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Etiology and Management of Branch Retinal Vein Occlusion

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Abstract: Retinal vein occlusion is one of the vascular disorders affecting vision. Branch retinal vein occlusion and central retinal vein occlusion are the two basic types of vein occlusion. Branch retinal vein occlusion is three times more common than central retinal vein occlusion and is second only to diabetic retinopathy as the most common retinal vascular cause of visual impairment. The origin of branch retinal vein occlusion includes systemic factor-hypertension and local anatomic factor-arteriovenous crossings. Branch retinal vein occlusion results in misty or distorted vision. Retinal vein occlusion is a multifactor process. There is no single magic bullet that cures retinal vein occlusion. A comprehensive management of patients with retinal vein occlusion is necessary to correct associated diseases or predisposing abnormalities that could lead to local recurrences or systemic event. This paper reviews the etiology and treatment of retinal vein occlusion and recommends the collaboration between other branches for its management.

Key words: Branch retinal vein occlusion . Hypertension . Arteriovenous crossing . Vein anterior . Vein posterior

Abbreviations: CRVO: Central Retinal Vein Occlusion . BRVO: Branch Retinal Vein Occlusion . RVO: Retinal Vein Occlusions

INTRODUCTION

Retinal Vascular Occlusive (RVO) disorder collectively constitutes one of the major causes of blindness and yet its pathogenesis, clinical features and particularly its management is not well understood [1, 2]. Early diagnosis and treatment are important to avoid visual morbidity. RVO is an obstruction of the retinal venous system by thrombus formation. First described as retinal apoplexy [3] it was later established as a clinical entity resulting from thrombosis [4]. Since that time the condition has been the subject of almost continuous research. However, the etiology and mechanism of obstruction is still not well understood.

INCIDENCE AND PREVALENCE

The occurrence of RVO in male and female populations is evenly distributed. RVO occurs especially in middle-aged and older individuals with a history of systemic arterial hypertension, diabetes or generalized atherosclerotic disease [5].

TYPES

Retinal vein occlusion may develop to varying extent at different sites. 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 [6]. Branch Retinal Vein Occlusion (BRVO) and Central Retinal Vein Occlusion (CRVO) are the two basic types of vein occlusion. In CRVO (Fig. 1) the main vein of the eye is occluded. CRVO is classically characterized by disc edema, increased dilatation, tortuousity of retinal veins, widespread hemorrhages, cotton wool spots, retinal edema and capillary non perfusion [6]. BRVO has similar features but they are confined to a portion of fundus [5].

DIAGNOSIS OF RETINAL VEIN OCCLUSION

Fundus photography [7] and fluorescein angiography [7] are useful tools in the diagnosis of retinal diseases. Fluorescein angiography is a widely used, non-invasive and reasonably safe procedure for

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Fig. 1: Fundus photograph of right eye showing crvo

the detection and localization of the disease. The diagnosis of retinal vein occlusion is based on the fundoscopic finding of retinal vein dilatation in association with retinal hemorrhages and cotton-wool spots. The pathology can involve the entire venous system or can be limited to a branch of the central retinal vein [6] Retinal vein occlusion can be distinguished clinically from diabetic retinopathy and other retinal disease [16]. There has been renewed interest in the orientation of crossing retinal vessels at arteriovenous intersections particularly as it relates to the risk of BRVO (Fig. 2) [8].

BRANCH RETINAL VEIN OCCLUSION (BRVO)

BRVO is amongst the most common retinal diseases seen in clinical practice. It is a disease of the elderly age group with 90% of the patients older than 50 BRVO was first described by Leber in 1877 [9]. One of the branches of the main vein is blocked in BRVO. It is defined as a segmental intra-retinal hemorrhage, not exceeding the midline, caused by obstruction in the vein draining the corresponding retinal area. It is usually unilateral, but occurs bilateral only in 9% of the patients [10] (Table 1).

BRVO is three times more prevalent than CRVO and second only to diabetic retinopathy as the most common retinal vascular cause of visual loss [11]. Clinically, patients with BRVO may complain of decreased vision or may be asymptomatic. Vision loss is related to the extent of macular damage from intra-retinal edema, hemorrhage or capillary non-perfusion [12]. The characteristic fluorescein angiographic findings in BRVO include delayed venous filling in the area of occlusion, capillary non-perfusion and macular edema in the acute phase, as well as micro vascular abnormalities in later stages [13].

RISK FACTORS

The origin of BRVO undoubtedly includes both systemic factors such as hypertension (Table 2) and local anatomic factors such as arteriovenous crossings. Systemic risk factors for BRVOs include cardiovascular disease and hypertension [14]. Ocular risk factors include glaucoma and hyperopia [14]. High blood pressure is the most common cause for BRVO [15]. Arterial hypertension, diabetes mellitus and hyper-viscosity syndrome are among the thrombogenic factors that are reported to be responsible for BRVO [16]. The strong association of BRVO with systemic atherosclerosis and the observation that blockage usually occurs at the site of an arteriovenous crossing has led to the postulation that focal narrowing of the vein at the site of obstruction is the initiating factor for BRVO [17]. Factors that determine location of BRVO include inflammation, abnormalities of blood factors, angulations 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 [19]. Compression of the vein may lead to turbulent flow in the vein. The turbulent flow in combination with the preexisting endothelial vascular damage from the different conditions creates a local environment favorable to intravascular thrombus formation [20]. Hypertension, diabetes mellitus, hyperlipidaemia and haematological disorders are important associated systemic conditions [21]. The presence of a particular systemic disorder does not necessarily reflect the 'cause and effect relationship' with that type of retinal vein occlusion. It could be a chance occurrence [24].

Table 1: Number o f subjects and associated diseases

Associated diseases	Patients
Hypertension	57 (81.4%)
Diabetes	2 (2.85%)
Diabetes and hypertension	7 (10%)
No disease	4 (5.7%)

Table 2: Comparison of features of arteriovenous crossings

	Eyes	Determinable crossings	Arterial overcrossings N (%)	Venous overcrossings N (%)
Brvo sites	72	65	63 (96.1%)	2 (3.1%)
Brvo eyes	72	283	197 (69.6%)	86 (30.4%)
Fellow eyes	68	271	164 (60.5%)	107 (39.4%)

p-value (venous and arterial overcrossings) Brvo sites v/s fellow eyes.oo1

p-value (venous and arterial overcrossings) Brvo eyes v/s fellow eyes.o25

Using test of proportion(chisquare) for comparison between affected eye and fellow eye

PATHOPHYSIOLOGY

BRVO occurs at arteriovenous crossing site [22, 23]. This observation is attributed to Leber, a German ophthalmologist, who over 100 years ago first suggested the vulnerability of arteriovenous crossing and the importance of arteriosclerosis in the pathogenesis of BRVO [9]. This observation has been reaffirmed by recent studies. The blocked venous branch can almost always be localized to a nearby arteriovenous crossing [8]. In the majority of retinal arteriovenous crossings within the eye the artery is situated anterior to the vein towards the vitreous cavity [18]. It was observed that venous over crossings occur at 30% of all crossings in the retinas of normal eyes [19]. Artery lies over the vein in 97% of arteriovenous crossings where BRVOs occur [19]. Both types of crossings have been demonstrated histologically [26]. Approximately in 60% of normal arteriovenous crossings, artery lies anterior to vein and few crossings are affected by branch retinal vein occlusion [23]. 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 (Table 3).

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 patho-etiologic role in BRVO [20]. Two studies found that 2.4% or less of BRVOs occur at vein-anterior crossings [19].

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 [23]. Retinal artery and vein share a common adventitial sheath at the crossing site. This sheath may predispose this site to BRVOs [33]. There is varying degrees of fusion of the vascular wall at the AV crossing [30]. Venous compression by the relatively rigid artery may result in turbulent flow, endothelial damage, thrombosis and occlusion [31]. Histologically,

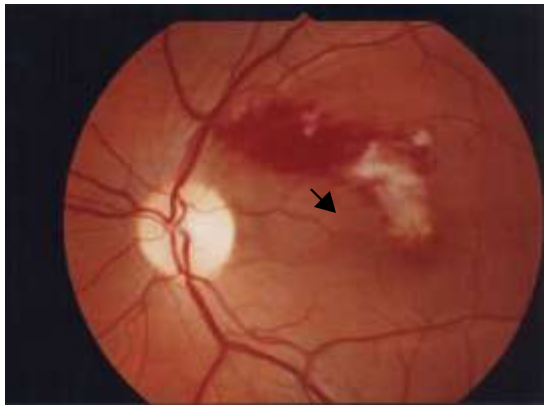

Fig: 2: Fundus photograph of left eye showing superotemporal brvo with artery over vein

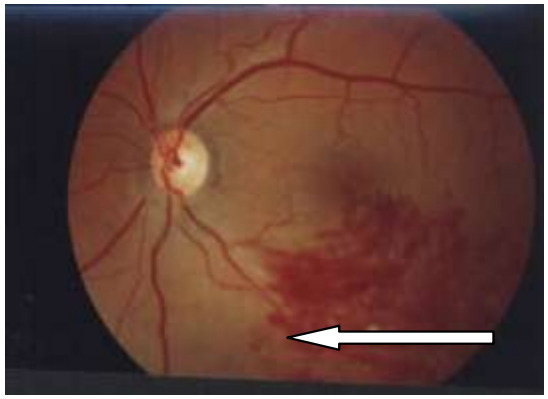

Fig. 3: Fundus photograph showing inferotemporal brvo with vein over artery

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 [35]. The incidence of arterial over crossing was significantly higher in the BRVO [31]. 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 supero-temporally and one third develops infero-temporally [22]. The predilection of BRVO for supero-temporal 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 supero-temporal quadrant. This may be related to the increased number of arterio-venous crossings in this quadrant with respect to the rest [24]. Significantly more supero-temporal quadrant crossings than infero-temporal 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 [24]. Upper temporal vascular arcade is more often involved than the lower temporal vascular arcade [20]. Most BRVOs involve the area inside the temporal vascular arcade whereas peripheral BRVOs are rarely seen [30]. Nasal occlusions are less likely to be diagnosed and are probably less reported because of their asymptomatic nature. Females have a higher risk of RVO than males because of their arterial over crossing ratio However, this cannot be explained by local anatomical factors only [32]. The pathogenesis of retinal branch vein occlusion and central retinal vein occlusion still remains speculative. Evidences suggest that the pathogenesis of various types of RVO like many other ocular vascular occlusive disorders, is a multifactor process and there is no single cause for RVO.

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 [12]. 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 edema, macular hemorrhage, macular ischemia and foveal hemorrhage, vitreous hemorrhage, epi-retinal membrane and retinal detachment [44]. Even if macular edema occurs [33], some of the BRVO eyes can attain good visual acuity. Over time, the retinal edema and hemorrhage may resolve spontaneously with recovery of vision.

TREATMENT

Therapeutics for improvement of RVO has limited success in the past for all types of retinal vein occlusions (branch, central and hemi-central retinal vein occlusion). Current management is based on the recommendations of the BRVO study and surgical techniques. Treatment options don't address the underlying etiology of BRVO. Instead focus on treating sequelae of the occluded venous branch, such as macular edema, vitreous hemorrhage

SURGICAL TREATMENT

Sheathotomy, a surgical technique to separate the closely associated vessels at the arteriovenous crossing has been developed to treat macular edema in an attempt to improve visual acuity [35, 36]. 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 edema. Arteriovenous sheathotomy [38, 39] led to a transient improvement of the retinal blood flow and was effective in reducing macular edema. Collateral vessels in branch retinal vein occlusion have a favorable effect on visual prognosis [37]. Argon-laser-photocoagulation can prevent the development and treat neo-vascularization.Off-label use of intra vitreous triamcinolone acetonide is being increasingly used for the treatment of macular edema unresponsive to laser [40, 41]. 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.Thrombolytic therapy applied systemically is limited due to serious side effects but may be helpful when injected intra-ocular.

MEDICAL TREATMENT

The medical treatment [42] 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.

CONCLUSION

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 [43].

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