REVIEW ARTICLE

BRANCH RETINAL VEIN OCCLUSION

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Retinal vein occlusions (RVO) are the second commonest sight threatening vascular disorder. Branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO) are the two basic types of vein occlusion. Branch retinal vein occlusion is three times more common than central retinal vein occlusion and- second only to diabetic retinopathy as the most common retinal vascular cause of visual loss. The origin of branch retinal vein occlusion undoubtedly includes both systemic factors such as hypertension and local anatomic factors such as arteriovenous crossings. Branch retinal vein occlusion causes a painless decrease in vision, resulting in misty or distorted vision. Current treatment options don't address the underlying aetiology of branch retinal vein occlusion. Instead they focus on treating sequelae of the occluded venous branch, such as macular oedema, vitreous haemorrhage and traction retinal detachment from neovascularization. Evidences suggest that the pathogenesis of various types of retinal vein occlusion, like many other ocular vascular occlusive disorders, is a multifactorial process and there is no single magic bullet that causes retinal vein occlusion. A comprehensive management of patients with retinal vascular occlusions is necessary to correct associated diseases or predisposing abnormalities that could lead to local recurrences or systemic event. Along with a review of the literature, a practical approach for the management of retinal vascular occlusions is required, which requires collaboration between the ophthalmologist and other physicians: general practitioner, cardiologist, internist etc. as appropriate according to each case.

Keywords: branch retinal vein occlusion, hypertension, arteriovenous crossing, vein anterior.

INTRODUCTION

Retinal vascular occlusive disorder collectively constitutes one of the major causes of blindness and yet there is marked controversy on its pathogenesis, clinical features and particularly its management.[1,2] Early recognition and treatment are important to avoid potentially significant visual morbidity. Retinal vein occlusion is an obstruction of the retinal venous system by thrombus formation Its clinical picture was first described as retinal apoplexy.[3] Later on it was established as a clinical entity resulting from thrombosis.[4] Since that time the condition has been the subject of almost continuous research but nevertheless even today many points both in aetiology and intimate mechanism of obstruction are still un-elucidated.

INCIDENCE AND PREVALENCE

Retinal vein occlusion occurs with equal sex distribution. It occurs especially in middle-aged and older individuals with a history of systemic arterial hypertension, diabetes or generalized atherosclerotic disease.[5] Its incidence in the Australian population was 0.7% at 49–60 years and 4.6% at 80 years.[6] The prevalence of retinal vein occlusions has been shown to vary from 0.7% to 1.6%.[6]

TYPES

Retinal vein occlusion may develop at different sites and to varying extent. Depending on the location of occlusion it can be classified into occlusions of central vein, hemi central vein, major branch vein and macular branch vein.[7] BRVO and CRVO are the two basic types of vein occlusion. Relatively little information is available on the natural history of BRVO. In CRVO the main vein of the eye is occluded. CRVO is classically characterized by disc oedema, increased dilatation, tortuousity of retinal veins, widespread haemorrhages, cotton wool spots, retinal oedema and capillary non perfusion.[7] BRVO has similar features but they are confined to a portion of fundus.

DIAGNOSIS OF RETINAL VEIN OCCLUSION

Fundus photography and fluorescein angiography are useful tools in the diagnosis of retinal diseases. Fluorescein angiography is a widely used, minimally invasive procedure which provides the practitioner with information regarding the extent and location of disease. Although complications can occur, the procedure is generally accepted as reasonably safe.[8] The diagnosis of retinal vein occlusion is based on the fundoscopic finding of retinal vein dilatation in association with retinal haemorrhages and cotton-wool spots. The pathology can involve the entire venous system or can be limited to a branch of the central retinal vein.[7] Retinal vein occlusion can be distinguished clinically from diabetic retinopathy and other retinal diseases. There has been renewed interest in the orientation of crossing retinal vessels at arteriovenous intersections particularly as it relates to the risk of branch retinal vein occlusion.[9]

BRANCH RETINAL VEIN OCCLUSION

BRVO is amongst the most common retinal diseases seen in clinical practice. It is usually a disease of the

elderly age group with ninety percent of the patients being above the age of 50 years in a large series. Recognition of the disease is of paramount importance because its complications are a cause of significant visual morbidity. Epidemiological data from the Beaver Dam Eye Study suggest a prevalence and five-year incidence of 0.6% each.[10]

BRVO was first described by Leber in 1877.[11] In BRVO one of the branches of the main vein is blocked. It is defined as a segmental intraretinal haemorrhage not exceeding the midline caused by obstruction in the vein draining the corresponding retinal area. It is usually unilateral occurring bilaterally only in 9% of the patients.[12] It is three times more common than CRVO and second only to diabetic retinopathy as the most common retinal vascular cause of visual loss.[13] Clinically, patients with BRVO may complain of decreased vision or may be asymptomatic. Vision loss at presentation is related to the extent of macular damage from intraretinal oedema, haemorrhage or capillary non-perfusion.[14] The characteristic fluorescein angiographic findings in BRVO include delayed venous filling in the area of occlusion, capillary non-perfusion, and macular oedema in the acute phase, as well as micro vascular abnormalities in later stages.[15] More recently, serous macular detachment and sub retinal haemorrhage have been documented using optical coherence tomography.[16]

RISK FACTORS

The origin of BRVO undoubtedly includes both systemic factors such as hypertension and local anatomic factors such as arteriovenous crossings. Systemic risk factors for BRVOs include cardiovascular disease and hypertension.[17] Ocular risk factors include glaucoma and hyperopia.[17] Most people know high blood pressure and other vascular diseases pose risks to overall health, but many may not know that high blood pressure can affect vision by damaging veins in the eye. High blood pressure is the most common condition associated with BRVO.[18] Arterial hypertension, diabetes mellitus and hyperviscosity syndrome are among the thrombogenic factors.[19] The strong association with systemic atherosclerosis coupled with the observation that blockage usually occurs at the site of an arteriovenous crossing has led to the assumption that focal narrowing of the vein at the site of obstruction is the initiating factor inBRVO.[20] Various local factors that determine location of BRVO include inflammation, abnormalities of blood factors, angulation and narrowing of vein, number of arteriovenous crossings and presence of crossing in which artery is anterior to vein. Arterial compression of the vein is believed to be the main cause of BRVO.[21,22] Compression of the vein may lead to turbulent flow in the vein. The turbulent flow in combination with the pre-existing endothelial vascular damage from the different conditions creates a local environment favourable to intravascular thrombus formation.[23] Hypertension, diabetes mellitus, hyperlipidaemia and haematological disorders are important associated systemic conditions.[17] The presence of a particular systemic disorder does not necessarily mean cause and effect relationship with that type of retinal vein occlusion. It may well simply be a chance occurrence.[24]

PATHOPHYSIOLOGY

BRVO occurs at arteriovenous crossing site.[25,26] This observation is attributed to Leber, a German ophthalmologist over 100 years ago, who first suggested the vulnerability of arteriovenous crossing and the importance of arteriosclerosis in the pathogenesis of BRVO.[11] This observation has been reaffirmed many times since. The blocked venous branch can almost always be localized to a nearby arteriovenous crossing.[15] In the majority of retinal arteriovenous crossings within the eye the artery is situated anterior to the vein towards the vitreous cavity.[27] It was observed that venous over crossings occur at 30% of all crossings in the retinas of normal eyes.[28] Artery lies over the vein in 97% of arteriovenous crossings where BRVOs occur.[5] Both types of crossings have been demonstrated histologically.[29] Approximately 60% of normal arteriovenous crossings, artery lies anterior to vein and few crossings are affected by branch retinal vein occlusion.[21] Arterial over crossings are at relatively higher risk of BRVO than venous over crossings, and that the risk of BRVO in an eye is proportional to the number of arterial over crossings in the eye.[9] It is suggested that a crossing with artery lying anterior to the vein possibly be one of the risk factors of BRVO and the artery exerting mechanical pressure upon the vein be the main cause in the pathogenesis of BRVO. Mechanical narrowing of the venous lumen at this intersection is thought to play a pathoetiologic role in BRVO.[25] A monograph on BRVO was published in which it was observed that BRVO rarely occurs at crossing where vein crosses over the artery.[28] Two studies found that 2.4% or less of BRVOs occur at vein-anterior crossings.[9,26] The likelihood that the artery will lie anterior to the obstructed vein at the site of blockage in a BRVO is substantially greater than what would be expected by chance alone.[27]

Retinal artery and vein share a common adventitial sheath at the crossing site. This sheath may predispose this site to BRVOs.[30] At the AV crossing there is varying degrees of fusion of the vascular wall.[11] Venous compression by the relatively rigid artery may result in turbulent flow, endothelial damage, thrombosis and occlusion.[23] Histologically, the adventitia of the vessels fuse at the arteriovenous crossing site, while in some cases, the retinal artery and vein share a common media as they cross.[31] The incidence of arterial over crossing was significantly higher in the BRVO eyes.[22] Retinal branch

vein occlusion most often involves temporal retinal veins at the arteriovenous crossing. The precise cause is unknown. It was noted that two third of occlusions develop superotemporally and one third develops inferotemporally.[32] The predilection of BRVO for superotemporal quadrant was caused by greater number of crossings in this quadrant and location of macula temporal to disc. Up to two thirds of BRVOs occur in the superotemporal quadrant. This may be related to the increased number of arteriovenous crossings in this quadrant with respect to the rest.[33] Significantly more superotemporal quadrant crossings than inferotemporal quadrant crossings had the artery anterior to the vein. This suggested that variation in the pattern of arteriovenous crossings may have a role in the clinical distribution of branch retinal vein occlusion.[25] Upper temporal vascular arcade is more often involved than the lower temporal vascular arcade.[9] Most BRVOs involve the area inside the temporal vascular arcade whereas peripheral BRVOs are rarely seen.[34] Nasal occlusions are less likely to be diagnosed and are probably underreported because of their asymptomatic nature. Females have a higher risk than males because of their arterial over crossing ratio and BRVO prefer arterial over crossing. However the insignificant difference between the female and male patients led to the assumption that the effect of sex on BRVO cannot be explained only by local anatomical factors since their effect is only slight.[35] The pathogenesis of retinal branch vein occlusion and central retinal vein occlusion remain speculative. Evidences suggest that the pathogenesis of various types of retinal vein occlusion, like many other ocular vascular occlusive disorders, is a multifactorial process and there is no single magic bullet that causes retinal vein occlusion.

VISUAL EFFECTS

BRVO induces variable functional deficits depending on the grade of vascular occlusion and its localization. BRVO may lead to significant reductions of central and paracentral retinal function.[14] It causes a painless decrease in vision, resulting in misty or distorted vision. Its visual effects range from nil to severe visual loss. Multiple factors interplay in the pathogenesis of this visual loss, including macular oedema, macular haemorrhage, macular ischemia and foveal haemorrhage, vitreous haemorrhage, epiretinal membrane and retinal detachment.[36] Even if macular oedema occurs,[37] some of the BRVO eyes can attain good visual acuity. Over time, the retinal oedema and haemorrhage may resolve spontaneously with recovery of vision.

TREATMENT

Therapeutic armamentarium for functional improvement was very limited in the past for all types of retinal vein occlusions (branch, central and hemi-central retinal vein occlusion). Despite its frequency treatments for retinal vein occlusions are unsatisfactory and include several that have not been tested by large, well designed, prospective, randomized controlled trials. Current management is based on the recommendations of the Branch Vein Occlusion Study and newer evolving surgical techniques. Current treatment options don't address the underlying aetiology of BRVO. Instead they focus on treating sequelae of the occluded venous branch, such as macular oedema, vitreous haemorrhage and traction retinal detachment from neovascularization.[38] Sheathotomy, a surgical technique to separate the closely associated vessels at the arteriovenous crossing has been developed to treat macular oedema in an attempt to improve visual acuity.[39,40] Argon-laser-photocoagulation can prevent the development and treat neovascularizations successfully. Collateral vessels in branch retinal vein occlusion have a favourable effect on visual prognosis Careful laser treatment is recommended to avoid destroying collaterals in BRVO.[41] Since 1999 numerous reports on successful surgical techniques were published. It could be shown that the dissection of the adventitial sheath with separation of the artery from the vein at the arteriovenous crossing where branch retinal vein occlusion occurs can re-establish the retinal blood flow with reduction of macular oedema. But it is still unclear which step of the surgery,[42,43] Vitrectomy, internal limiting membrane peeling and sheathotomy is causative for the results. Arteriovenous sheathotomy[44,45] led to a transient improvement of the retinal blood flow and was effective in reducing macular oedema. It is not clear whether the transient effect of sheathotomy affects the long-term visual acuity and macular oedema. Off-label use of intra vitreous triamcinolone acetonide is being increasingly used for the treatment of macular oedema unresponsive to laser.[46,47] Two or four milligrams (0.05 or 0.1 ml, respectively) of triamcinolone acetonide (Kenalog, Bristol-Myers Squibb) is injected through the inferior pars plana under sterile conditions in the out patient clinic. Serial Optical Coherence Tomography is used as a rapid and less invasive way of monitoring the macular oedema improvement in visual acuity and macular oedema is probably secondary to stabilization of the blood-retinal barrier. Potential complications include infections,[48] sterile, or pseudo-endophthalmitis, elevated intraocular pressure, cataract formation, retinal detachment, and intraocular haemorrhage. Thrombolytic therapy applied systemically is limited due to serious side effects but may be helpful when injected intraocularly. The medical treatment of retinal vein occlusion is comprised of three main stages: identification and therapy of the detectable risk factors, specific treatment aimed at the occlusive form and treatment of retinal vein occlusion complications. Even though the possible medical management of retinal vein occlusion includes several treatments, the most interesting approaches have been: anticoagulant/anti-aggregating agents, troxerutin,

corticosteroid, fibrinolytic/thrombolytic agents, and haemodilution. Overall, the medical approach to retinal vein occlusion is still awkward and unsatisfactory. Randomized clinical trials are needed to assess the degree of efficacy of the medical treatment of the specific forms of retinal vein occlusion.[49] Retinal vascular occlusions may result of loco-regional ocular causes. They more often occur in patients with cardiovascular pathologies or risk factors, or sometimes other systemic diseases that need to be recognized for a proper treatment. Therefore, a comprehensive management of patients with retinal vascular occlusions is necessary to correct associated diseases or predisposing abnormalities that could lead to local recurrences or systemic event.[50] Along with a review of the literature, a practical approach for the management of retinal vascular occlusions is required, which requires a collaboration between the ophthalmologist and other physicians: general practitioner, cardiologist, internist... as appropriate according to each case.

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