

Combined central retinal artery occlusion and central retinal venous occlusion with bilateral carotid artery disease in a patient with protein C deficiency

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Abstract

Central retinal artery occlusion and central retinal venous occlusion are rare entities of retinal vascular disorders that can cause sudden visual loss and combined occurrence results in devastating outcomes. The role of protein C deficiency is well established in venous thrombosis however the occurrence of concurrent arterial thrombosis is rare and the combination in association with carotid artery occlusion is an exceptionally rare occurrence. Here we report a case of protein C deficiency presenting as combined central retinal artery occlusion and central retinal venous occlusion with bilateral carotid artery disease.

Keywords: Central retinal artery occlusion, central retinal vein occlusion, protein C deficiency, carotid artery disease

INTRODUCTION

Protein C forms a major component in the regulation of coagulation cascade system. The importance of protein C as an anticoagulant and hence its deficiency resulting in a procoagulant state and increases the occurrence of venous thrombosis as explained by the Virchow's triad.¹ The other manifestations of protein C deficiency include arterial thrombosis and warfarin induced cutaneous necrosis. However, though the risk of arterial thrombosis is augmented, the data is sparse.²

Retinal vascular disease causes sudden painless visual loss with devastating outcomes if not addressed in a timely manner. Central retinal vein occlusion (CRVO) may be associated with risk factors such as age, diabetes mellitus, hypertension, obesity, smoking, hypercoagulable disorders. Central retinal arterial occlusion (CRAO) may be associated etiology and risk factors such as carotid artery disease, cardiogenic, small vessel disease, hematological and inflammatory causes. Common etiological and risk factors to CRVO and CRAO can result in combined occurrence.³ Here we report a rare and unique case of protein C deficiency in causing CRAO with CRVO and carotid artery disease in a young patient.

CASE REPORT

A 42 year old male presented with sudden onset diminution of vision in his right eye one month prior to presentation. He had previous episodes of transient weakness of left upper and lower limbs which resolved spontaneously in 5-10 minutes that was not evaluated. On examination the patient was able to perceive only hand movements close to face in his right eye. Visual acuity was 20/30 in his left eye. Fundus examination showed multiple hemorrhages in all four quadrants and multiple soft exudates around the disc, which were suggestive of ischemic CRVO (Figure 1). Pale retina, arterial attenuation, cherry red spot over the posterior pole were present, suggestive of associated CRAO (Figure 1). Fundus was normal in the left eye.

Subsequently fluorescein angiography was done which showed a delayed filling of the disc vessels and choroidal filling at 20 seconds. No further filling of arterial, AV phase, venous phase till 3 minutes in the right eye (Figure 2) suggestive of severely impaired circulation. It confirms the diagnosis of CRAO with macular ischemia.

During the course in the hospital, the patient developed multiple episodes of transient ischemic attack manifesting as weakness of left upper and lower limb lasted for 5-10 minutes. Imaging of brain was done which was normal. Carotid Doppler ultrasound showed complete occlusion of

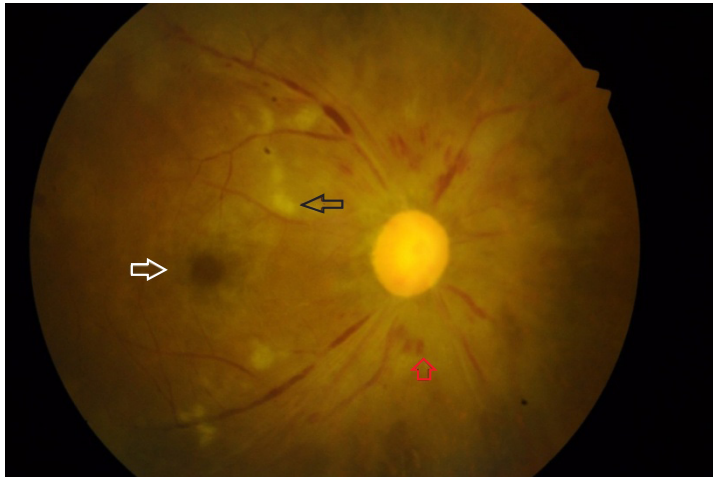


Figure 1. Fundus photograph showing multiple cotton wool spots (black arrow) and haemorrhage (red arrow) suggestive of ischaemic CRVO with cherry Red spot (white arrow), arterial attenuation, suggestive of associated CRAO

internal carotid artery on the right side with 90% occlusion on the left side. CT angiography was done which showed occlusion of bilateral internal carotid artery, noted from its origin to termination (Figure 3) with bilateral middle cerebral artery and anterior cerebral artery is reformed from circle of Willis (Figure 4).

Protein C levels which were significantly reduced to 16 %, suggestive of severe protein C deficiency. Autoimmune workup were negative. 2D echocardiography was normal. Patient was started on heparin followed by warfarin. International normalized ratio was maintained between 2-3. His neurological symptoms

improved with treatment. He was advised close follow up in ophthalmology department.

One month later, he developed pain and redness in his right eye with intraocular pressure found to be 40 mm Hg. He was treated with anti-glaucoma medications and advised pan retinal photo coagulation. He was getting pan retinal photocoagulation in the ophthalmology department on an outpatient basis and was under close monitoring. He was advised lifelong anticoagulation.

DISCUSSION

Protein C deficiency has both homozygous

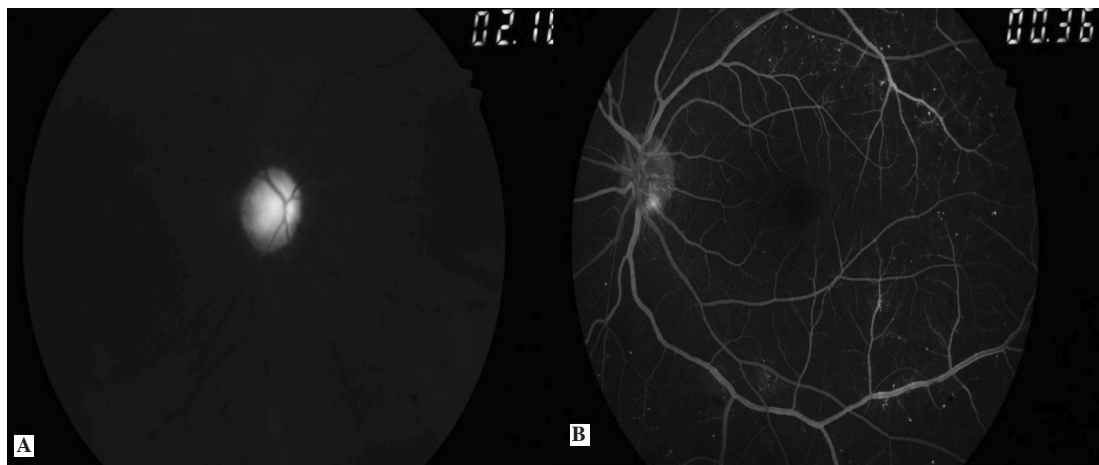


Figure 2. Fundus fluorescein angiography of retina shows no filling of arterial, AV phase, venous phase till 3 minutes in the right eye (A). It is suggestive of severely impaired retinal circulation with normal filling in the left eye (B)

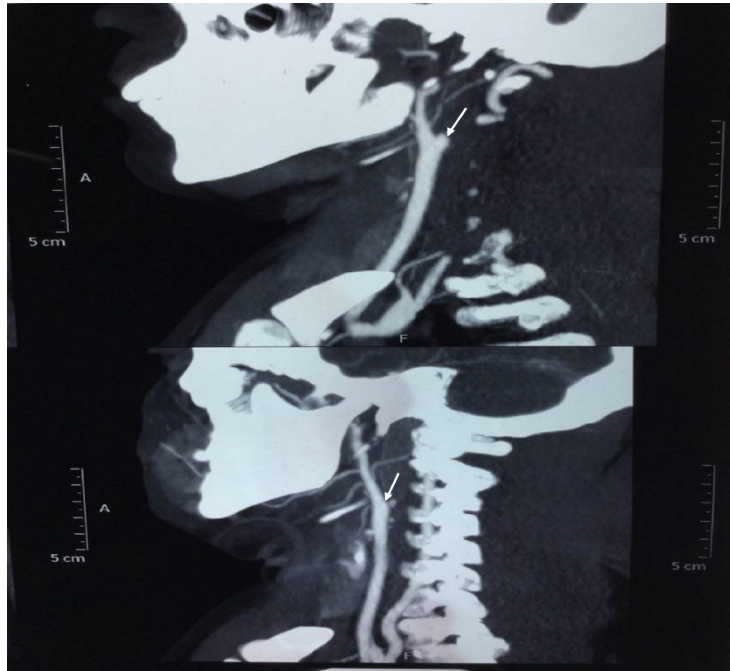


Figure 3. CT carotid angiogram showing occlusion of bilateral internal carotid artery noted from its origin to termination (arrow)

and heterozygous state. Homozygous state is a rare entity that causes purpura fulminans like syndrome in neonates.⁴ Heterozygous individuals present later in life and have an increased risk of thromboembolism at a younger age.⁵

Since our patient presented for the first time at around 40 years of age, he was probably suffering from heterozygous protein C deficiency. There are

two types of protein C deficiency– type 1 being the most common, in which the concentration and functional activity of protein C are reduced. In type 2, the concentration is normal with only the functional activity being reduced. Protein C deficiency can also be acquired by many conditions like acute thrombosis, drugs like warfarin and oral contraceptive pills and liver

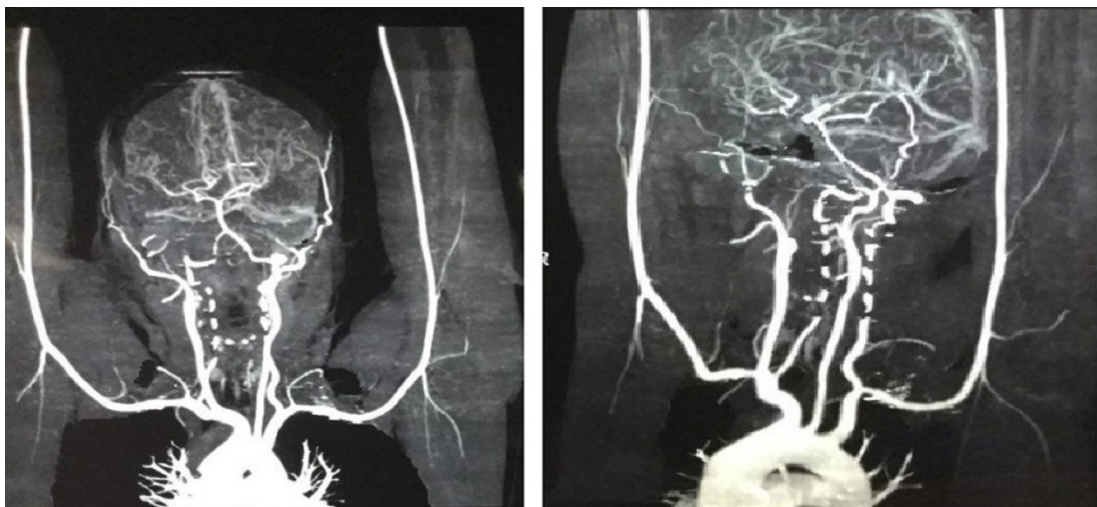


Figure 4. CT cerebral angiogram reformatted showing flow of middle cerebral artery and anterior cerebral artery from circle of Willis.

disease. Our patient presented to us after one month of visual loss and the workup for the secondary causes of protein C deficiency were negative.

The most common cause for isolated CRAO is embolism, with the major source being atherosclerotic carotid artery disease. CRAO and CRVO can occur either simultaneously or sequentially.⁶ Desai *et al.* reported a similar case of combined CRAO and CRVO in a patient with protein C deficiency.⁷ Schwartz *et al.* reported a case of combined CRAO with CRVO secondary to thrombotic thrombocytopenic purpura.⁸

In our patient, CRAO and carotid artery disease may have developed from the same systemic risk factors³ and coexisting CRVO may have also developed secondary to the protein C deficiency¹ which is associated with high incidence of thromboembolism. But Hayreh's theory states that after the event of a CRVO, a complete block in the retinal circulation occurs leading to secondary CRAO and presents with combined CRAO-CRVO.⁹ This may be another explanation for the combined CRAO-CRVO in our patient.

Combined CRAO-CRVO usually has poor visual prognosis. A study done by Valle *et al.* showed that among 7 of 12 patients there was a drastic improvement in vision after fibrinolytic therapy¹⁰ when instituted in the acute phase. It is effective mainly within 72 hours, as suggested by dramatic improvements in some of the cases. Our patient had severe visual loss in the affected eye as he presented late. He also developed complications like neovascular glaucoma for which he received treatment with pan retinal photo coagulation and anti-glaucoma medications.

In conclusion, combined CRAO-CRVO is a disease with devastating visual outcome and is often not an isolated ocular event. A detailed investigation is always needed in younger patient, as ocular pathology may be followed by severe cerebrovascular and cardiovascular events if not addressed in a timely manner. Long term anti coagulation therapy is needed in such patient to prevent life threatening systemic complications.

REFERENCES

1. Allaart CF, Poort SR, Reitsma PH, Bertina RM, Briët E, Rosendaal FR. Increased risk of venous thrombosis in carriers of hereditary protein C deficiency defect. *Lancet* 1993;341(8838):134-8.
2. Folsom AR, Ohira T, Yamagishi K, Cushman M. Low protein C and incidence of ischemic stroke and coronary heart disease: the Atherosclerosis Risk in Communities (ARIC) Study. *J Thromb Haemost* 2009;7(11):1774-8.
3. Recchia FM, Brown GC. Systemic disorders associated with retinal vascular occlusion. *Curr Opin Ophthalmol* 2000;11(6):462-7.
4. Seligsohn U, Berger A, Abend M, *et al.* Homozygous protein C deficiency manifested by massive venous thrombosis in the newborn. *N Engl J Med* 1984;310(9):559-62.
5. Bovill EG, Bauer KA, Dickerman JD, Callas P, West B. The clinical spectrum of heterozygous protein C deficiency in a large New England kindred. *Blood* 1989;73(3):712-7.
6. Schmidt D. Comorbidities in combined retinal artery and vein occlusions. *Eur J Med Res* 2013;18(1):27.
7. Desai S, Rai N, Kulkarni P, Natarajan S. Combined CRVO with CRAO in a patient with protein C deficiency. *Retin Cases Brief Rep* 2014;8(2):145-9.
8. Schwartz SG, Puliafito CA. Bilateral CRAO and CRVO from thrombotic thrombocytopenic purpura: OCT findings and treatment with triamcinolone acetonide and bevacizumab. *Ophthalmic Surg Lasers Imaging* 2006;37(5):420..
9. Hayreh SS. Prevalent misconceptions about acute retinal vascular occlusive disorders. *Prog Retin Eye Res* 2005;24(4):493-519.
10. Vallée JN, Paques M, Aymard A, *et al.* Combined central retinal arterial and venous obstruction: emergency ophthalmic arterial fibrinolysis. *Radiology* 2002;223(2):351-9.