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

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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 cellophane 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, 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 ×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
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. Re-injections 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. 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](image-url) 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.

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**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%) | Homocysteine (µmol/L) | Initial BCVA | Quadrant Involved | Macula | Neovascularization | Anti-VEGF (mg) | 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| Yes | No  | 198         | 111      | 128      | 24.7     | 5/60                | Superior hemiquadrant** | Ischemia     | No     | No         | Yes (1)   | 6/24  | Normal    |          |
| 4      | 60  | Female| RE | Yes | Yes | Yes | 112        | 239      | 198      | NA       | 2/60                | ITO        | CME            | No     | Yes (3)      | Yes         | 6/24  | Normal    |          |
| 5      | 53  | Male| RE  | Yes| No  | Yes | 132        | 205      | 484      | NA       | 1/60                | Superior hemiquadrant | Ischemia     | No     | NVD        | Yes (1)   | 1/60  | Macular RVO|          |
| 6      | 57  | Male| LE  | Yes| No  | Yes | 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, ITO: 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.
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. We previously reported another case of a 39-year-old man with hyperhomocysteinemia and combined branch occlusion. 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.

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 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. Of the cases reported in literature, NVD occurred in one case and NVG in two patients. 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.

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.

References
1. Richards RD. Simultaneous occlusion of the central retinal artery and vein. Trans Am Ophthalmol Soc 1979;77:191-209.
2. Brown GC, Duker JS, Lehman R, Eagle RC Jr. Combined central retinal artery-central vein obstruction. Int Ophthalmol 1993;17:9-17.
3. Shukla D, Arora A, Hadi KM, Kumar M, Baddela S, Kim R.
Combined central retinal artery and vein occlusion secondary to systemic non-Hodgkin’s lymphoma. Indian J Ophthalmol 2006;54:204-6.

4. Hayreh SS, Fraterrigo L, Jonas J. Central retinal vein occlusion associated with cilioretinal artery occlusion. Retina 2008;28:581-94.
5. McLeod D. Central retinal vein occlusion with cilioretinal infarction from branch flow exclusion and choroidal arterial steal. Retina 2009;29:1381-95.
6. Ozturk T, Takes O, Saatci AO. Dexamethasone implant (ozurdex) in a case with unilateral simultaneous central retinal vein and branch retinal artery occlusion. Case Rep Ophthalmol 2015;6:76-81.
7. Karapetyan A, Ouyang P, Tang LS, Zeng J, Ying MD. Detection of underdiagnosed concurrent branch retinal artery occlusion in a patient with central retinal vein occlusion using spectral domain optical coherence tomography. BMC Ophthalmol 2014;14:91.
8. Schmidt D. Comorbidities in combined retinal artery and vein occlusions. Eur J Med Res 2013;18:27.
9. Lee YJ, Kim JH, Ko MK. Neovascularization in branch retinal vein occlusion combined with arterial insufficiency. Korean J Ophthalmol 2005;19:34-9.
10. Sengupta S. Combined branch retinal artery and vein occlusion in hyperhomocysteinemia. JAMA Ophthalmol 2014;132:1255.
11. Nicolò M, Artioli S, La Mattina GC, Ghiglione D, Calabria G. Branch retinal artery occlusion combined with branch retinal vein occlusion in a patient with hepatitis C treated with interferon and ribavirin. Eur J Ophthalmol 2005;15:811-4.
12. Conway MD, Tong P, Olk RJ. Branch retinal artery occlusion (BRAO) combined with branch retinal vein occlusion (BRVO) and optic disc neovascularization associated with HIV and CMV retinitis. Int Ophthalmol 1995-1996;19:249-52.
13. An TS, Kwon SI. Neovascular glaucoma due to branch retinal vein occlusion combined with branch retinal artery occlusion. Korean J Ophthalmol 2013;27:64-7.
14. Kaur S, Sachdev N. Unilateral branch retinal arterial occlusion following administration of bevacizumab for branch retinal vein occlusion. Int Ophthalmol 2013;33:549-52.
15. Okamoto N, Matsumoto C, Shimomura Y. Sequential occlusion of the branch retinal artery and branch retinal vein in a patient with hypertension: An interventional case report. Clin Ophthalmol 2014;8:2121-3.
16. Shah VA, Wallace B, Sabates NR. Spectral domain optical coherence tomography findings of acute branch retinal artery occlusion from calcific embolus. Indian J Ophthalmol 2010;58:523-4.
17. Mennel S, Droutsas K, Meyer CH, Schmidt JC, Kroll P. Radial optic neurotomy in combined cilioretinal artery and central retinal vein occlusion. Br J Ophthalmol 2005;89:642-3.