INTRODUCTION

Ocular vascular occlusive disorders collectively constitute the most common cause of visual disability[1]. Retinal vein occlusion (RVO) is the second most common retinal vascular disorder after diabetic retinopathy and is considered to be an important cause of visual loss[2,3].

While the exact pathogenesis of RVO remains unclear and controversial, it has been suggested that multiple factors including local anatomical susceptibility, degenerative changes of the vessel wall and abnormal hematological abnormalities may all contribute to the development of vascular obstruction. While arterial disease is considered to be the predominant aetiology in both central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO), the other risk factors are different in both presentations.

LOCAL ANATOMICAL SUSCEPTIBILITY

In CRVO, obstruction of retinal blood flow in the region of lamina cribrosa and just posterior of it occur as a result of different contributing factors. Unique anatomical features of CRVO in the region of lamina cribrosa may predispose to obstruction.

Central retinal artery and central retinal vein share a common adventitial sheath at the lamina cribrosa. The central retinal vein could be compressed by right next to artery especially in eyes with arteriosclerotic vascular disease. Rigid and hyperplastic arteriosclerotic artery wall causes mechanical narrowing of thin-walled vein[4]. High blood velocities in the CRVO also lead to endothelial cell damage, endothelial proliferation and possible thrombus formation[5]. Narrowing of central venous lumen and

ABSTRACT

Retinal vein occlusion (RVO) has multiple pathogenetic mechanism that including local anatomical susceptibility, degenerative changes of the vessel wall and abnormal hematological abnormalities. All of these mechanisms could contribute to develop vascular obstruction. Anatomic features of arteriovenous crossings and common adventitial sheath shared by artery and vein could cause turbulent flow. Turbulence in vessel flow promotes endothelial phenotypic changes that cause endothelial f-actin expression increase. Intercellular adhesions and endothelial functions are affected by high f-actin levels. Damaged arteries and hypoxic tissues express endothelin-1 (ET-1). Endothelin-1 can diffuse from the neighboring veins and stimulate venous vasoconstriction. Vasoconstriction of veins lead to an increase in pressure. High blood viscosity is another important factor in pathogenesis of RVO. Pathogenesis of RVO is very complex and these factors can lead to a vicious cycle of worsening the other factor.

Key words: Central; Branch; Retinal vein occlusion; Endothelial dysfunction

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turbulent flow in this region results occlusion at the lamina cribrosa. The association between BRVO and arteriovenous (A/V) crossing was first reported by Koyanagi in 1928[1]. Branch RVOs occur almost invariably at a site where the artery crosses over the vein. In approximately 60-70% of eyes that are unaffected by BRVO the artery has been reported to be anterior to the vein whereas in 98-99 % of eyes with BRVO it crosses the vein[9-11].

Anatomic features of A/V crossings and secondary effects of arteriolar sclerosis may prone the crossing site to venous occlusion. The thin-walled vein lies between the rigid thick-walled artery and the highly cellular retina in the majority of A/V crossings. Common adventitial sheath shared by artery and vein and the narrowing of the venous provide the setting for BRVO[12-14]. Increased rigidity of the crossing artery induced by arteriolar sclerosis may increase the risk of occlusion. Studies investigating the vulnerability of A/V crossing sites to BRVO have reported focal thickening of the venous basement membrane and hyperplasia of extracellular matrix and adventitia at A/V crossings[15-19].

However, an additional pathogenic mechanism has recently been postulated for development of venous occlusion. Atherosclerotic arteries may be producing increased endothelin-1 (ET-1), which may diffuse across to the neighboring vein, stimulating venous vasoconstriction[19] and increase retinal venous pressure[20]. While vascular endothelial cells produce ET-1 under a physiological condition but also all cells under stress produce ET-1. Potential sources of ET-1 could be systemic circulation , diseased artery and hypoxic neighboring tissue[20].

It was assumed that ocular perfusion pressure decreases progressively as a result of increased retinal vein pressure. If the critical limit for perfusion pressure is exceeded, hypoxic retina could secrete more ET-1 .There would be dangerous vicious cycle that causes retinal hemorrhages and retinal edema[21-24].

DEGENERATIVE CHANGES OF THE VESSEL WALL

It has recently been postulated that retinal and choroidal endothelial cells has functional and structural site (like geometrics, phenotype and intracellular cytoskeleton) specific heterogeneity. Possible relationship between the site specific changes of vascular endothelial phenotype and endothelial dysfunction have been investigated in many literature. The endothelium is subjected to the mechanical forces due to shear stress related to blood flow. Endothelial cells converts these mechanical signals into chemical signals and it starts a series of signal transduction pathways and differentiation in endothelial cell phenotype. Endothelial phenotypic heterogeneity is a core property of the endothelium and has been described at the endothelial cell phenotype. Endothelial phenotypic heterogeneity starts a series of signal transduction pathways and differentiation in endothelial cells in prelaminar region were transiently changed cause endothelial phenotype changes localizations of CRVO. Both environmental and genetic factors may cause endothelial phenotype changes[25]. Polygonal morphology of endothelial cells in prelaminar region were transiently changed to spindle shaped in the lamina cribrosa. Lamina cribrosa region is the site of greatest endothelial phenotypic changes identify. In patients with vascular comorbidities, endothelial f-actin expression also increases in central retinal vein[26]. The force transduction mechanisms in endothelial cells are a combination of force transmission via cytoskeletal elements and transduction of the physical forces to biochemical signals at mechanotransducer sites. F-actin microfilaments are basic structure at transmission and transduction. Endothelial f-actin intercellular adhesions and regulate the effect of endothelial cells on external mechanical forces induced internal mechanical stress. All these changes are suggested as part of high hemodynamic force in lamina cribrosa region contributing to CRVO.

HEMATOLOGICAL DISORDERS

Two main hematological disorders in the pathogenesis of BRVO are dysregulation of the thrombosis-fibrinolysis balance and conditions leading to high blood viscosity[26-28]. They create more favorable environment to intravascular thrombus formation and venous occlusion. Association between BRVO and hyperviscosity due to high hematocrit was demonstrated in literature[28-31]. Results of published studies conflicting and the role of coagulation factors in the development of RVO is not fully understood.

CONCLUSION

Pathogenesis of RVO is complex and multifatorial. Different anatomical, vascular and inflammatory factors may contribute to its pathophysiology.

COMPETING INTERESTS

The authors declare that there is no conflict of interest regarding the publication of this paper.

REFERENCES

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