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Loading Doses of Bevacizumab in Branch Retinal Vein Occlusion (BRVO): a Case Report

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ABSTRACT

Background: Branch retinal vein occlusion (BRVO) is a sight threatening condition which may result well when promptly diagnosed and treated. Current trend of BRVO therapy uses anti-vascular endothelial growth factor (anti-VEGF) such as bevacizumab, ranibizumab and aflibercept as agents of choice. Previous studies have proven effectiveness of six monthly injections of anti-VEGF as loading doses before switching to pro-renata regimen in BRVO. We would like to report a case with lower frequency of bevacizumab injection as anti-VEGF in a case of BRVO with satisfactory outcome. **Case presentation:** A 52-year old male presented with sudden painless vision loss on right eye since 2 months prior to examination. Patient had been taking medications regularly for hypertension and dyslipidemia. Patient had also been previously diagnosed with peripheral artery disease. Patient came with BCVA of 0.1 and negative pinhole on right eye while BCVA for left eye was 1.0. Relative afferent pupillary defect was positive on the right eye. Intraocular pressure and anterior segment were within normal limits for both eyes. Upon fundus examination of the right eye, findings included 0.3 CDR, dilated and tortuous retinal veins, multiple scattered preretinal hemorrhages, and macular edema. Upon posterior segment evaluation of the left eye, no abnormalities was found. Patient was then diagnosed with BRVO of the right eye and received three monthly injections of bevacizumab. Patient's BCVA and anatomic condition improved with final BCVA of 0.5 on the right eye. Patient was monitored monthly for the next six months and there was no deterioration on the anatomical and functional outcomes.
Conclusion: Lower frequency of monthly bevacizumab injection could be beneficial in some cases of BRVO. Monthly monitoring is essential to maintain anatomical and functional outcomes.

Keywords: BRVO, bevacizumab, anti-VEGF, loading doses

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Background

Branch retinal vein occlusion (BRVO) is one of the most common retinal vascular disease. It endangers sight by causing ischemia to retinal tissue due to compression at the arteriovenous (AV) crossing site of the retina. This condition triggers the production of various substances along with transfer of proteins and fluid to interstitial as well as release of inflammatory mediators and cytokines.[1] Among these substances, vascular endothelial growth factor (VEGF) plays major role as it increases vascular permeability and induces angiogenesis. As a result of VEGF, macular edema occurs and usually becomes the main cause of visual impairment in BRVO. Compared to central RVO (CRVO), BRVO occurs more often and has better prognosis when treated appropriately.[2] Hence, prompt treatment of BRVO is essential to preserve anatomical and visual function of the patients.

Currently there are wide range of therapeutic options of BRVO with anti-VEGF remains the preferred among all. There are three anti-VEGF available: ranibizumab, aflibercept and bevacizumab. Earlier two has been approved by US Food and Drug Administration while the latest is used off label for RVO cases.[3] These drugs have been proven by various randomised controlled trials (RCTs) to improve ocular structure and function after episodes of RVO.[4,5]

Large trials tend to use Anti-VEGF regimen of six injections administered monthly.[4,5] However, more frequent injections means more financial burden for patients and family as well as for healthcare system especially in low- and middle-income countries. Nowadays, there is growing evidence of lesser amount of injections given to patients with BRVO, switching the trend to pro-renata (PRN) dosing.[6] Here, we would like to present a case of BRVO with satisfactory and lasting result after three monthly injections of bevacizumab.

Case Presentation

A 52-year old male came to Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia with chief complaint of sudden painless vision loss on right eye since 2 months prior toe examination. Patient denied any red eye nor pain. Patient was previously diagnosed with peripheral artery disease (PAD) and had also been taking regular medication for hypertension and dyslipidemia. Patient came with BCVA of 0.1 and negative pinhole on right eye while best corrected visual acuity (BCVA) for left eye was 1.0. Relative afferent pupillary defect was positive on the right eye. Intraocular pressure and anterior segment were within normal limits for both eyes. Fundus examination of the right eye showed cup disk ratio (CDR) of 0.3, fundus examination showed dilated and tortuous retinal veins, multiple scattered preretinal hemorrhages, and macular edema. Fundus examination of left eye showed no abnormalities. Patient was diagnosed with BRVO of right eye and was given three monthly injections of intravitreal ranibizumab. Patient came for monthly routine follow up with final BCVA of 0.5 on right eye and 1.0 on left eye along with significant improvement of retinal conditions. During the course of six months follow up period, patient's BCVA remains and anatomic condition improved.

Discussion

BRVO Is a sight threatening disease with 15-year cumulative incidence of 1.8%.[7] Its risk factors include age, cardiovascular disease, hypertension, body mass index (BMI), hyperviscosity syndrome, and autoimmune.[8,9] BRVO is usually caused by compression of nearby vessel, mostly in arterio-venous crossing site.[10] Those with BRVO usually develop visual impairment due to macular edema. Over a year, visual loss occurs in 5-15% of patients with BRVO.[11]

Recent studies have proven that anti-VEGF provides a promising solution for macular edema in cases of BRVO. Bevacizumab is an anti-VEGF originally used originally for colorectal cancer. However, recent trend has shown

increased use of bevacizumab in ocular diseases, such as BRVO. The drug works against VEGF-A and has been proven to relieve macular edema in patients with RVO.[12]

BRVO has better prognosis with reports of spontaneous resolution. Approximately 50-60% of eyes were found to have visual acuity (VA) of 20/40 or better without treatment.[13] However, persistent macular edema and bleeding from neovascularisation will contribute to poorer prognosis.[13] Hence, timely recognition and management must be carried out.

As anti-VEGF including bevacizumab has been widely proven to benefit patients with RVO. There are still inconsistency on the dosing regimen. Recent trend has shifted to PRN dosing in comparison to six monthly injections. However, there has not been many RCTs

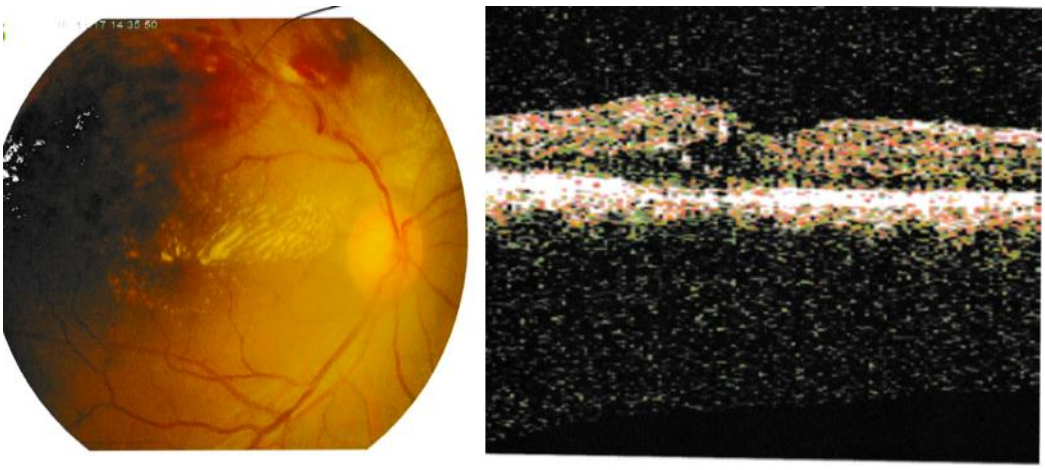

Figure 1. **[Left]** Fundus photo of patient 3 prior to injection. **[Right]** OCT of patient in case 3 prior to anti VEGF injection

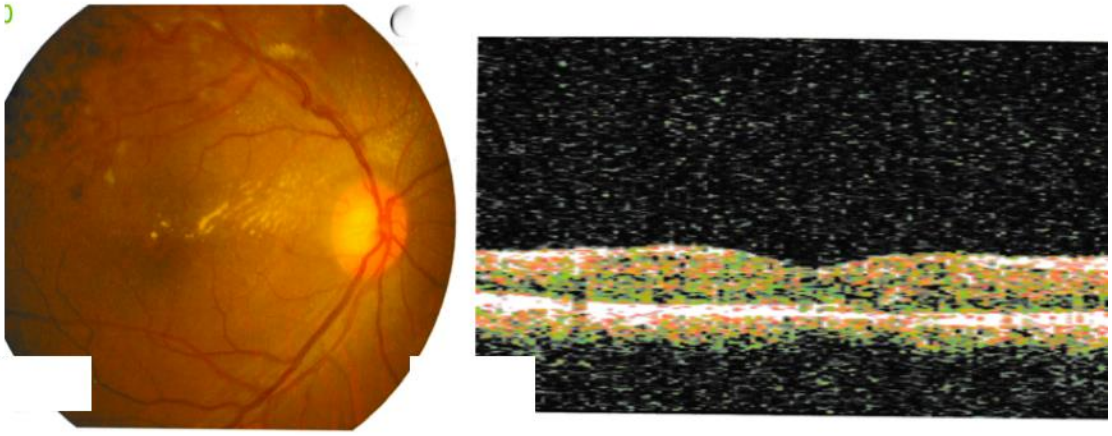

Figure 2. [Left] Fundus photo patient 3 after third anti-VEGF injection. **[Right]** OCT of patient in case 3 prior to anti VEGF injection

showing benefits of less than six monthly injections.

A study conducted in Macedonia showed significant VA improvement of patient with both CRVO and BRVO (p=0.001 and p<0.001, respectively) treated with intravitreal bevacizumab with number of injections averaging in 1.98.[14] The study also showed significant improvement of central macular thickness (CMT) of both CRVO and BRVO cases (p<0.001). A prospective RCT conducted

in India by Narayanan, et al showed promising result of PRN dosing, as patients treated in bevacizumab group obtained +15.6 letters ($p<0.0001$; 95% CI +12.0 to +20.5) compared to start of therapy with average of 3.0 ± 1.4 injections. Hence, lower frequency of bevacizumab injection may benefit the patient.[15]

Patient in our case showed marked improvement after three monthly injections of bevacizumab. The result was also maintained after six months routine follow up. Hence, we believe that three injection may be suffice to improve condition of patients with BRVO. We still strongly recommend routine monitoring of these patients to prevent deterioration. We also believe that lower frequency of anti-VEGF injections, especially in low- and middle-income countries could benefit patients and their families.

Conclusion

Patients with BRVO could benefit from three monthly injection of anti-VEGF. We strongly recommend monthly follow-up to ensure patient's functional and anatomical outcomes.

List of Abbreviations

BCVA : best corrected visual acuity

BMI : body mass index

BRVO : branch retinal vein occlusion

CMT : central macular thickness

CRVO : central retinal vein occlusion

PAD : peripheral artery disease

PRN : pro-renata

RVO : retinal vein occlusion

VA : visual acuity

VEGF : vascular endothelial growth factor

Declarations

Ethics and Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by Editor-in-Chief of this journal.

Availability of Data and Materials

All data generated or analysed during this study are included in this published article

Competing Interest

Author declare no competing interest

Funding

None

Authors' Contribution

AAV conducted the examination, performed the injections and analysed patient's data as well as wrote this manuscript. Author has approved this final manuscript.

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