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A rare case of bilateral central retinal vein occlusion in a patient with Vitamin D deficiency

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ABSTRACT

One of the most important differentials for painless sudden loss of vision is CRVO (Central retinal vein occlusion). It is one of the leading diseases causing vision loss especially in elderly population. However, bilateral simultaneous CRVO in a young patient with no other co morbidities is rare. This case illustrates a young male of 40 years with no well-known comorbidities who experienced sudden onset diminution of vision in right eye followed by left eye in 2 weeks gap. No history of smoking, diabetes, hypertension, dyslipidemia or any other systemic disorders. Patient is not on any topical or systemic medications. There was no significant family history. On evaluation of right eye, the BCVA (best corrected visual acuity) was 6/36 and left eye was finger counting 3 meters. Intra ocular pressure in both eyes was 18 mm Hg. Anterior segment showed all normal findings. Dilated fundus evaluation in both eyes showed multiple superficial and deep hemorrhages with hard exudates and macular edema. OCT (Optical Coherence tomography) displayed macular edema in both eyes. Blood investigations showed all values within normal limits except Vitamin D levels which were found to be deficient.

Keywords: Optical Coherence tomography, Central retinal vein occlusion, co morbidities, diabetes, hypertension, dyslipidemia

1. INTRODUCTION

CRVO (Central retinal vein occlusion) is a potentially lethal disease condition involving majorly the older population. It ranks second next to diabetic retinopathy as vascular disease-causing vision loss especially in elderly population (Cugati et al., 2006). Although CRVO is often a frequent condition, bilateral CRVO is rather uncommon. According to reports, bilateral CRVO accounts for between 0.41% and 7.7% of all CRVO cases (Ziaei et al., 2013). In central retinal vein occlusion, occlusion of the major retinal vein occurs dorsal to the lamina cribrosa and is often brought about by thrombosis.

The pathogenesis of retinal vein occlusion is thought to involve vascular

injury, stasis and hypercoagulability, which are all components of Virchow's triad for thrombogenesis. Atherosclerosis injury to the retinal vascular wall changes the rheologic characteristics of the nearby vein, causing stasis, thrombosis and ultimately occlusion. There are a lot of other theories proposed regarding the pathogenesis of CRVO, but the complete pathogenesis is still not fully understood (Browning, 2012).

CRVO is categorized into ischemic and non-ischemic variants according to the range of retinal capillary ischemia seen on FFA (fundus fluorescein angiography) (Baseline and early natural history report, 1993). CRVO is characterised by superficial and deep intraretinal haemorrhages in all the quadrants along with varying degrees of retinal venous tortuosity, edema of the optic disc, cotton wool patches and cystoid macular oedema. Other significant risk factors include older age, hypertension, hyperlipidemia, diabetes mellites and hyperhomocystinemia (Hayreh et al., 2001).

Vitamin D is one of the fat-soluble vitamins, obtained from either food sources or by transformation of 7-dehydrocholesterol available in subcutaneous fat to pro-Vitamin D in the presence of UV rays. Bone and mineral homeostasis are maintained by Vitamin D and its deficiency can lead to a raised occurrence of several disorders, including osteoporosis, malignancies, cardiovascular and autoimmune disorders (Bendik et al., 2014). By influencing an extensive scale of cell types to maintain healthy vasculature, Vitamin D performs several biological activities in new vessel development, inflammation, atherosclerosis, stiffness of arteries and calcification.

The nuclear hormone activity of the functional form of Vitamin D is mediated by the binding Vitamin D receptor (VDR), which is found in the majority of cells, including cells of immune system, vascular endothelium, myocardium, retina, osteoblasts, pericytes, smooth muscle and fat cells. Vitamin D prevents vascular damage in the endothelial cells of retina by preventing vascular smooth muscle migration and proliferation (Carlberg, 2014). Thus, Vitamin D and retinal vasculature are closely related.

2. CASE PRESENTATION

The patient is a young male aged 42, with no familiar comorbidities who experienced sudden onset, painless diminution of vision in the right eye followed by the left eye in 2 weeks gap. No history of redness, watering, floaters, flashes or trauma. No history of smoking, diabetes, hypertension, dyslipidemia or any other systemic disorders. Patient did not give any history regarding the use of any topical eye drops. There was no significant family history.

On further evaluation, right eye gave a best corrected visual acuity of 6/36 and left eye showed finger counting 3 meters. Intraocular pressure in both eyes was 18 mm Hg. Pupil size and reaction to light was normal in both eyes. There was no iris neovascularization. Anterior segment findings were within normal limits. On dilated posterior segment examination, right eye revealed a normal disc with a 0.3:1 cup disc ratio, tortuous blood vessels, foveal reflex dull, multiple superficial and intraretinal hemorrhages along the blood vessels, hard exudate in inferonasal to the disc with macular edema (Figure 1A) and left eye showed normal disc with 0.3:1 cup disc ratio, tortuous vessels, multiple superficial and intraretinal hemorrhages along the blood vessels, multiple hard exudates and macular edema (Figure 1B).

Optical coherence tomography (OCT) done displayed macular edema in both eyes with central foveal thickness of 501µm in the right eye and 348µm in the left eye. Blood investigations (Table 1) including complete blood count, lipid profile, blood sugar, liver function test, renal function test, homocysteine and thyroid function tests were within normal limits. Thrombophilia screening, antinuclear antibody (ANA), anti-DNA antibody, rheumatoid factor, angiotensin-converting enzyme and antineutrophil cytoplasmic antibody (ANCA) were also found to be normal. ECG, Chest X-ray and carotid Doppler were done and there were no abnormal findings found. However, the Vitamin D level of the patient was 8.34 µL.

Physician call was done for a complete systemic assessment and all examinations were found to be within normal limits. The patient was started on Vitamin D supplementation of 60,000 IU once a week. We started the patient on a monthly Intravitreal Bevacizumab injection (1.25mg/0.05ml).

After 3 months of treatment with Vitamin D supplementation and monthly intravitreal bevacizumab, patients' vision in the right eye improved to 6/9 and left eye to 6/36p. Post intervention fundus photo (Figure 3) and OCT (Figure 4) showed significant improvement. The macular edema of the patient had completely resolved with central foveal thickness improving to 276µm in the right eye and 283µm in the left eye. The patient has been on regular follow up since then and shown positive results.

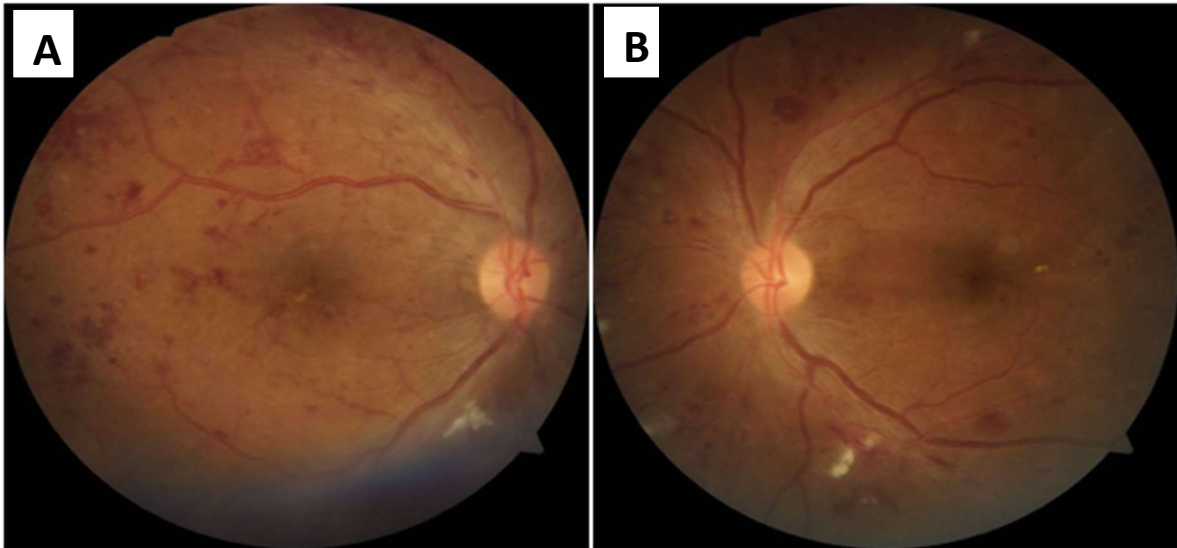


Figure 1 A) Fundus photo of right eye on presentation. B) Fundus photo of left eye on presentation

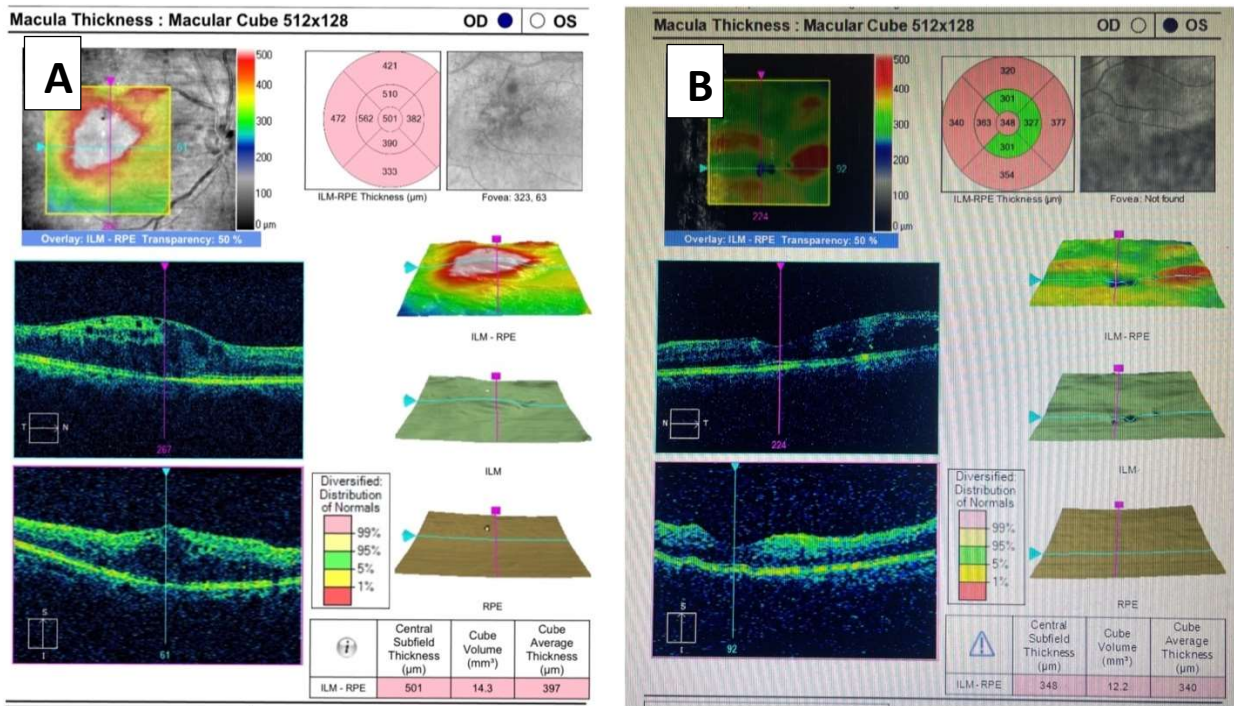


Figure 2 A) OCT of right eye on presentation. B) OCT of left eye on presentation

Table 1 Blood investigations

Investigation	Values
Hemoglobin	14 grams %
ESR (Erythrocyte Sedimentation Rate)	8 mm/1 st hour
Urea	28 mg/dL
Creatinine	1.0 mg/dL
Sodium	141 mmol/L
Potassium	3.9 mmol/L
ALT (Alanine Aminotransferase)	17 U/L
AST (Aspartate Aminotransferase)	28U/L

ALP (Alkaline Phosphatase)	83 U/L
Total Protein	6.2 g/dL
Total Bilirubin	0.6 mg/dL
Total Cholesterol	150 mg/dL
Triglycerides	130 mg/dL
LDL (Low density lipoprotein)	120 mg/dL
VLDL (Very low-density lipoprotein)	29 mg/dL
dHDL (High density lipoprotein)	45 mg/dL
Vitamin D	8.0 ng/ml
Homocysteine	10.8 μ mol/L

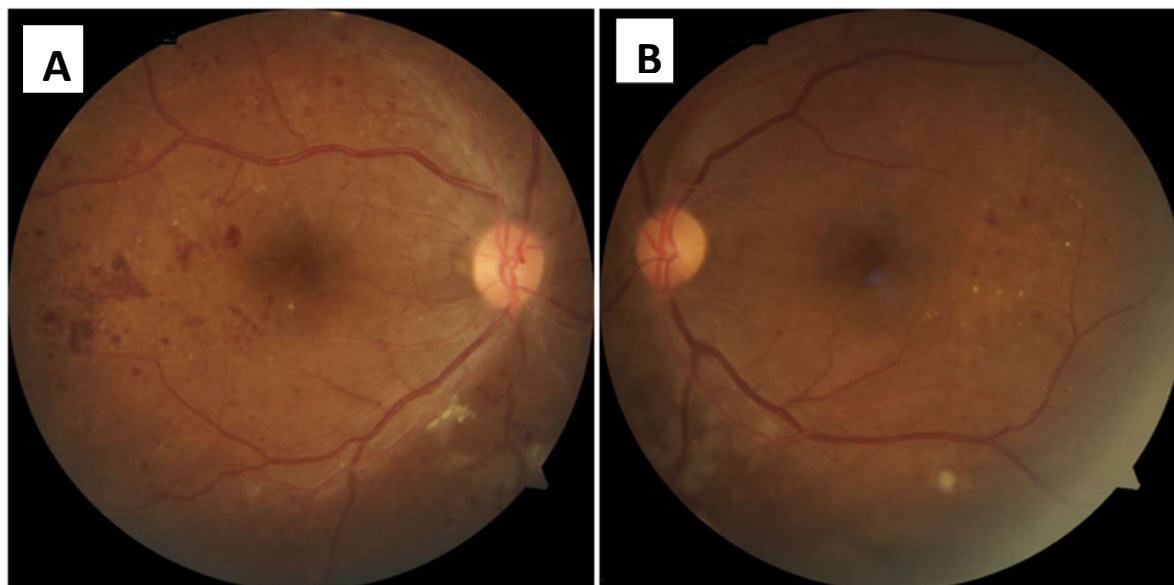


Figure 3 A) Fundus photo of right eye post intervention. B) Fundus photo of left eye post intervention

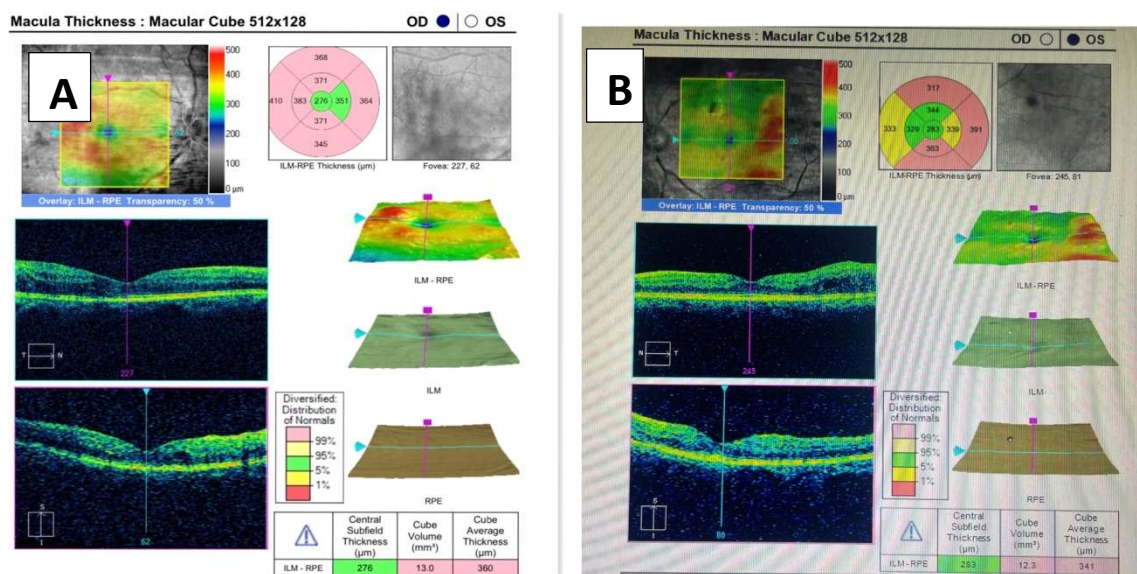


Figure 4 A) OCT of right eye post intervention. B) OCT of left eye post intervention

3. DISCUSSION

Vitamin D deficiency and its positive association with retinal vein occlusion is a topic of increasing interest. Multiple studies have discussed this association in the past. However, occlusion of central retinal vein in a young patient with no other comorbidities is a rare phenomenon. It is even rarer when it is simultaneous bilateral occlusion of central retinal vein in a patient with Vitamin D deficiency and no other co-morbidities. Multiple reasons might be proposed regarding the relation of Vitamin D with the damage of renal microvasculature. First, by activating the endothelium, Vitamin D may change the shape and order of the microvasculature.

Endothelial cell activity is modified by Vitamin D receptors produced on these cells through binding to these receptors. The result is that the activated endothelium encourages proliferation and migration of endothelial cells by increasing nitric oxide production and decreasing reactive oxygen species generation (Molinari et al., 2013). Additionally, it lowers vascular tone by producing constricting factors produced from endothelium and suppresses innate inflammatory process by altering particular signaling pathways (Wong et al., 2010). Therefore, it is plausible that low Vitamin D levels could prevent these antioxidative and vasodilatory mechanisms from starting, resulting in blood vessel damage.

In a study, Ziaei et al., (2013) found that venules, not arterioles, were notably affected by Vitamin D deficiency. In a case-control study, Karimi et al., (2022) found that patients receiving oral Vitamin D supplements had greater reductions in central macular thickness and better improvements in best-corrected visual acuity after undergoing intravitreal bevacizumab therapy in comparison to control groups. This case illustrates the case of a 40-year aged with no other comorbidities presenting with complaints of sudden loss of vision in the right eye followed by the left eye in a gap of 2 weeks.

Retinal examination suggested occlusion of central retinal vein with macular edema in both eyes. The patient is under regular follow-up and was treated with 3 doses of Intravitreal bevacizumab and oral Vitamin D supplementation. Patients' vision improved and macular edema subsided drastically after 3 doses of intravitreal injection and Vitamin D3 supplementation. The Vitamin D levels of the patient were restored and the patient is on regular follow-ups since then. There was no further deterioration in vision or fundus changes in the patient since then.

4. CONCLUSION

Vitamin D deficiency is a lesser-known risk factor for retinal vein occlusions and hence is often overlooked. Vitamin D deficiency can damage the retinal vascular endothelium resulting in vision loss. Hence in any patient with retinal vein occlusions Vitamin D levels should be investigated. This can help in prophylaxis and therapy of retinal vein occlusions.

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Author Contribution

Dr Varsha Kandambeth collected all the information and prepared the manuscript which has been thoroughly reviewed by Dr Swapneel M and Dr Daigavane.

Informed Consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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