

Retinal vein occlusion – Diagnosis and management

A great deal is known about the aetiology, pathogenesis and management of retinal vascular disease as it applies to venous occlusion. Retinal vein obstruction correlates to the anatomical occlusion site.

The three major variants are central retinal vein occlusion (CRVO), hemiretinal vein occlusion (HRVO) and branch retinal vein occlusion (BRVO). Up to 98% of all BRVOs occur temporally, with 66% occurring superotemporally¹. The inferotemporal venous branch is affected in almost all other cases. A macular branchlet vein occlusion can also occur and involves smaller venous tributaries that drain only a portion of the macula².

Approximately two in 1,000 persons aged 40 years or older developed a retinal vein occlusion over a four-year period in a population-based study performed in Israel³. In persons aged 65 years or older, this increased to five per 1,000 individuals. Overall, 90% of patients who develop vein occlusion are over 50 years of age⁴.

Aetiology

The underlying cause for vein occlusion has been proposed to occur from compression of the vein by a thickened artery resulting in thrombus formation. At both the arteriovenous crossings in the retina and just behind the lamina cribrosa, arteries and veins share a common adventitial sheath. Additionally, CRVO may result because both artery and vein are limited in their expansion as their lumens narrow when they pass through the sieve-like lamina cribrosa. This adjacent positioning of the vessels may itself lead to thrombus formation from turbulent blood flow^{2,5}.

Based on the mechanical nature of this disorder (constriction of the fibrous sheath which surrounds the arteriovenous crossing), new treatment strategies have been evaluated which may potentially revolutionise the therapeutic approach to venous occlusions. Investigators have shown that if the fibrous sheath surrounding the arteriovenous crossing at

the point of a BRVO is opened surgically, the flow of blood can be re-established and vision improved^{6,7}. The artery and vein can be separated using retinal scissors – or a sheathotomy performed using a microvitreoretinal blade can be employed^{6,7}.

Another experimental procedure addresses the thrombus, which is formed in both central retinal and hemiretinal cases. Removal of the thrombus and re-establishment of retinal blood flow has been shown to be successful with systemic intravenous tissue plasminogen activator (t-PA)⁸. Tissue plasminogen activator is a synthetic, clot-selective, fibrinolytic protein which converts plasminogen to plasmin, specifically in the presence of fibrin. Unfortunately, delivery via this route has been associated with severe haemorrhagic complications, including stroke and death. A new retinal procedure is being refined in which a microcannula is inserted next to the thrombus after retinal venipuncture. Then t-PA is injected causing thrombolysis of the clot⁹.

A chorioretinal anastomosis between a retinal vein and the choroid may bypass the occluded vein and relieve the venous obstruction. This may both decrease the likelihood of conversion of a non-ischaemic vein occlusion to an ischaemic status and diminish macular oedema, with consequent improvement in visual acuity¹⁰. A high-powered laser is used to disrupt the retinal vein wall and rupture the underlying Bruch's membrane¹¹. Complications of this procedure include choroidal or choroidovitreous

neovascularisation, pre-retinal fibrosis with or without vitreal detachment and vitreal haemorrhage^{12,13}.

Predisposing factors

The predisposing factors vary depending on the age of the patient with a vein occlusion. Most patients who develop this problem are over 50 years of age⁴. These patients may have generalised arteriosclerotic disease and often are found to have associated systemic hypertension, cardiovascular disease or diabetes mellitus. They may have elevated cholesterol or triglyceride levels, are presently smokers or have a recent history of quitting smoking. Some have other signs and symptoms of a possible vasculitis, such as temporal arteritis (**Table 1**)^{2,5}.

There is also a smaller and younger group (under 50 years of age) of patients who may present with venous obstruction. These patients do not neatly fit into the arteriosclerotic or thrombotic category as their older counterparts. These patients may have a family history significant for vascular disease, especially at a young age or may have an unusual clinical appearance upon presentation, i.e. bilateral simultaneous vein occlusion. These patients may have an underlying collagen vascular disease or some type of blood dyscrasia. Our ability to identify such underlying disease entities has vastly improved and these individuals warrant an appropriate work-up (**Table 2**). Examples of collagen-vascular disease, which may cause venous obstruction, include

Table 1
Work-up for patients with venous obstruction – patients over 50 years of age

Disorder	Testing
Hypertension	Blood pressure
Diabetes	Fasting blood sugar
Cardiovascular	Duplex ultrasonography
	Electrocardiogram
Hyperlipidemia	Cholesterol level
	Triglyceride level
Temporal Arteritis	Erythrocyte sedimentation rate
	C-reactive protein
	Complete blood count

Table 2
Work-up for patients with venous obstruction – patients under 50 years of age

Disorder	Testing
Scleroderma	Antinuclear antibody
Polyarteritis nodosa	Erythrocyte sedimentation
	Complete blood count
Lupus	Antinuclear antibody
	Anti-doublestranded DNA
Inflammatory phlebitis	Rapid Plasma Reagin
	Fluorescent Treponemal Antibody Absorption
	Chest X-ray
	Antinuclear antibody
Hyperviscosity	Complete blood count with differential
	Prothrombin time
	Partial thromboplastin time
Coagulation	Protein S deficiency
	Protein C deficiency
	Antithrombin III
	Factor V Leiden (Activated protein C resistance)
Dysproteinemia	Complete blood count
	Serum protein electrophoresis
Anti-phospholipid Syndrome	Lupus anticoagulant
	Anticardiolipin profile
Homocysteine	Plasma homocysteine
	Folate, vitamins B6 and B12 levels

temporal arteritis, scleroderma, polyarteritis nodosa, lupus erythematosus and inflammatory phlebitis^{2,5}.

Blood dyscrasias can result in hyperviscosity as a result of either an increased number of circulating cells (chronic leukaemias, polycythemia) or change in plasma proteins (Waldenstrom's macroglobulinemia, multiple myeloma). Genetic predisposition to venous thrombosis may cause increased levels of clotting factors VII and XI, and deficiency of specific anticoagulants such as protein S, protein C and antithrombin III. Activated protein C resistance and factor V Leiden recently have been described as the most common genetic predisposition to venous thrombosis⁵. Antiphospholipid antibodies and serum homocysteine elevation affect the coagulation homeostasis peripherally. Homocysteine levels are increased by dietary deficiency of folate and vitamins B6 and B12 and hence are potentially reversible. The treatment of hyperhomocystenemia is safe, readily available, and affordable, and vitamin supplementation has been shown to reduce homocysteine levels by up to 25%¹⁴.

Signs and symptoms

The most common presenting complaint is an abrupt decrease of central vision. Less frequently, patients may present with a history of transient obscuration of vision, lasting a few

seconds to minutes, with complete recovery to normal. These symptoms may recur over several days to weeks followed by a decrease in vision¹⁵. Metamorphopsia and visual field defects have also been described¹⁶.

Ophthalmoscopy will show dilated and tortuous veins, flame-shaped haemorrhages, dot-blot haemorrhages, retinal and macular oedema, and cotton-wool spots affecting the part of the retina drained by the obstructed vein or the whole fundus in a CRVO (Figures 1 and 2). With time, as the haemorrhages absorb, hard exudate formation will occur. Old vein occlusions show vascular sheathing, cholesterol crystal deposition and retinal pigment epithelial degeneration at the macula. Young patients especially seem to have a good ability to form secondary collaterals, thereby compensating for the occlusion. Collaterals develop between the retinal circulation and the ciliary vessels at the optic disc. Called optociliary shunt vessels, collaterals are sometimes so prominent and tortuous that they can be confused with optic disc neovascularisation (Figures 3 and 4)⁵. The two main vision threatening complications are neovascularisation and chronic macular oedema¹⁶.

Fundus fluorescein angiography of an acute CRVO will show a delayed arteriovenous transit time, which is the period from the time the dye is first seen in the retinal arterioles to the time it is first seen in the retinal veins. Intraretinal

haemorrhages will cause fluorescence blocking defects. Hypofluorescence is the result of areas that are not perfused. Ten or more of such areas of non-perfusion or capillary dropout result in the CRVO in being labelled as ischaemic (Figure 5). Less than 10 areas are found in the non-ischaemic CRVO.

If the haemorrhaging is extensive, it is often hard to calculate the amount of non-perfusion since the underlying fluorescence is hidden by the intraretinal blood. Diffuse leakage from the optic disc and retina is typical in later stage images of the angiogram. Neovascularisation of the disc is seen in about 10-15% of patients and leaks profusely late in the angiogram².

In BRVO, the fluorescein angiogram will show delayed filling in the involved branch vein in comparison to the other uninvolved veins. Fluorescein blocking defects can be seen in the involved quadrant from the intraretinal blood. Collateral vessels may develop between retinal capillaries in the affected area and nearby unaffected veins. If retinal neovascularisation develops, it will enhance prominently from the underlying leakage.

Patients with ischaemic CRVO more often develop iris neovascularisation and neovascular glaucoma than patients with BRVO. Conversely, patients with BRVO more often develop optic disc and retinal neovascularisation than patients with CRVO (Figure 6)⁵.



Figure 1
Central retinal vein occlusion with macular oedema



Figure 2
Supratemporal BRVO note cotton wool spots

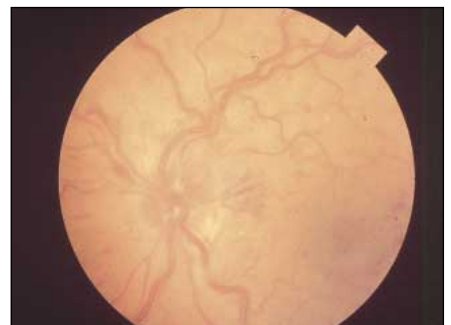


Figure 3
Central retinal vein occlusion



Figure 4
Same patient as in Figure 3. Four years later, optociliary shunt vessels can be seen on optic nerve head

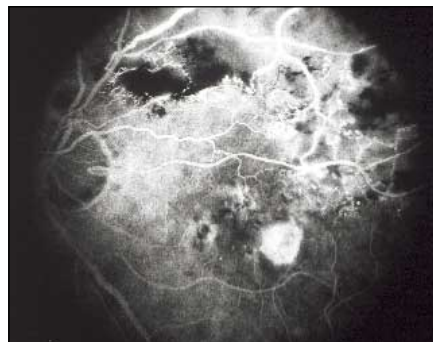


Figure 5
Fluorescein angiogram. Ischaemic vein occlusion with extensive capillary dropout



Figure 6
Superotemporal BRVO. Also visible is retinal neovascularisation, paramacular blot haemorrhage, inferior pre-retinal ("keel-shaped") haemorrhage

Management

The patients who can benefit from laser treatment with vein obstruction have been defined by both the Collaborative Branch Retinal Vein Occlusion Study (BVOS) and the Central Vein Occlusion Study (CVOS)¹⁷⁻²¹. All of these patients should undergo a fluorescein angiogram to outline the pattern of leakage, identify ischaemia, and help guide the laser photocoagulation application if it is indicated.

According to the BVOS, focal grid photocoagulation is recommended for chronic macular oedema with intact perfoveal capillary perfusion after at least three months' delay for spontaneous resolution of macular oedema. Laser is done if visual acuity is 20/40 to 20/200. Retreatment is recommended every three months if areas of leakage persist. Panretinal photocoagulation is done if there is retinal or iris neovascularisation. Patients with a branch retinal vein occlusion should be followed every one to two months for the first six months, then every three to 12 months if the haemorrhage clears.

A central retinal vein occlusion may be categorised by fluorescein angiography into perfused (non-ischaemic), non-perfused (ischaemic) or indeterminate. Approximately one third of initially non-ischaemic eyes, usually in the first four months, progress to an ischaemic status. All of these patients need to be followed monthly for the first six months, decreasing to once per year as the clinical condition stabilises. Gonioscopy is performed on each visit, looking for rubeosis.

The CVOS showed that there was no benefit of grid photocoagulation for macular oedema in older patients. However, there was a trend toward improved vision in patients younger than 65 years of age who were treated with focal grid laser for their chronic macular oedema. The CVOS also found that patients who develop intraocular neovascularisation benefit from laser panretinal photocoagulation. This treatment should be applied promptly to minimise the risk of developing neovascular glaucoma or vitreous haemorrhage.

Summary

Venous occlusive disease is second to diabetic retinopathy as the most common retinal vascular disease. Prompt diagnosis and timely referral for laser photocoagulation therapy will help patients avoid devastating complications such as neovascular glaucoma and chronic macular oedema. New, unique and promising techniques are on the near horizon in the more proactive treatment of venous occlusive disease.

About the author

Leonid Skorin Jr is a licensed optometrist and board-certificated ophthalmologist. He is fellowship-trained in neuro-ophthalmology. He has written numerous publications and has lectured internationally.

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