Case Report

Central Retinal Vein Occlusion in young with Hyperhomocysteinemia – A Case Report and Review of Literature

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Abstract

We present a case of unilateral non-ischemic CRVO in a 22 year male without hypertension, diabetes and open angle glaucoma. Laboratory tests including complete coagulation profile and thrombotic workup were negative, except for raised serum homocysteine level(23.03 µmol/L). The patient was given vitamin supplements for 8 weeks to control homocysteine levels and a single intravitreal bevacizumab injection was given to treat macular edema. The vision and macular thickness improved to normal at 8 weeks, with no recurrence or new cardiovascular complications over a follow-up of one year. We also reviewed the literature and found hyperhomocysteinemia to be a important risk factor for CRVO in the young, and vitamin supplements help in quicker recovery and can prevent recurrence.

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Introduction

Retinal vein occlusion (RVO) is one of the most common retinal vasculopathy causing blindness, second only to diabetic retinopathy. It typically affects old individuals with associated risk factors, such as vascular disease, hypertension and glaucoma.[1] RVO is uncommon in younger adults, under 40 years of age and occur with unusual causes such as hypercoagulability disorders, collagen vascular diseases, lymphoproliferative disorders, malignant hypertension, medications (most notably oral contraceptives and isotretinoin), and trauma.[2-11] So, a comprehensive workup is needed in a young patient with CRVO. The role of hyperlipidemia and hyperhomocysteinemia has been evaluated in some studies as a risk factor for RVO of the young, wih contradictory results.[12-14]

We report a case of CRVO in a young patient with elevated serum homocysteine, with an excellent outcome. We also reviewed the literature on the relationship of hyperhomocysteinemia and CRVO of young.

Case Report

A 22-year-old student presented in Out Patient Department (OPD) of a tertiary care hospital with the complaint of sudden onset decreased visual acuity (VA) in his right eye for 25 days. There was no pain, redness and discharge. The patient had no previous systemic or ocular medical history and did not use any medication.

His best corrected VA was 20/150 OD and 20/20 OS. His intraocular pressure was 14 mm Hg OD and 12 mm Hg OS. The range of ocular movements was full, and there was no relative afferent pupillary defect. In both eyes, the anterior segments were normal. Fundus examination of the right eye showed a swollen and hyperemic disc, numerous retinal hemorrhages all over the fundus, tortuous and dilated retinal vasculature and macular edema (ME) (Figure 1), while fundus of the other eye was normal (Figure 2). Fundus fluorescein angiography demonstrated disc leakage with areas of blocked fluorescence due to retinal hemorrhages. Capillary non-perfusion areas were not observed (Figure 1). ÓCT showed increased central macular thickness (CMT) with irregular foveal contour in the right eye (Figure 1). He was diagnosed with CRVO in young.

The workup included a normal complete hemogram (Hb-14.1 gm percent, MCV-93.1 fl, MCH- 31.3 picogram, MCHC-33.7 gm/dl, TLC- 7400 mg/dl, Platelet count- 1.8 Lakhs/cumm), lipid profile and coagulation tests (PT-12 sec and PTT-30 sec, INR- 0.98). The erythrocyte sedimentation rate was normal (18 mm/h), and a complete collagenogram, including the serum rheumatic factor, serum antinuclear antibodies (ANA) and serum antineutrophil cytoplasmic antibodies were also normal. Serum homocysteine level was 23.03 µmol/L,which was significantly higher than the normal range of 6-15 µmol/L.

The patient was treated with one intravitreal injection of bevacizumab (1.25 mg/0.05 ml) in the right eye and oral multivitamins to control serum homocysteine level. VA improved to 20/20 at 2 months follow-up and the homocysteine level also returned to normal i.e. 13 µmol/L. The retinal haemorrhages got resorbed significantly (Figure 3) and CMT decreased (Figure 3). At 6 months follow up, the fundus examination was normal, CMT was 215 µm with the restoration of a normal macular architecture. The patient was followed for an additional one year with no recurrence. Intraocular pressure remained normal with no evidence of NVE/NVI/NVA on all follow up examinations.

Discussion

CRVO is increasingly being recognized in younger patients and elevated serum homocysteine is a potential risk factor for the disease.[13-21] There is a significant contradictory evidence regarding the role of homocysteine in CRVO in literature.[22-29]

Homocysteine is a sulfur-containing amino acid with a free thiol (sulfhydryl; SH) group, formed from methionine in blood and its metabolism is dependent on vitamins or

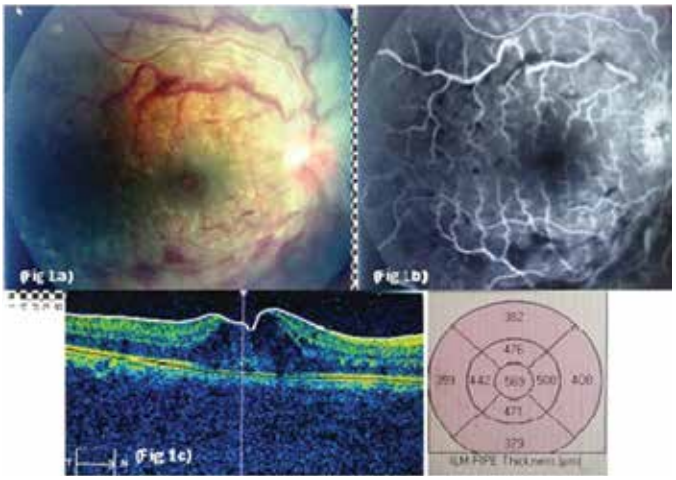

Figure 1: *Fundus and OCT picture of the right eye*

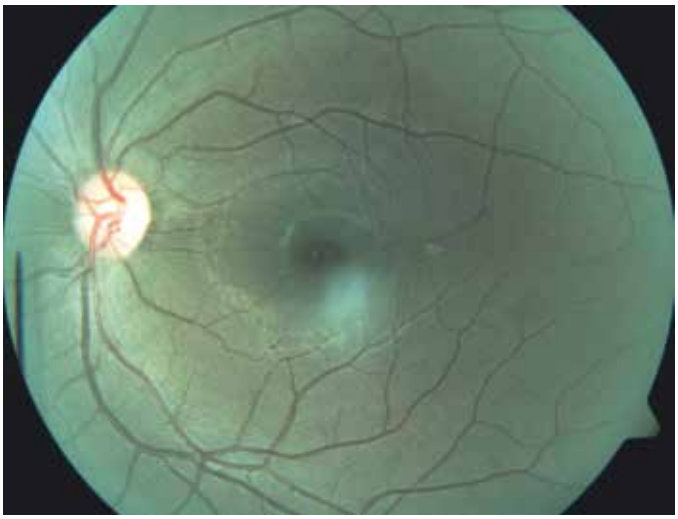

Figure 2: *Fundus picture of normal left eye*

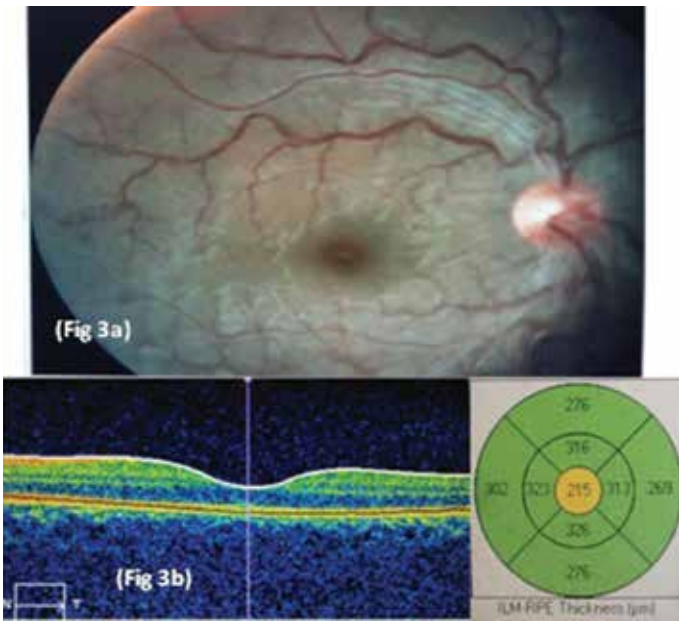

Figure 3: *Fundus and OCT picture of the right eye at 2 months*

vitamin derivatives (folate, vitamin B12, vitamin B6 and flavin adenine dinucleotide).[30] Homocysteine can either be metabolised to cysteine by vitamin B6 dependent trans-sulfuration pathway or converted back to methionine by a pathway that depends on folate and vitamin B12. Therefore, a deficiency of these vitamins can cause elevation of serum homocysteine.[31]

Hyperhomocystenemia can be either acquired or inherited.[32] It causes dysfunction of the endothelium of the vessel wall, with proliferation of smooth muscle leading to prothrombic changes. Thus, it increases the risk of cardiovascular events.[33] It is also associated with ocular complications like retinal arterial atherosclerosis, macular degeneration and optic atrophy due to retinal micro vascular occlusions, non-arteritic ischemic optic neuropathy (NA-ION), cataract, glaucoma and exudative age related macular degeneration.[34]

There have been a few reports of CRVO with elevated plasma homocysteine. Biousse and colleagues described a 24-year-old male with bilateral CRVO who had normal hematologic testing except for an elevated plasma homocysteine of 26.2 pimol/L.[35] Similarly, De Bruijne and coworkers described a high prevalence of hyperhomocysteinemia in a series of 22 patients with venous occlusive disease.[36] Fourteen patients had an elevated plasma homocysteine, either fasting or following methionine loading. Moghimi et al[22] found significantly elevated homocysteine in acute CRVO in the Iranian population compared to controls (p=0.005), supporting the necessity of screening. A study has even found fasting hyperhomocysteinemia to be second only to hypertension as an independent risk factor for the disease.[37]

An inverse relation is reported between both red-cell folate and serum vitamin B12 levels with hyperhomocysteinemia.[38-40] Folic acid administered alone or with pyridoxine, even to subjects without folate deficiency, can reduce homocysteine concentrations.[41] Homocysteine Lowering Trialist's Collaboration also demonstrated the role of 6 week intake of folate and B12 0.5 mg each, in reducing plasma homocysteine by 25% and 7%, respectively.[42,43] Thus, it is assumed that by reducing their levels, we can shorten the course of CRVO with complete resolution and can also prevent further vascular morbidities.

Bevacizumab (Avastin) is an anti-VEGF drug for treatment of macular edema due to CRVO. It was first reported by Rosenfeld in 2005[44] and has since been widely used in the treatment of CRVO with macular edema.

Our case thus illustrates an interesting presentation of unilateral non-ischemic CRVO in young, where hyperhomocystenemia was found to be the only risk factor. Treatment of hyperhomocysteinemia resulted in an excellent outcome with no recurrence or any other neurological and cardiovascular complications during one year follow-up.

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