

# Intravitreal bevacizumab injection and carotid artery stent replacement for neovascular glaucoma in internal carotid artery occlusion

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**Abstract:** Neovascular glaucoma (NVG) secondary to internal carotid artery (ICA) occlusion is usually resistant to treatment. We report a case of NVG with ICA occlusion improved by intravitreal bevacizumab (IVB) injection and carotid artery stent replacement (CAS), even though we did not perform panretinal photocoagulation. A 67-year-old male with NVG noted visual loss in his left eye. Magnetic resonance angiography showed left ICA occlusion. He was diagnosed with NVG secondary to ICA occlusion. The next day, we carried out IVB injection in his left eye, following which the iris and angle neovascularization regressed, and the intraocular pressure decreased to normal within a day after the injection. CAS was performed on his left ICA at a month post injection. Two months later, we reinjected bevacizumab in his left eye. His condition remained stable with no recurrence over two years. This case indicates that IVB injection and CAS are useful for early-stage NVG secondary to ICA occlusion.

**Keywords:** bevacizumab, neovascular glaucoma, internal carotid artery occlusion, carotid artery stent replacement, vascular endothelial growth factor

## Introduction

Patients with internal carotid artery (ICA) occlusion/stenosis develop ocular ischemia and present with various ocular signs. The clinical course and presentation may be quite varied, with some cases showing rapid advancement of neovascularization following high intraocular pressure (IOP). ICA occlusion often progresses without symptoms, and when the patient notices ocular disorders and visits a clinic, the condition is often at an advanced stage of ocular ischemia where neovascular glaucoma (NVG) has developed with severe ICA stenosis. In such cases, due to the remarkable decline in ophthalmic arterial blood pressure, even a slight increase in IOP causes severe damage to the eye and leads to loss of vision. Prompt countermeasures to lower IOP are essential to ameliorate the ischemia.<sup>1</sup> Thorough panretinal photocoagulation (PRP) is the most effective procedure performed to resolve neovascularization, but sometimes the desired decline in IOP cannot be reached. In such cases, an invasive filtering surgical procedure, such as trabeculectomy, is needed to lower IOP.

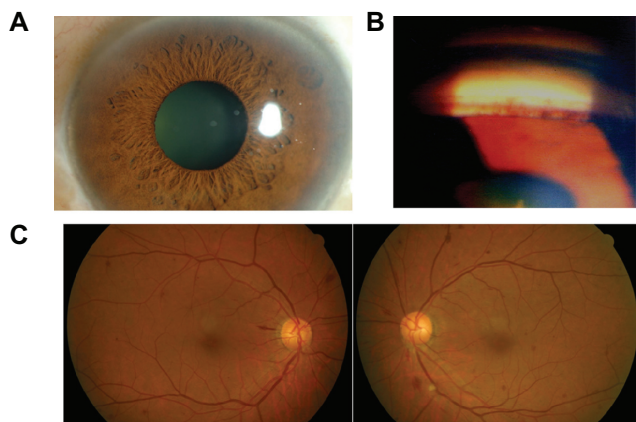
Recently, the involvement of vascular endothelial growth factor (VEGF) in neovascular diseases has been discussed.<sup>2</sup> Bevacizumab is an anti-VEGF antibody and angiogenesis inhibitor developed in the US and approved in 2004 by the Food and Drug Administration as a treatment for colorectal cancer. It has also been used off-label for ocular diseases, and its efficacy has been reported for choroidal neovascularization in age-related macular degeneration and myopic choroidal neovascularization, central retinal vein occlusion, diabetic retinopathy, postoperative macular edema, NVG, and

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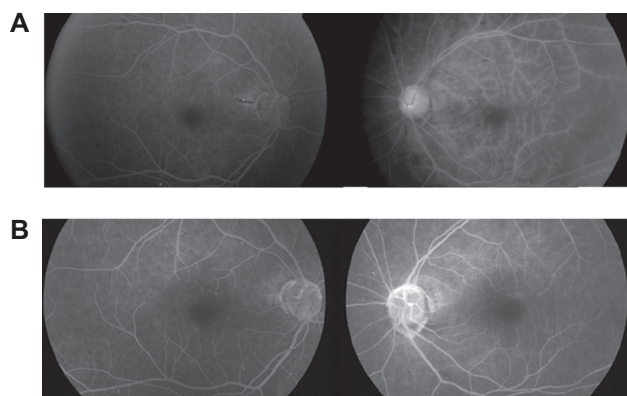
other ocular diseases.<sup>3-9</sup> Because ocular administration of bevacizumab is not yet approved, its off-label use needs approval of the relevant institutional review board and written consent of the patient, after a detailed explanation of the drug's effects and confirmation of the patient's free will in undertaking the treatment. This article describes the efficacy of intravitreal bevacizumab (IVB) injection in a patient with NVG secondary to ICA occlusion.

## Case report

A 67-year-old male had intermittent vision difficulty and trouble with seeing things in purple with his left eye since April 2006, but did not pursue treatment until he gradually sensed decreasing visual acuity (VA). He visited a nearby clinic on April 26, 2007, when he was diagnosed with NVG. He was referred to Kinki University Hospital on April 27, 2007. At his initial visit to our hospital, his VA was 1.0 for both eyes, with IOP values of 13 mmHg OD and 31 mmHg OS. He had a 30-year history of type 2 diabetes mellitus. Slit lamp examination of his left eye demonstrated neovascularization of the iris and all hours of the angle, and peripheral anterior synechiae (PAS) was present at the directions of 3 o'clock and 6 o'clock (Figure 1A and 1B). Funduscopy revealed peripheral blot hemorrhages in both eyes (Figure 1C). Fluorescein angiography (FA) revealed that the arm-to-retina circulation time was prolonged to 21.9 sec, and the intraretinal transit time was also prolonged. At the late phase of FA, diffuse leakage was seen, probably caused by hyperpermeability of the retinal artery, but no avascular areas were seen in his left eye (Figure 2A). We referred him to our neurosurgery department for examination. Magnetic resonance angiography (MRA) of his carotid arteries demonstrated branching of the left ICA



**Figure 1** Clinical findings at the initial patient visit. **A)** Neovascularization of the iris. **B)** Neovascularization of the angle. **C)** The fundus photograph of both eyes. The images show bilateral peripheral dot hemorrhages.



**Figure 2** Fluorescein angiography of the left eye shown over time. **A)** At the initial visit. **B)** Six months after carotid artery stent replacement. Angiogram taken six months after carotid artery stent replacement shows normalized arm-to-retina circulation time and the leakage of the dye from the retinal artery was improved, with no avascular areas observed.

from the common carotid artery and occlusion at 15.59 mm from the branching point (Figure 3).

The patient was diagnosed with ocular ischemic syndrome secondary to ICA occlusion. He had also had a cerebral infarction two years previously and was diagnosed at that time with ICA occlusion, but was given only oral antiplatelet medication and followed up.

In order to regress the neovascularization, 1.25 mg (0.05 mL) of bevacizumab (Avastin® 100 mg/4 mL) was injected into the vitreous through the pars plana of the left eye on April 28, 2007. Before the injection of bevacizumab, approval from the institutional review board of Kinki University Hospital and the patient's informed consent

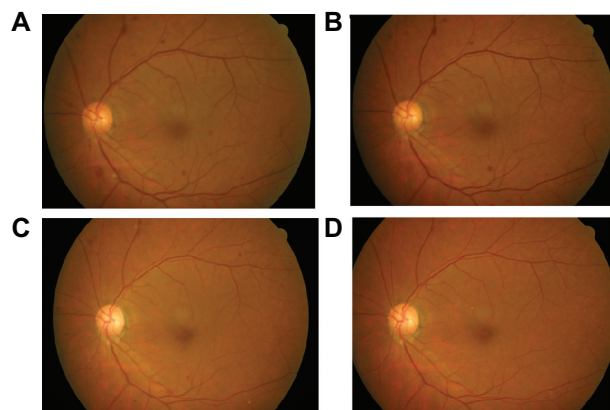


**Figure 3** Magnetic resonance angiography of the carotid, showing occlusion of the left carotid artery at 15.59 mm from its branching from the common carotid artery.

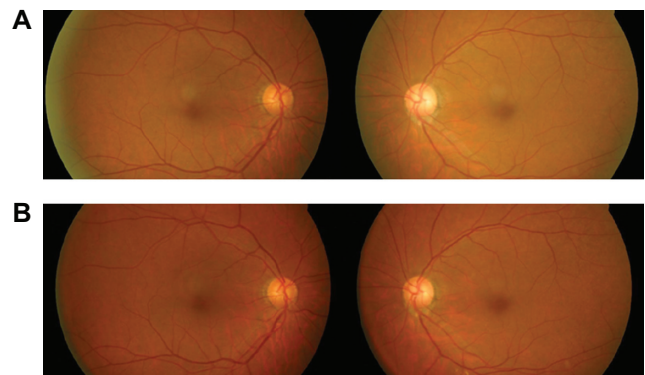
were obtained. On the following day, the left eye IOP decreased to 18 mmHg and iris neovascularization vanished. Five days after the injection, the neovascularization at the angle had completely regressed, and left eye IOP remained 18 mmHg. The patient did not show any signs of deterioration, so we decided to follow him up without giving PRP. He underwent carotid artery angioplasty and stent placement on June 5, 2007. After the operation, the VA was 1.0 for both eyes with IOP of 17 mmHg OD and 16 mmHg OS. However, neovascularization was present at the directions of 3 o'clock and 6 o'clock, so we injected bevacizumab (1.25 mg/0.05 mL) again into the left eye. After the reinjection, his corrected VA remained at more than 1.0. He did not report any complications, and no evidence of IOP elevation or recurrence of neovascularization was seen. The fundoscopic findings were improved, with only slight blot hemorrhage remaining (Figure 4). No complications associated with the IVB injection were identified. FA at six months after carotid artery stent placement (CAS) showed improvement of the arm-to-retina circulation time and the leakage of the dye from the blood vessels (Figure 2B). Avascular areas of the retina were not observed. More than two years have passed and his condition remains stable, although additional treatment, such as PRP, has not been performed (Figure 5A and 5B).

## Discussion

We report here our experience with a case where NVG regressed and good VA was maintained following IVB injection without PRP. Bevacizumab treatment resolved iridal and angle rubeosis and lowered IOP quickly after the injection.



**Figure 4** Fundus photos of the left eye showing the clinical course. **A)** Five days after intravitreal bevacizumab injection. **B)** Thirty-two days after intravitreal bevacizumab injection. **C)** Forty-four days after carotid artery stent replacement. **D)** Six months after carotid artery stent replacement. The photo taken 44 days after carotid artery stent replacement shows slight dot hemorrhages remaining; this hemorrhage was resolved by six months after carotid artery stent replacement.



**Figure 5** Fundus photos over time. **A)** One year after intravitreal bevacizumab injection. **B)** Two years after intravitreal bevacizumab injection. Ophthalmoscopy shows an almost normal fundus.

Conventionally, complete PRP has been the only established method of treatment for neovascularization. However, PRP is a destructive method, and substantial lowering of visual function often occurs. To the best of our knowledge, there have been no reports that the combination of IVB and CAS resulted in a favorable long-term prognosis for NVG secondary to ICA occlusion without necessitating PRP application.

Because PRP has the advantage of permanent neovascular suppression, we have considered whether this procedure might be necessary in this case, and if necessary, when the most appropriate timing for PRP application might occur. However, two years have passed without any signs of neovascular recurrence and our patient remains stable and in a good condition.

When we attend a patient with NVG, we have to treat the underlying causes, and nosotropic measures are also necessary to counter the symptoms of NVG. For a case like the present one, while giving carotid endarterectomy (CEA) or CAS as a fundamental treatment, we have to prescribe measures to resolve neovascularization and to suppress the development of secondary-angle glaucoma.

The fundamental therapy for this type of case is to improve ocular ischemia by widening the ischemic part of the ICA and reconstructing the blood circulation. The “gold standard” for treatment of an occluded ICA is CEA, a surgical treatment, and its effectiveness has been shown in many studies. For some cases in which CEA is considered a high-risk procedure, CAS has been performed, and it has been reported to be as effective as CEA.<sup>10</sup> Our case was given CAS, and thereafter blood circulation was restored, and his fundoscopic and FA findings have improved remarkably, and neovascularization in the iris and angle has been resolved.

On the other hand, there are reports of complications caused by CAS, therefore we need to judge the indication

for CAS very carefully. While waiting for the operation to become feasible, we need to control IOP and give treatment to resolve neovascularization.

Recently, IVB injection has been reported to be very useful for NVG in the early stages.<sup>7</sup> The clinical course of NVG is divided into three stages, ie, Stage I (preglaucoma), Stage II (open-angle glaucoma), and Stage III (angle-closure glaucoma).<sup>11</sup>

Wakabayashi et al<sup>7</sup> reported their IOP control outcomes in patients with NVG who had received IVB injection as an initial treatment, although most of their cases had NVG secondary to diabetic retinopathy. Their findings show that IVB was very effective at the preglaucoma stage or early neovascularization stages, but IOP control was increasingly difficult with more advanced NVG.

Our patient was diagnosed with Stage II NVG (open-angle glaucoma), and the IVB injection produced prompt resolution of the neovascularization, resulting in a lowering of IOP, as well as suppression of angle-closure development.

As stated, IVB injection has the advantages of rapid and dramatic efficacy with low invasiveness. However, it is not flawless. The ocular use of bevacizumab is not yet approved by regulatory agencies, so we need institutional review board approval and adequate informed consent from the patient. Proper administration methods, correct dosages, and long-term patient prognosis have not yet been identified. The effect of an IVB injection is estimated at present to persist for one to several months and there is a chance of recurrence. Furthermore, there are some researchers<sup>12</sup> reporting a high probability of IOP increase immediately after intravitreal injection, therefore we need to assess the damage to the optic nerve caused by the injection using a larger number of cases. The left eye in our case had decreased IOP the day after the injection, and we presume this is showing the efficacy of bevacizumab injection in IOP reduction. Fortunately, we have not experienced deterioration of the visual field. On the other hand, the IOP of the right eye was 17 mmHg one month after the injection, but it has been fluctuating between 11 mmHg and 18 mmHg for two years afterwards. We consider this to be within the diurnal variation for the right eye.

Future study is needed to identify countermeasures for cases where the angle is already closed, where systemic complications are hindering neurosurgical procedures, where neurosurgical operations are not indicated (such as proliferative vascular occlusive disease), and where ocular circulation is not improved even after a neurosurgical procedure.

In conclusion, IVB injection can be a useful treatment for NVG secondary to ICA occlusion. While waiting for surgery like CEA or CAS as a fundamental treatment, we are able to control IOP quickly with IVB to suppress the development of secondary-angle glaucoma and maintain visual function for the patient.

## Disclosure

The authors report no conflicts of interest in this work.

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