Retinal periphlebitis associated with branch retinal vein occlusion and complicated by subfoveal hemorrhage: a case report

Abdulrahman AlZaid¹, Moustafa Magliyah¹,², Amjad Ameen Saifaldein³, Hani B AlBalawi⁴, Marco Mura¹ and Hassan Al-Dhibi¹,⁵

Abstract
Retinal periphlebitis is a subtype of retinal vasculitis affecting the retinal veins. We report a case of bilateral branch retinal vein occlusion (BRVO) associated with idiopathic retinal periphlebitis and complicated by subfoveal hemorrhage (SFH). An 18-year-old woman presented with best-corrected visual acuity of 20/20 in the right eye and 20/30 in the left eye. Examination revealed bilateral retinal vascular sheathing predominantly involving the retinal veins and bilateral BRVO. Fundus fluorescein angiography revealed localized vascular leakage in the right eye and diffuse vascular leakage in the left eye. Spectral-domain optical coherence tomography showed mild nasal thickening with subfoveal fluid in the left eye. Oral steroids were started on a tapering dosage as well as oral methotrexate. A year later, she presented with regressed vascular sheathing in both eyes with 5/200 vision and SFH in the left eye. Pars plana vitrectomy, subretinal tissue plasminogen activator, intravitreal ranibizumab, laser photocoagulation, and gas injection were performed. The SFH resolved and the visual acuity improved to 20/100. Good vision was preserved in both eyes with no active inflammation. Timely management of SFH in idiopathic retinal periphlebitis can achieve a favorable visual outcome.

¹Vitreoretinal Division, King Khalid Eye Specialist Hospital, Riyadh, Saudi Arabia
²Department of Ophthalmology, Prince Mohammed Medical City, Aljouf, Saudi Arabia
³Department of Ophthalmology, King Faisal Medical Complex, Taif, Saudi Arabia

Corresponding author:
Hani B AlBalawi, Department of Ophthalmology, University of Tabuk, Al Douba Street, PO Box 7191, Tabuk 11462, Kingdom of Saudi Arabia.
Email: hb.albalawi@ut.edu.sa

¹Department of Surgery, Division of Ophthalmology, Faculty of Medicine, Ophthalmology Department, University of Tabuk, Tabuk City, Saudi Arabia
²Alfaisal University, College of Medicine, Riyadh, Saudi Arabia
Introduction

Retinal periphlebitis is a subtype of retinal vasculitis affecting the retinal veins. Retinal vasculitis, which predominantly involves veins, is found in tuberculosis, Eales’ disease, syphilis, sarcoidosis, Behcet’s disease, multiple sclerosis, cytomegalovirus retinitis, and human immunodeficiency virus infection. Idiopathic retinal periphlebitis is an uncommon retinal vasculitis and primarily affects the retinal veins, with only a few cases reported in the literature. Retinal vascular occlusion, including central retinal venous occlusion (CRVO) and branch retinal venous occlusion (BRVO), is a known feature of retinal periphlebitis. Occlusive periphlebitis can lead to retinal edema, intraretinal hemorrhages, and hemorrhagic infarction of the retina. Although BRVO is a prominent feature of retinal periphlebitis in Behcet’s disease, it can be associated with idiopathic vasculitis. Subfoveal hemorrhage (SFH) is not an uncommon feature in BRVO and may cause poor vision as a result of subsequent damage to photoreceptors. We report a case of bilateral BRVO associated with idiopathic retinal periphlebitis and complicated with SFH in one eye. The reporting of this study conforms to CARE guidelines.

Case presentation

The patient was an 18-year-old woman with no previous ocular or systemic conditions who presented with a 10-day history of blurred vision in the left eye. She denied similar previous episodes or a history of oral or genital ulcers. On examination, her best-corrected visual acuity (BCVA) was 20/20 in the right eye and 20/30 in the left eye. Anterior segment examination, including intraocular pressure, was unremarkable with no signs of inflammation in the anterior chamber in either eye. Fundus examination showed dense vascular sheathing of the superonasal and inferior blood vessels surrounded by scattered retinal hemorrhages, indicating BRVO (Figure 1a). Less severe exudates were found in other retinal quadrants of the right eye. In the left eye, dense sheathing was found in the inferotemporal retinal veins with diffuse scattered hemorrhages. Scattered areas of vascular sheathing were found in other retinal quadrants (Figure 1b). Fundus fluorescein angiography (FFA) showed leakage from superonasal and inferior blood vessels with nonperfusion of capillaries in the corresponding areas in the right eye (Figure 1c). In the left eye, FFA showed diffuse vascular leakage from retinal vessels, as well as leakage from a macular retinal venule with a limited area of capillary nonperfusion in the far periphery temporally (Figure 1d). Spectral-domain optical coherence tomography (SD-OCT) was unremarkable in the right eye and showed mild nasal thickening with subfoveal fluid in the left eye (Figure 1e and f). Systems review, including of the respiratory, gastrointestinal, neurological, and musculoskeletal systems, was negative. Systemic workup for uveitis, including a full blood count and renal and liver
function tests, a computed tomography scan of the chest, a fluorescent treponemal antibody absorption test, a purified protein derivative test, and the QuantiFERON-TB Gold test were negative for tuberculosis. Syphilis was also negative. Serum antinuclear antibody, antineutrophil cytoplasmic autoantibody,
cytoplasmic and perinuclear anti-neutrophil cytoplasmic antibodies, rheumatoid factor, and HLA-B51 were all negative. Magnetic resonance imaging of the brain and orbital cavities was unremarkable. Anterior chamber tap with polymerase chain reaction tests were negative for herpes simplex virus, varicella zoster virus, and cytomegalovirus.

The impression was bilateral retinal vasculitis with inflammatory BRVO in both eyes. She was started on oral prednisone 1 mg/kg to be tapered over a month and methotrexate 10 mg weekly. Her BCVA remained 20/20 in the right eye and 20/30 in the left eye. She was offered an intravitreal injection of ranibizumab 0.5 mg/0.05 mL for macular edema in the left eye but preferred to continue with systemic treatment and delay local therapy because she had acceptable vision in the right eye.

A year later, she presented again with a sudden decrease in vision in the left eye to 5/200, a newly formed subretinal hemorrhage in the macular area, and new retinal hemorrhages superiorly (Figure 2a). SD-OCT showed accumulation of blood in the subfoveal region, indicating SFH (Figure 2b). The patient underwent pars plana vitrectomy with subretinal injection of 12.5 μg of tissue plasminogen activator, intravitreal injection of ranibizumab 0.5 mg/0.05 mL, with laser photocoagulation for the ischemic retinal areas and sulfur hexafluoride gas injection.

Two months later, the patient presented with a BCVA of 20/100 in the left eye and complete resolution of the SFH, inactive vasculitis, and laser photocoagulation scars (Figure 3a). SD-OCT showed a normal retinal structure in the macular area (Figure 3b). She has maintained stable vision in both eyes with no active inflammation seen at 2-monthly follow-up visits for 1 year. Further follow-up at 3-monthly to 4-monthly intervals is planned.

Discussion

In this report, we describe a case of bilateral BRVO associated with idiopathic retinal periphlebitis and complicated with SFH in the left eye. The periphlebitis described herein resembled frosted branch angiitis, which is characterized by a thick inflammatory infiltrate surrounding all of the retinal veins. The diagnosis of idiopathic retinal periphlebitis is usually established after exclusion of other etiologies, including Behçet’s disease, tuberculosis, sarcoidosis, multiple sclerosis, pars planitis, and Eales’ disease. The clinical findings in this case, as well as the results of the systemic workup,
led to a diagnosis of idiopathic retinal periphlebitis. Eales’ disease is an idiopathic retinal vasculitis that primarily affects the peripheral retinal veins and is usually associated with a positive purified protein derivative test. Clinical features include perivascular phlebitis, diffuse peripheral nonperfusion, and neovascularization leading to vitreous hemorrhage. Although the retinal vasculitis in our patient was primarily venous, the peripheral retinal nonperfusion was localized and no neovascularizations were observed. Furthermore, all tests for tuberculosis were negative.

Another diagnosis of exclusion is IRVAN (idiopathic retinal vasculitis, aneurysms and neuroretinitis). Unlike idiopathic retinal periphlebitis, IRVAN mainly involves the retinal arterioles, and clinical findings include aneurysmal dilatations of arterioles in the retina and optic nerve head, peripheral capillary nonperfusion, retinal neovascularization, and macular exudate.

Kleiner et al classified patients with eyes that have the appearance of frosted branch angiitis into three subgroups. The first subgroup includes patients with lymphoma or leukemia whose disease is due to cellular infiltration (frosted branch-like appearance). The second subgroup includes patients who have associated viral infection or autoimmune disease. Frosted branch angiitis in these patients is a clinical sign of immune complex deposition (secondary frosted branch angiitis). The third subgroup is described as idiopathic retinal vasculitis in healthy young patients (acute idiopathic branch angiitis). There are few reports of CRVO in idiopathic vasculitis described as frosted branch angiitis. CRVO in these patients is often nonperfused and usually progresses to rubeosis iridis and neovascular glaucoma with a poor visual outcome despite treatment. The incidence of BRVO in idiopathic retinal vasculitis is believed to be as low as 9%. The good visual outcome in both eyes in our patient with no sequelae of retinal ischemia, such as retinal neovascularization, rubeosis iridis, or neovascular glaucoma, suggests a better prognosis than the CRVO in these patients. Nevertheless, the incidence of SFH in the left eye of this patient might have caused significant visual loss owing to loss of photoreceptors, especially if surgical intervention had not been performed in a timely manner. Pars plana vitrectomy with subretinal tissue plasminogen activator and gas tamponade remain the mainstay for management of SFH and achieve visual improvement. Addition of anti-vascular endothelial growth factor may

Figure 3. Fundus photograph of the left eye obtained 2 months after retinal surgery shows complete resolution of the foveal subretinal hemorrhage, inactive vasculitis, and laser photocoagulation scars and (b) Spectral-domain optical coherence tomography scan of the left eye showing a normal retinal structure in the macular area.
help to maintain the gains in visual acuity.\textsuperscript{12}

In conclusion, idiopathic retinal vasculitis is an uncommon cause of inflammatory retinal vascular occlusions that mainly include the retinal veins. Visual and structural outcomes of BRVO in idiopathic retinal periphlebitis are more favorable than those of CRVO. Timely surgical management is needed for SFH to prevent significant visual loss.

\textbf{Author contributions}

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

\textbf{Declaration of conflicting interests}

All authors report no conflicts of interest in this work.

\textbf{Ethics statement}

This research was conducted in compliance with the Declaration of Helsinki. Written informed consent for publication of this case, the deidentified patient details, and accompanying images was obtained. This project was exempted from review by the institutional review board at King Khaled Eye Specialist Hospital. Separate consent was obtained for administration of immunosuppressive medications.

\textbf{Funding}

The authors declare that this study has received no financial support.

\textbf{ORCID iDs}

Moustafa Magliyah \footnote{https://orcid.org/0000-0001-6350-7464}
Hani B AlBalawi \footnote{https://orcid.org/0000-0001-9396-6952}

\textbf{References}

1. Abu El-Asrar AM, Herbort CP and Tabbara KF. Differential diagnosis of retinal vasculitis. \textit{Middle East Afr J Ophthalmol} 2009; 16: 202–218.
2. Graham EM, Stanford MR, Sander MD, et al. A point prevalence study of 150 patients with idiopathic retinal vasculitis: I: Diagnostic value of ophthalmological features. \textit{Br J Ophthalmol} 1989; 73: 714–721.
3. Muraoka Y, Tsujikawa A, Murakami T, et al. Branch retinal vein occlusion-associated subretinal hemorrhage. \textit{Jpn J Ophthalmol} 2013; 57: 275–282.
4. Gagnier JJ, Kienle G, Altman DG, et al; CARE Group. The CARE guidelines: consensus-based clinical case reporting guideline development. \textit{Headache} 2013; 53: 1541–1547.
5. Das T, Pathengay A, Hussain N, et al. Eales’ disease: diagnosis and management. \textit{Eye (Lond)} 2010; 24: 472–482.
6. Kleiner RC. Frosted branch angiitis: clinical syndrome or clinical sign? \textit{Retina} 1997; 17: 370–371.
7. Foss AJ, Headon MP, Hamilton AM, et al. Transient vessel wall sheathing in acute retinal vein occlusions. \textit{Eye Lond Engl} 1992; 6: 313–316.
8. Seo MS, Woo JM, Jeong SK, et al. Recurrent unilateral frosted branch angiitis. \textit{Jpn J Ophthalmol} 1998; 42: 56–59.
9. Kaburaki T, Nakamura M, Nagasawa K, et al. Two cases of frosted branch angiitis with central retinal vein occlusion. \textit{Jpn J Ophthalmol} 2001; 45: 628–633.
10. Abu El-Asrar AM, Al-Obeidan SA and Abdel Gader AG. Retinal periphlebitis resembling frosted branch angiitis with non-perfused central retinal vein occlusion. \textit{Eur J Ophthalmol} 2003; 13: 807–812.
11. Kumawat B, Tripathy K, Venkatesh P, et al. Central Retinal Vein Occlusion-like Appearance: A Precursor Stage in Evolution of Frosted Branch Angiitis. \textit{J Ophthalmic Vis Res} 2017; 12: 440–442.
12. Chang W, Garg SJ, Maturi R, et al. Management of thick submacular hemorrhage with subretinal tissue plasminogen activator and pneumatic displacement for age-related macular degeneration. \textit{Am J Ophthalmol} 2014; 157: 1250–1257.