondary angle closure.

The interesting question in this clinical case is the etiology. It is well known that rubeosis iridis is a consequence of severe posterior segment ischemia, and in this patient there seems to be an obvious reason, namely, the CRVO — or is it?

Classically rubeosis iridis occurs about 3 months after the onset of CRVO, although this patient was diagnosed after 1 month. While this is not unheard of, we have nevertheless been given fluorescein angiographic evidence that the original CRVO was non-ischemic. If any deviation from the norm is contemplated, one would have expected the rubeosis

to occur later, rather than earlier. It would therefore be helpful to look for clues of any additional source(s) of ischemia. For example, has the diabetic retinopathy in the other eye worsened since the last examination? Also, is there any bruit in the area of the right carotid bifurcation? A finding for the latter may not only explain the worsening ischemia, but may save the patient from a devastating stroke.

On the treatment side, one would like to first ascertain from a careful history how long the elevated IOP has existed. If it has been for more than 1 week, the prognosis for any useful vision is poor, and one would choose more conservative therapy.

For argument's sake, what if a good historian tells you the blurred vision started 1 day ago and furthermore this is his only sighted eye? I would then elect the most aggressive treatment and try to solve the two main problems in one setting. For long term functional survival, the posterior segment ischemia must be controlled, and the IOP reduced. In a sterile environment, the corneal edema can be reduced with paracentesis assisted by topical application of glycerin. If panretinal photocoagulation can now be performed aggressively (via indirect laser ophthalmoscope if need be), then this should be done and a large-size glaucoma drainage device, such as a 350 mm^2 Baerveldt, implanted. If laser cannot be delivered ab-external, I would opt for vitrectomy and endolaser, followed by a Baerveldt implant with tube insertion into the posterior segment. The eye will be very inflamed after the procedure and it may be helpful to give an intravitreal injection of dexamethasone 400 μg as well as the usual subconjunctival and topical steroid treatment.

Conservative therapy ranges from medical treatment for pain control to a slightly more aggressive protocol consisting of retinal cryotherapy plus cyclocryotherapy or cyclophotocoagulation. Here, the desires and comfort of the patients play an important role and they can usually make an intelligent, informed choice after being presented with full information about the different choices.