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Branch Retinal Vein Occlusion and Serum Homocystein Level

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Abstract: ***This article delves into the intricate relationship between elevated homocysteine levels and Branch Retinal Vein Occlusion BRVO, a prevalent retinal vascular disease. Focusing on a study of 10 patients aged between 50 and 70 years, diagnosed with BRVO, it evaluates the implications of homocysteine in the pathogenesis and management of this condition. The study highlights how systemic conditions like hypertension, diabetes, and hyperlipidemia contribute to arteriosclerosis, thereby affecting BRVO development. It also examines the impact of homocysteine on endothelial cell damage and Vascular Endothelial Growth Factor VEGF activation, and the role of vitamins like folate, B6, and B12 in mitigating homocysteine levels. The findings from the patient group, including variations in visual outcomes and the effectiveness of treatments like anti-VEGF injections and vitamin supplementation, offer critical insights into the potential for therapeutic interventions in managing BRVO. This comprehensive analysis underscores the need for further research to establish a definitive link between homocysteine levels and retinal vein occlusions, potentially paving the way for innovative treatment strategies.***

Keywords: Retinal Vein Occlusion, Homocysteine, BRVO, Endothelial Damage, Vitamin Supplementation

1. Introduction

Retinal venous occlusion (RVO) is one of the most common retinal vascular diseases, second only to diabetic retinopathy. BRVO is the most common type of RVO with a prevalence which has been shown to vary from 0.7% to 1.6%affecting both men and women equally.[1]

BRVO is divided into two distinct entities based on anatomical location - Major BRVO, when one of the major branch retinal veins which supplies an entire quadrant is occluded, and macular BRVO, when one of the macular venules is occluded. In 66% of eyes with BRVO, there is occlusion of the major branch in the supero-temporal quadrant, followed by 22-43% of eyes with occlusion of the major branch in the inferotemporal quadrant.[2]

Major BRVO can be asymptomatic or with visual blurring, usually involving the sector of visual field corresponding to the area of the retina involved. In macular BRVO, there is always a central visual disturbance with normal peripheral vision.[3]

RVOs can be further characterized as *non-ischemic* (*i.e.*, perfused) or *ischemic* (*i.e.*, non-perfused) depending on the status of retinal perfusion.[4]

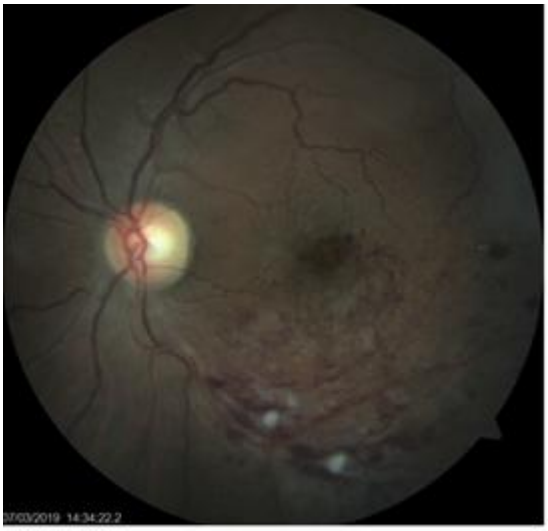
Although the exact mechanism of BRVO has not been completely elucidated, BRVO is thought to follow the principle of Virchow's triad for intravascular thrombus formation, such that there is endothelial damage, hemodynamic changes in blood flow, and hypercoagulability. The majority of patients with BRVOs have an underlying systemic arterial disease orchronic conditions such as hypertension, diabetes mellitus, and hyperlipidemia resulting in arteriosclerosis, a process that is characterized by thickening and hardening of the arterial wall with a loss of elasticity. Prothrombotic conditions, including hyperviscosity syndromes, vasculitides, and hypercoagulable states, such as hyperhomocysteinemia, Anti-cardiolipin antibodies are also considered important risk factors to the development of BRVOs.[5]

Elevated serum homocysteine, is a well-documented risk factor for peripheral, cardiac and cerebrovascular diseases, has recently been shown to be a risk factor for retinal venous occlusion also. Homocysteine, a metabolic product of methionine, can be converted back to methionine or cysteine via remethylation or transulfuration. The conversion of methionine to cysteine is the most significant metabolic pathway to reduce homocysteine concentration. Enzyme methylene tetrahydrofolate reductase deficiency is identified as a potential source for hyperhomocysteinemia. Elevated homocysteine leads to atherosclerosis and thromboembolism by endothelial cell damage and VEGF activation. Folate, B6, B12 are inversely related to homocysteine levels.[6]

We studied 10 patients in the age group of 50 -70 years, who presented to the ophthalmology OPD and were diagnosed with BRVO. Three out of the 10 patients had complaints of diminution of vision over a period of 1 to 2 months and a vision less than 6/24. The rest had a vision of 6/9 – 6/6 and had come for a regular ophthalmic check-up. On ophthalmological evaluation, anterior segment was normal in all patients and on fundus examination were found to have a BRVO. 7 had a supero-temporal BRVO [figure2]and 3 had an infero-temporal [figure1]. The three symptomatic patients had BRVO which were associated with macular oedema[figure3& 4] and the rest were an incidental finding. All patients underwent an extensive screening including blood pressure check, lipid profile, blood sugar levels (FBS, PPBS, HbA1c), Serum homocysteine levels, macular OCT.

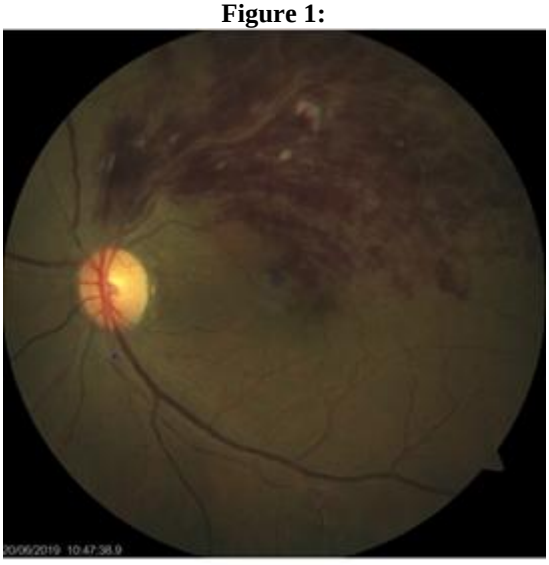
4 patients had normal homocysteine levels and the remaining 6 cases had elevated homocysteine. Visual outcome was not compared to homocysteine level in these patients due to variables like presence or absence of macular oedema, macular ischemia and the specific location of the branch occluded, which influence the visual outcome. The 3 patients with macular oedema were given 2 intravitreal anti-

VEGF injections over a period of 2 months and a significant improvement in visual acuity was noticed. The six patients with raised serum homocysteine levels were started on CapsuleHomocheck (folate and B12) for 1 month. There was spontaneous resolution of the BRVO in remaining seven patients.



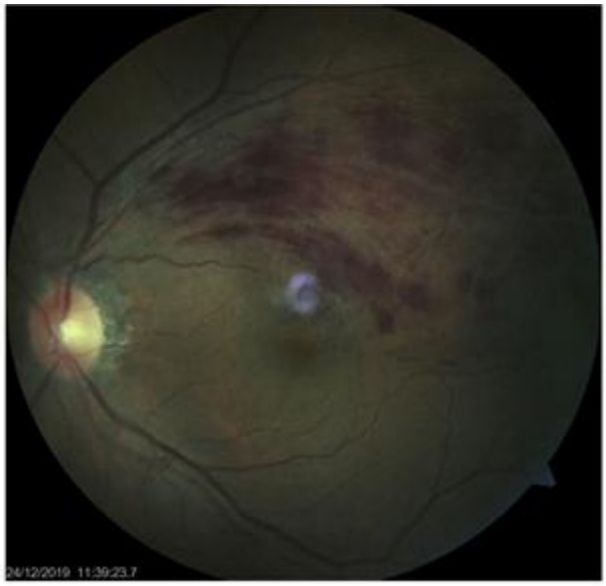
INFEROTEMPORAL BRVO

Figure 1:



SUPEROTEMPORAL BRVO

Figure 2:



SUPEROTEMPORAL BRVO WITH MACULAR EDEMA

Figure 3

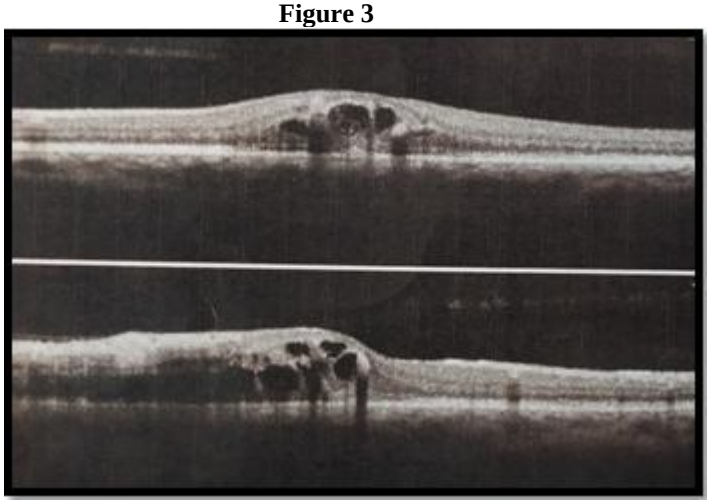


Figure 4: Cystoid Macular Edema on OCT

2. Discussion

The relationship between homocysteine and other vascular disease has been well documented and many studies support a similar relationship for ocular vascular disease. The etiology of elevated serum homocysteine is multifactorial. Homocysteine is a metabolite of methionine. It can be converted back to methionine or to cysteine via remethylation or transulfuration, respectively. The conversion to methionine or cysteine is the most significant metabolic pathway to reduce homocysteine concentrations. The enzymemethyelenetetrahydrofolate reductase is needed for remethylation of homocysteine and has been blamed as a potential source for hyperhomocystinemia.[7]The genetically determined thermolabile variant of methyelenetetrahydrofolate reductase, which exerts less enzymatic activity and therefore is associated with elevated homocysteine, has received considerable attention because the mutation is fairly common in the general population. The most important nutritional factors include the vitamins folate, B6 (pyridoxine), and B12 (cyanocobalamin) because homocysteine levels are inversely related to blood levels for each vitamin. Folate is required to remethylate homocysteine to methionine. Vitamin B6 is required for conversion of

homocysteine to cysteine by the enzyme cystathionine ß-synthase, for which vitamin B6 acts as a co-factor. Vitamin B12 is a co-factor for methionine synthase, which helps in the conversion of homocysteine to methionine. A 6 week intake of folate and B12 in doses of 0.5 mg each has been demonstrated to reduce homocysteine by 25% and 7%, respectively, by the Homocysteine Lowering Trialist's Collaboration. In a study by Lobo et al, low dose folic acid (400 µg) combined with B6 and B12 lowered homocysteine levels by 30%. The reduction was similar to that found in patients taking 1 mg and 5 mg folic acid supplements.[7]

The exact mechanism by which homocysteine affects the vascular system is poorly understood. Previous studies have demonstrated that homocysteine decreases production of prostacyclin, nitric oxide and thrombomodulin production by endothelial cells. In addition, endothelial cell damage leading to thrombi formation occurs by the generation of oxygen free radicals during the oxidation of homocysteine. Finally, the actual proliferation of smooth muscle cells and inhibition of vascular endothelial cell growth that occurs with elevated homocysteine has been demonstrated.[8,9]

Treatment of hyperhomocystinemia is relatively simple, safe and inexpensive with dietary supplementation of folate in combination with vitamins B6 and B12. Therapeutic studies are required to determine if lowering homocystiene with vitamin supplementation will decrease future risk of retinal vein occlusions.[10]

3. Conclusion

Patients presenting with such kind of clinical picture should be investigated thoroughly to rule out any modifiable risk factor such as hyperhomocysteinemia to prevent any further vaso-occlusive event. It may also be considered that serum homocysteine levels be made a part of the routine screening in patients over the age of 50 years who are suffering from diabetes and hypertension, in an attempt to prevent the development of retinal venous occlusions. Therapeutic studies are required to determine if lowering homocystiene with vitamin supplementation will decrease future risk of retinal vein occlusions.

References

[1] Megan L. Cochran; NavidMahabadi; Craig N. Czyz.Branch Retinal Vein Occlusion (BRVO). StatPearls [Internet]
[2] Jiri Rehak, MatusRehak. Branch Retinal Vein Occlusion: Pathogenesis, Visual Prognosis, and Treatment Modalities.Curr Eye Res. 2008 Feb; 33(2): 111–131.
[3] Musa Abdelaziz, Mahdi Rostamizadeh, Baseer Ahmad.Branch retinal vein occlusion. AAO.
[4] Brittni A. Scruggs, Tyler S. Quist, Olga Kravchuk, Elliott H. Sohn. Branch Retinal Vein Occlusion. Ophthalmology and visual sciences.
[5] Branch Retinal Vein Occlusion: Classification and Treatment. International Journal of Ophthalmology. May 2009;223(5):298-305.
[6] Kapil D. Lahiri, Jayanta Dutta, Himadri Datta, and Harendra N. Das. Hyperhomocysteinemia, as an Independent Risk Factor for Retinal Venous Occlusion in an Indian Population. Indian J Clin Biochem. 2013 Jan; 28(1): 61–64.
[7] Lobo A, et al. Reduction of homocysteine levels in coronary artery disease by low-dose folic acid combined with vitamins B6 and B12.Am J Cardiol. 1999 Mar 15;83(6):821-5.
[8] Fahad Al Wadani, Rajiv Khandekar, Gigani Salim, Mohammed Al Ali, Salman Ramzi. Hyperhomocysteinia is a risk factor for retinal venous occlusion: A case control study. Indian J Opthalmol.2014;62:291-4.
[9] Sayli Mahesh Gavaskar, Vijay Karambelkar, Mihir Anil Paranjpe.Retinal Venous Occlusive Diseases and Study of their Risk Factors. International Journal of Contemporary Medical Research. July 2019;6(7).
[10] Petr Kolar. Risk Factors for Central and Branch Retinal Vein Occlusion: A Meta-Analysis of Published Clinical Data. Journal of Ophthalmology.2014.