

Combined branch retinal vein and branch retinal artery occlusion – clinical features, systemic associations, and outcomes

Sabyasachi Sengupta, Utsab Pan

Purpose: Retinal vascular occlusions affecting both the arterial and venous systems are rare events. Combined branch retinal artery (BRAO) and vein (BRVO) occlusion are exceedingly rare and not well characterized. **Methods:** Six patients with combined BRAO and BRVO underwent a comprehensive eye examination, fundus fluorescein angiography, optical coherence tomography, and cardiovascular evaluation. **Results:** Mean age at presentation was 54 ± 7.8 years (range: 39–60), and five of the six were men. Patients had a combination of systemic comorbidities such as diabetes (5), hypertension (4), dyslipidemia (5), and hyperhomocysteinemia (1). All had unilateral combined occlusion characterized by narrowing and cattle tracking of blood in arteries and dilated tortuous veins in the involved quadrant. Fluorescein angiography demonstrated complete capillary drop out and a clear demarcation between the perfused and nonperfused retina. Presenting vision ranged from 6/9 to 1/60 Snellen's, and final vision depended on the macular perfusion status. All eyes were treated with angiography-guided sectoral laser photocoagulation, and three eyes required intravitreal bevacizumab due to macular edema or retinal neovascularization. **Conclusions:** Combined BRAO and BRVO is rare, may have unique underlying pathogenetic mechanisms, is associated with multiple systemic comorbidities and can yield good visual outcome if macula remains well perfused.

Key words: Branch retinal artery occlusion, branch retinal vein occlusion, combined

Combined vascular occlusions involving the parts of the retinal arterial and venous systems have been reported in the past. Among these, simultaneous occlusion of the central retinal artery (CRAO) and vein (CRVO) is well characterized.^[1-3] Coexistent cilioretinal artery occlusion along with CRVO is most frequently reported and is equally well described.^[4,5] Rarely, branch retinal arterial occlusion has been reported to coexist with CRVO.^[6,7] Many of these combined vascular occlusions have been described in association with comorbidities such as diabetes, dyslipidemia, systemic lupus, and hyperhomocysteinemia.^[8]

Combined branch retinal vein (BRVO) and artery (BRAO) occlusion affecting the same retinal quadrant or hemisphere has been rarely reported in the past. Lee *et al.*, in a study of 308 eyes of BRVO, reported 56 eyes with simultaneous arterial insufficiency but not frank obstruction.^[9] Most other reports have been anecdotal and describe single cases.^[10-15] We present a series of six cases of combined BRAO and BRVO and describe the clinical, angiographic, and optical coherence tomographic (OCT) features along with comorbid systemic associations and visual outcomes in these eyes.

Methods

All individuals attending the vitreoretina services of our institution between November 2013 and November 2015 and diagnosed with combined BRAO and BRVO were enrolled in this prospective study. The study was approved by the

Institutional Ethics Committee, and Informed consent was obtained.

All participants underwent comprehensive ophthalmic assessment by a single fellowship – trained vitreoretina specialist (SS). A thorough review of the patient's medical history was done with special attention to the presence and duration of diabetes mellitus, hypertension, cardiac disease, renal disease, and dyslipidemia.

At baseline and every follow-up visit, best-corrected visual acuity was recorded, undilated slit lamp evaluation was done with $\times 45$ magnification to detect iris neovascularization (NVI), gonioscopy was performed to detect the neovascularization of the anterior chamber angle, and dilated fundus examination was done to document findings associated with BRAO and BRVO such as quadrantic involvement, macular status, and retinal neovascularization at disc (NVD) or elsewhere (NVE). Fundus fluorescein angiography (FFA) was done once at baseline, and OCT was done at every visit (Cirrus spectral domain-OCT, Carl Zeiss Meditec, Dublin, USA).

All patients underwent a thorough systemic evaluation including measurement of blood pressure (BP), fasting and

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postprandial blood sugar levels, renal profile including blood urea and serum creatinine levels, fasting lipid profile, including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein, very LDL, total triglycerides, and serum homocysteine levels. Inflammatory markers tested were anti-nuclear antibody, double-stranded DNA, c-ANCA, and RA factor. All patients also underwent electrocardiogram, echocardiography, and cardiologist's consultation to determine underlying cardiovascular disease.

All eyes were treated with scatter laser photocoagulation in the involved quadrant or hemisphere and laser was guided by the extent of capillary drop out seen on the FFA. Intravitreal bevacizumab (1.25 mg/0.05 ml) was injected in eyes that showed the presence of macular edema or persistent neovascularization despite laser. Reinjectations were based on the persistence of macular edema at every visit.

Results

The mean age at presentation was 54 ± 7.8 years (Interquartile range: 53–60 years, range: 39–60 years), patients were predominantly men (83%) and both right and left eyes were equally involved.

Systemic associations, clinical characteristics, and treatment outcomes of all six patients are presented in Table 1. Four eyes had quadrant, and two had hemispheric involvement. Fundus evaluation revealed narrowing and cattle tracking of blood in arteries and dilated tortuous veins in the involved quadrant or hemisphere. In addition, retinal whitening and/or featureless retina and flame shaped and blot hemorrhages were noted in the involved quadrant [Figs. 1a, e and 2a]. FFA revealed delay in filling of the involved artery and gross delay in venous filling [Figs. 1b-d, f-h, and 2b-d] along with large areas of capillary nonperfusion (CNP). A clear demarcation zone was seen between the ischemic and perfused retina in all the eyes. The OCT done through the region of occlusion showed hyperreflectivity and increased thickness of inner retinal layers and decreased reflectivity in the outer retinal

layers suggestive of arterial occlusion.^[16] Follow-up OCT's revealed thinning of the ganglion cell layer after the resolution of the occlusion [Fig. 3].

One eye developed NVD even after scatter laser to the involved area and was given intravitreal bevacizumab along with additional panretinal photocoagulation, following which the NVD resolved. Two separate eyes received intravitreal bevacizumab due to the presence of cystoid macular edema [Table 1]. One eye with NVE had massive neovascularization with a tractional retinal detachment involving the macula at presentation itself.

Discussion

We describe the largest series of cases of combined BRAO and BRVO. Most of our patients were relatively young, predominantly men and had multiple cardiovascular risk factors such as diabetes, hypertension, and dyslipidemia.

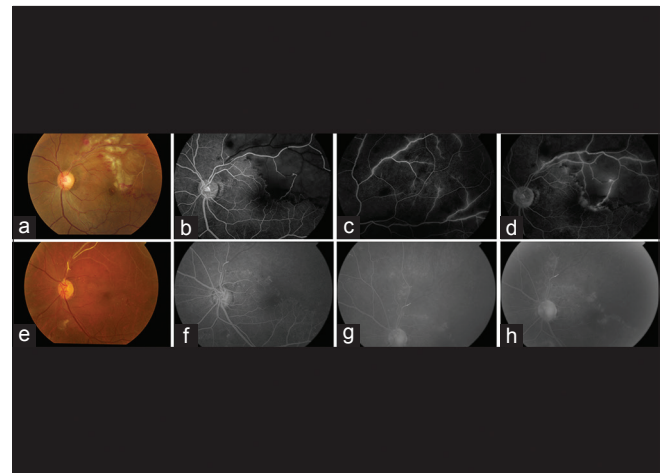


Figure 1: Clinical (a and e) and early (b and f), mid (c and g), and late (d and h) phase angiographic features of combined branch retinal artery and vein occlusion in the superotemporal quadrant in two of the participants

Table 1: Systemic associations, clinical characteristics, treatment, and outcomes of eyes with combined branch retinal vein occlusion and branch retinal artery occlusion

Number	Age	Sex	Eye	DM	HTN	Dyslipidemia	FBS (mg%)	TC (mg%)	TG (mg%)	Homocystein (µmol/L)	Initial BCVA	Quadrant Involved	Macula	Neovascularization	Anti-VEGF (n)	Laser	Final BCVA	Other eye
1	39	Male	LE	No	Yes [#]	Yes [#]	98	268	168	9.6	6/24	STQ [§]	CME	No	Yes (1)	Yes	6/6	Normal
2	60	Male	LE	Yes	Yes [#]	Yes	75	192	185	6.7	6/9	STQ [*]	Normal	No	No	Yes	6/9	Mild NPDR
3	53	Male	RE	Yes [#]	No	Yes	198	111	128	24.7 [#]	5/60	Superior hemiquadrantic ^{**}	Ischemia	No	No	Yes	6/24	Normal
4	60	Female	RE	Yes	Yes	Yes	112	239	198	NA	2/60	ITQ [§]	CME	No	Yes (3)	Yes	6/24	Normal
5	53	Male	RE	Yes	No	Yes	132	205	484	NA	1/60	Superior hemiquadrantic	Ischemia	NVD	Yes (1)	Yes	1/60	Macular RVO
6	57	Male	LE	Yes	Yes	No	102	171	144	NA	1/60	ITQ	TRD	NVE	No	Yes	1/60	Mild NPDR

*Figure 1, **Figure 2, [§]OCT images, [#]Diagnosed during workup for vascular occlusion. RE: Right eye, LE: Left eye, NA: Not available, FBS: Fasting blood sugar, TC: Total cholesterol, TG: Triglyceride, BCVA: Best-corrected visual acuity (Snellen), STQ: Superotemporal, ITQ: Inferotemporal, CME: Cystoid macular edema, TRD: Tractional retinal detachment, NVD: Neovascularization of disc, NVE: Neovascularization elsewhere, NPDR: Nonproliferative diabetic retinopathy, RVO: Retinal vein occlusion, OCT: Optical coherence tomography

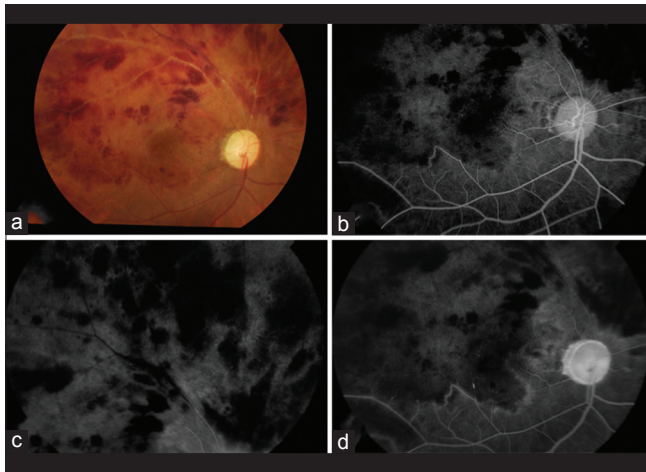


Figure 2: Shows clinical (a) and early (b), mid (c), and late (d) phase angiographic features of combined branch retinal artery and vein occlusion in the superior hemisphere

Vision at presentation and visual recovery after treatment were determined by perfusion status of the macula. All eyes received scatter laser irrespective of retinal neovascularization.

Combined BRVO and BRAO appear to be an unusual and extremely rare combination affecting both young and old patients with significant visual morbidity and systemic associations. Of six reported cases in literature, two patients were in their third decade, one associated with cytomegalovirus retinitis in a 26-year-old man with acquired immunodeficiency syndrome and the second case following hepatitis C treatment with interferon and ribavirin in a 29-year-old man.^[11,12] We previously reported another case of a 39-year-old man with hyperhomocysteinemia and combined branch occlusion.^[10] The other three cases were in their sixth decade, one being a hypertensive man who developed BRAO 5 weeks after intravitreal bevacizumab for BRVO associated macular edema and the other two being women with uncontrolled hypertension and diabetes.^[13-15]

Pathogenetic mechanisms by which combined BRVO and BRAO occur are unclear. We postulate that BRVO may be the initial event occurring due to the compression of the vein by atherosclerotic arteries at arterio-venous crossing sites leading to turbulent blood flow and dynamic obstruction or actual thrombus formation and mechanical blockage. If severe enough, sudden rise in intravascular pressure in the venous tree to levels above the systolic BP may lead to transmission of "back-pressure" to the arterial circulation and subsequent compromise in arterial perfusion which manifests as BRAO. Although the widespread CNP and vein occlusion are similar features, our cases should not be mistaken for ischemic BRVO as sludging of arteries and such well-demarcated, wedge-shaped complete capillary drop out is not a feature of ischemic BRVO. Similar mechanisms have been postulated to explain the occurrence of combined CRVO and CRAO.

We performed scatter laser photocoagulation at the time of initial presentation even without the presence of retinal neovascularization. Although this may be controversial; we believe that, due to very high "ischemic index" and resultant vascular endothelial growth factor load, these eyes are at a high

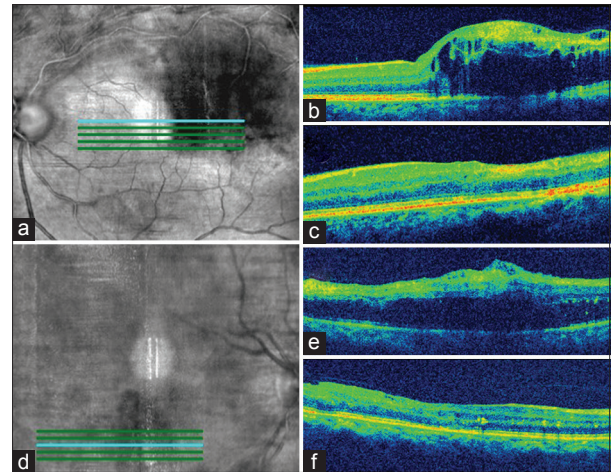


Figure 3: Serial spectral domain-optical coherence tomography images through the area of occlusion (a and d) showing hyperreflectivity and increased thickness of inner retinal layers, and decreased reflectivity in the outer retinal layers suggestive of arterial hypoperfusion (b and e). Follow-up optical coherence tomographics reveal thinning of the ganglion cell layer (c and f)

risk for retinal and iris neovascularization and can progress to neovascular glaucoma (NVG) within a few weeks. Lee *et al.* reported neovascularization rate of 21.4% in cases of BRVO with arterial insufficiency.^[9] Of the cases reported in literature, NVD occurred in one case and NVG in two patients.^[10,12,13] In our series, NVD occurred in one case despite sectoral laser and one had NVE at presentation. In addition to laser photocoagulation and use of intravitreal bevacizumab that we describe, radial optic neurotomy, though not popular, may be a therapeutic option as described by Mennel *et al.* for the management of combined CRVO and cilioretinal artery occlusion with good results.^[17]

We found a very high association of systemic comorbidity as most of our patients had a combination of diabetes mellitus, elevated lipids, hypertension, or hyperhomocysteinemia. A thorough systemic evaluation and close monitoring for cardiovascular events are critical in all cases of combined occlusion.

Conclusions

Combined BRAO and BRVO are exceedingly rare, are associated with significant systemic comorbidity and can have a good visual outcome if recognized early and treated appropriately.

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Conflicts of interest

There are no conflicts of interest.

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