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# Symmetrical Shadows: Unravelling the Mystery of Bilateral Central Retinal Vein Occlusion

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## Abstract

A 50y/M, on erratic medications for diabetes and hypertension came with the complaint of sudden diminution of vision in both eyes since 5 days. On ophthalmic examination, patient had a vision of 6/60 in both the eyes, with sluggish pupillary reaction. On fundoscopic examination, patient had the picture of bilateral central retinal vein occlusion with macular edema, confirmed on OCT Macula. Blood investigations were done to rule out systemic causes. Blood pressure was found to be significantly high apart from rest normal investigations, thus making the diagnosis of bilateral central retinal vein occlusion in the setting of hypertensive retinopathy.

**Keywords:** Hypertension; Central Retinal Vein Occlusion; OCT Macula

## Introduction

Retinal vascular occlusive disorders collectively constitute one of the major causes of seriously impaired vision. Retinal vaso-occlusive disease is the second most common cause of visual loss in older population after diabetic retinopathy [1]. Mainly it can be divided into branch retinal vein occlusion (BRVO), central retinal vein occlusion (CRVO) and hemi retinal vein occlusion (HRVO) depending on the site of occlusion.

Central retinal vein occlusion is an occlusion of the central retinal vein posterior to the lamina cribrosa of the optic nerve. And it is divided into two categories: non-ischemic (perfused) and ischemic (nonperfused) [2].

It is believed that the pathogenesis of CRVO includes a classical triad of endothelial damage, venous stasis and hypercoagulability (virchow's triad). The close anatomic relation of central retinal vein to artery could explain the turbulent flow and thrombus formation in cases when artery is affected but causing vein obstruction [3]. Hypertension and diabetes are one of the most common associations known to cause CRVO. Some other systemic causes being sarcoidosis, syphilis, systemic lupus erythematous [4-6]. However, none of the studies have been able to clearly establish the pathogenesis.

All these are merely blocks in a jigsaw puzzle which need to fit in order to unravel the pathogenesis of CRVO. For now, we can merely speculate the intricacies that occur in our body in case of CRVO. Here, we present an unusual case of bilateral CRVO, the cause of which is yet to be diagnosed.

## Methods

A 50 year male, known case of diabetes and hypertension for past 15 years came to the ophthalmology OPD with the chief complaint of sudden painless impairment of vision in both eyes since 5 days. Besides presbyopia, the patient had no

previous ophthalmological history. On examination, patient had visual acuity of 6/60 in both eyes, projection of rays accurate in all quadrants not improving on refraction. The torchlight examination was normal, except sluggish pupillary reaction. There was no neovascularization seen at angles on gonioscopy. On fundoscopy, there was a significant bilateral disc edema with blurring of margins. The arteriovenous ratio was attenuated. There were multiple flame shaped hemorrhages and cotton wool spots in all quadrants in both eyes. On investigations, patient had an Intraocular pressure of 14 mmHg & 15 mmHg and a blood pressure of 160/90 mmHg. Apart from raised lipid profile and HbA1c rest all blood investigations were found to be normal. OCT Macula showed central subfoveal thickness of 836 and 889 micrometer with macular edema (Figures 1 & 2). The fundus fluorescein angiography showed delayed arteriovenous transit time, masked by retinal hemorrhages, and capillary non perfusion areas less than 10 disc diameters, confirming the diagnosis of non-ischemic CRVO which was further planned to be managed with intraviterial Anti VEGF and laser photocoagulation (Table 1).

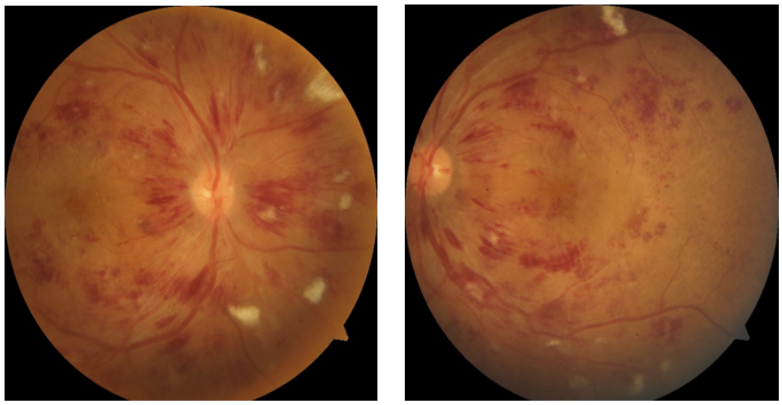

**Figure 1:** Fundus picture showing bilateral macular edema with multiple flame shaped hemorrhages and cotton wool spots in all quadrants in both eyes.

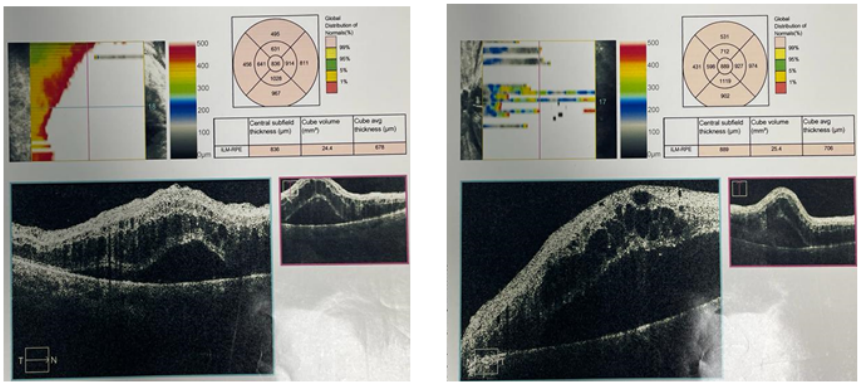

**Figure 2:** OCT Macula showing showed central subfoveal thickness of 836 and 889 micrometre respectively with macular edema.

| Investigations | |
|---|---|
| Blood Urea | 37.3 |
| Serum Creatinine | 1.06 |
| Serum Uric Acid | 5.2 |
| Calcium | 8.3 |
| Phosphorous | 5 |

| | |
|---|---|
| Sodium | 135 |
| Potassium | 4.5 |
| Chloride | 103 |
| Haemoglobin | 11.2 |
| Total Leucocytes Count (Tlc) | 8.39 |
| RBC Counts | 2.46 |
| PCV/Haematocrit | 21.6 |
| Platelet Count | 79.9 |
| RDW | 17.2 |
| ESR | 12 |
| Total Cholesterol | 370 |
| Triglyceride | 352 |
| Hdl Cholesterol | 42.5 |
| Ldl Cholesterol | 79.9 |
| Vldl Cholesterol | 17.2 |
| Bleeding Time | 5 min |
| Clotting Time | 8 min |
| PT | 11s |
| INR | 0.98 |
| Protein-C, S | 78 |
| Factor V Leiden | 82 |
| Apla | 10 |
| S.Homocysteine | 9 |
| Quantity | Pale Yellow |
| Colour | Clear |
| Transparency | Acidic |
| Reaction | ++ |
| Albumin | Nil |
| Sugar | 1.015 |
| Specific Gravity | 02-Mar |
| PUS Cells | 03-Apr |
| RBC'S | 02-Mar |
| Epithelial Cells | Yeast Cell seen |
| Bacteria | NIL |
| Vitamin B12 | 268 |
| Folic Acid | 3.4 |
| HBSAG,HCV,HIV I & II | Non-Reactive |
| S. Bilirubin Total | 0.57 |
| S. Bilirubin Direct | 0.12 |
| S. Bilirubin Indirect Total | 0.45 |

| | |
|---|---|
| Protein | 6.4 |
| Albumin | 2.7 |
| Globulin (Calculated) | 3.7 |
| A/G Ratio (Calculated) | 0.73 |
| AST | 17 |
| ALT | 24 |
| S. Alkaline Phosphatase | 177 |
| GGT | 57.3 |
| Serum LDH | 245.9 |
| HBA1C | 6.4 |

**Table 1:** Showing various blood investigations done for the patient.

## Discussion

CRVO typically presents as a unilateral sudden painless diminution of vision. In rare case scenarios, it can have bilateral presentation. In 1904, Coats described 2 types of CRVO- ischemic/non perfused and non-ischemic/perfused types. Commonly, in ischemic types, visual acuity is less than 6/60, with relative afferent pupillary defect present. There is higher risk of neovascularization, especially neovascularization of iris. There is patchy capillary hypo fluorescence with delayed arteriovenous transit time and delayed b wave amplitude in electroretinogram. This is in contrast to non-ischemic type where visual acuity is better than 6/60, absent/minimal afferent pupillary defect, low risk of neovascularization, uniform capillary fluorescence on angiography with normal/supernormal electroretinogram. It is imperative to distinguish between the two since the prognosis depends on it. Non ischemic CRVO has better prognosis.

Our patient has presented with bilateral CRVO. In patients less than 50 years of age, it is imperative to investigate further to rule out any blood dyscrasias. The typical fundus picture of dilated and tortuous vessels is lacking in our patient. This can be a rare case of bilateral non ischemic CRVO as a sequelae of hypertension, where the vessels got sclerosed, thus losing its tortuosity. Apart from raised lipid profiles and HbA1c the normalcy of blood investigations poses a great difficulty in determining the etiology. A close observation and a more aggressive approach needs to be required in finding out the cause as it can be a mere representation of a potentially life threatening disease.

A close differential that can be considered is hypertensive retinopathy. But, the absence of disc edema and any arterio-venous nicking changes makes it unlikely. However, it can't be excluded completely. Various theories were given to explain the pathogenesis of central retinal vein occlusion. It is important to explain some of them. Hayreh SS, et al. [7-9] suggested that non ischemic CRVO occurred because of venous flow obstruction, while ischemic CRVO occurred because of obstruction of both retinal arterial and venous occlusion. The limitation to this model being, it was based on animal models with occlusion of retinal vessels just at the entry into optic nerve. Fujino T, et al. [10] emphasized that CRVO, especially the ischemic type occurred merely by occlusion of retinal vein occlusion alone.

Green WR, et al. [11] suggested a different viewpoint. His research was a histopathological study where he gave a theory supporting the fact that the inciting agent leading to CRVO was in fact thrombus formation. In his study, he took 29 eyes and observed old or new thrombus in patients of CRVO. Time taken to evaluate this situation was in fact 6 hours to 10 years from the onset of disease. This temporal association in fact explained the morphologic features of the occlusion to a certain extent.

Many risk factors have been identified in case of CRVO. The Eye Disease Case-Control Study found that the risk for CRVO increased in people with hypertension, diabetes, less physical activity and decreased alcohol consumption, of greater significance in ischemic rather than non-ischemic CRVO [12]. In a study conducted by Rath EZ, et al. [13] he found that systemic hypertension along with open angle glaucoma was associated in males with CRVO. The risk increased with increased levels of serum lipid levels [14].

In women, the risk was higher with raised erythrocyte sedimentation rate, lower in post-menopausal women on estrogen therapy [14,15]. The panorama of risk factors was completely different in young individuals presenting with CRVO. It is typically associated with blood dyscrasias like protein C, protein S deficiency, factor V Leiden mutation

deficiency, antithrombin deficiency, antiphospholipid antibodies, activated protein C resistance, prothrombin gene mutation, anticardiolipin antibodies, abnormal fibrinogen levels, and lupus anticoagulant, hyperhomocystenemia [12,16-30].

However, none of the causes have been fully able to explain the pathogenesis in our patient. In a meta-analysis conducted in 2015 by Song P, et al. [31] it was found out that the prevalence of RVO in people aged 30-89 years was 0.77% (95% confidence interval CI = 0.55-1.08, equivalent to 28.06 million as compared to CRVO, where the prevalence was 0.13% (95% CI = 0.08-0.21), equivalent to 4.67 million affected people. CRVO typically presents as unilateral cause of sudden diminution of vision. However, in rare cases, it can have bilateral presentation. In such cases there is often any systemic illness associated. Narang S, et al. [32], reported a case of bilateral CRVO in the backdrop of chronic myeloid leukemia, a potentially life threatening hematological illness. Toohey TP, et al. [33] reported another case of bilateral CRVO in a patient of diffuse large B-cell lymphoma.

Thus, we can conclude that vaso-occlusive diseases are not merely a single disease. Rather they are a myriad of diseases, which need to be evaluated and investigated in a great depth. Sufficient data is lacking in its pathogenesis which needs to be further studied.

## Financial disclosures

The case report and its contents, including the results of investigations and images, was discussed with the patient, and informed.

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