

Preoperative Intracameral and Intravitreal Aflibercept Injection, Pars Plana Vitrectomy and Ahmed Glaucoma Valve Implantation in Refractory Neovascular Glaucoma

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ABSTRACT

Background: Medical and surgical management of one-eyed patient with neovascular glaucoma secondary to proliferative diabetic retinopathy, chronic myeloid leukemia and chronic renal failure.

Case report: A 68-year-old male patient with type 2 diabetes mellitus, chronic myeloid leukemia and chronic renal failure presented with sudden loss of vision in the right eye. In the left eye, there was visual acuity at the level of light perception and glaucomatous optic atrophy. In the right eye, the best-corrected visual acuity was 0.1 and anterior segment examination revealed rubeosis iridis and diffuse peripheral anterior synechia. In fundus examination, there were findings of diabetic retinopathy with cup: disc ratio of 4:10, peripapillary splinter hemorrhage and intraocular pressure of 40 mmHg. Despite initiation the maximal medical anti-glaucomatous treatment, it was failed to reduce IOP. Optical medium did not allow panretinal laser photocoagulation. Anterior chamber (half dose) and intravitreal (full dose) anti-VEGF (aflibercept) injections were performed. Following regression of rubeosis iridis, pars plana vitrectomy and panretinal endolaser photocoagulation were performed in combination with cataract surgery. Ahmed valve tube implantation was performed because the postoperative intraocular pressure was 28 mmHg. Intraocular pressure decreased to 10 mmHg. Here, we highlighted the points to be considered in the management of a one-eyed neovascular glaucoma case.

Conclusion: Intracameral and intravitreal anti-VEGF (aflibercept) injection, panretinal laser photocoagulation, pars plana vitrectomy are effective and reliable treatments for regression of rubeosis iridis in patients with neovascular glaucoma. Also, in these patients, glaucoma drainage implants have an important role in the control of intraocular pressure and glaucoma management.

Key Words: Neovascular glaucoma, Rubeosis iridis, Aflibercept, Ahmed glaucoma valve implantation.

INTRODUCTION

Neovascular glaucoma (NVG) is a secondary glaucoma due to ocular ischemia caused by several disorders such as proliferative diabetic retinopathy (PDR), retinal vein occlusion, ocular ischemic syndrome and chronic uveitis.¹ Several angiogenic factors including vascular endothelial growth factor (VEGF) are released from hypoxic retina, causing neovascularization and iris surface and anterior chamber angle. Abnormal fibrovascular tissue resulting from ischemia is proliferated at iris and anterior chamber angle, evolving to peripheral anterior synechia (PAS) and angle closure. These histopathological changes eventually lead elevated intraocular pressure (IOP) and severe loss of vision. In the treatment, first step is to treat underlying

ischemic condition accounting for neovascular stimuli while second step is to control elevated IOP which can result in optic nerve injury.

Retinal ischemia leading formation of abnormal vessels in NVG is typical treated by panretinal photocoagulation (PRP). In addition, there is evidence that VEGF play an important role in the development of NVG.² It has been reported that, as similar to intravitreal bevacizumab injection (Avastin, Genentech, South San Francisco, CA, USA), intracameral injection is also effective for regression of anterior chamber neovascularization.³ Aflibercept (Eylea, Regeneron, New York; Bayer, Berlin, Germany) is a recombinant fusion protein that binds and inhibits VEGF and placental growth factor (PIGF).⁴ When

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compared previous anti-VEGF molecules, it appears as a potent VEGF inhibitor due to its superior affinity and pharmacokinetics.⁵ It was reported that aflibercept is effective to regress neovascularization at iris and angle.⁶ Secondary goal is IOP control in the treatment of neovascular glaucoma. At this point, Seton surgery seems to be beneficial when trabeculectomy is failed in patients with uveitic and aphakic glaucoma.⁷

Case Report

A 68-years old man with known type 2 diabetes mellitus (DM), chronic myeloid leukemia (CML) and chronic renal failure (CRF) presented with sudden loss of vision in right eye. In his history, it was found out that the patient received multiple intravitreal injections to both eyes and intravitreal dexamethasone implant (Ozurdex, Allergan Inc., Irvine, California) in right eye for diabetic macular edema (DME). In addition, the patient was already using brinzolamide plus timolol fixed combination and brimonidine due to primary open angle glaucoma in both eyes. In the ophthalmological examination, best-corrected visual acuity as measured by Snellen chart was 0.1 in right eye and at light perception level in the left eye. In biomicroscopic examination, there

was nuclear sclerosis and rubeosis iridis (NVI) in the right eye (Figure 1-A) while diffuse peripheral anterior synechia (PAS) was observed in gonioscopy (Figure 1-B). The right was pseudophakic and had undergone trabeculectomy. In fundus examination, there was splinter hemorrhage at temporal margin of optic disc in right eye and vertical C: D ratio was 4:10 (Figure 1-C). In addition, there was glaucomatous optic atrophy in the left eye. The IOP was measured as 40 mmHg in right eye and 15 mmHg in the left eye. In the patient diagnosed as NVG in right eye, retinal nerve fiber layer (RNFL) thickness, computed visual field (VF) test, gonioscopy and fundus images were documented.

Bimatoprost eye drop (1x1), oral acetazolamide (250 mg, 3x1) and potassium tablet (1x1) were added to anti-glaucomatous therapy in the patient. PRP was planned to regress neovascularization; however, PRP could not be performed due to blurred optic media. Thus, aflibercept was given at full dose (2 mg/0.05 ml) via intravitreal injection and half dose (1 mg/0.025 ml) via intracameral injection. On day 6 after aflibercept injections, a marked regression in NVI was noted (Figure 1-D). At this point, phacoemulsification and intraocular lens implantation

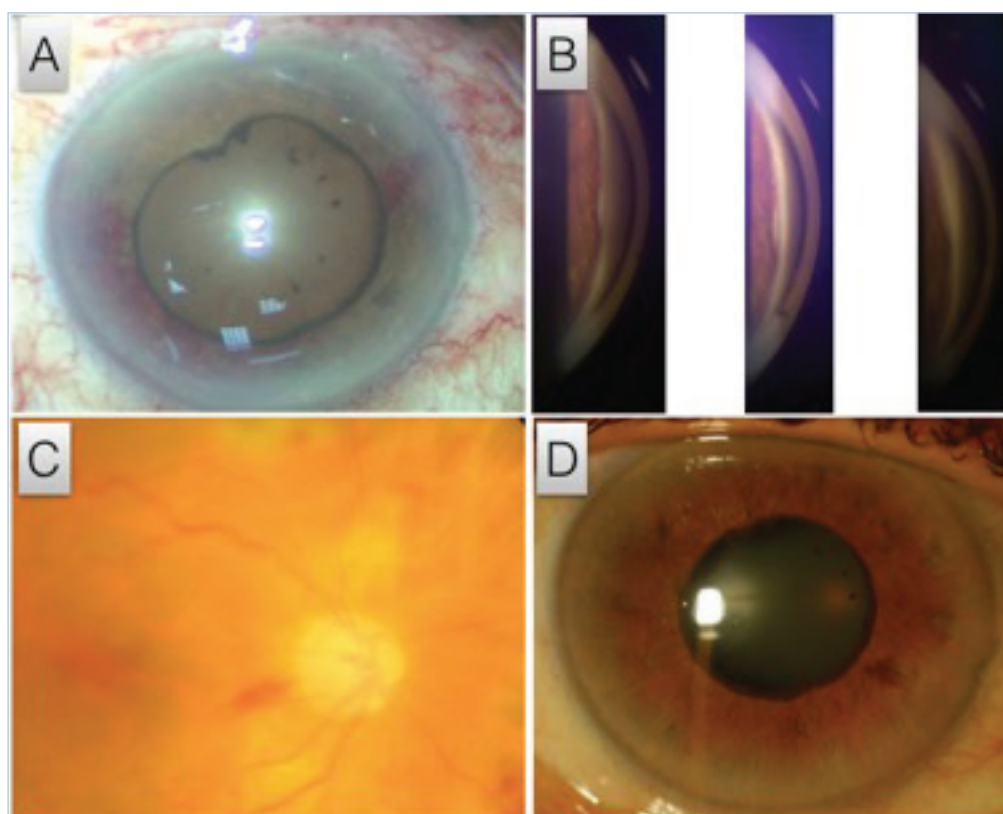


Figure 1: **A.** Diffuse NVI is seen in the right eye of patient; **B.** Generalized PAS is present in gonioscopy; **C.** Fundus image shows peripapillary splinter hemorrhage; **D.** Fundus image on day 6 after intravitreal (full dose) and intracameral (half dose) Aflibercept injection shows regression of NVI.

with pars plana vitrectomy and panretinal endolaser photocoagulation were performed (Figure 2-A). However, Ahmed valve tube implantation was performed at postoperative week 3 since visual acuity was 0.2 and IOP was 29 mmHg with progression to small island of central vision in VF test at postoperative weeks 1 and 2 (Figure 2-B and 2-C). One week after Ahmed valve tube implantation, visual acuity was 0.2 while IOP was 10 mmHg.

DISCUSSION

Commonly, primary source of neovascularization secondary to PDR and ischemic retinal vein occlusion are angiogenic growth factors, mainly VEGF, released from hypoxic retina. Both elevated IOP and underlying cause should be treated in neovascular glaucoma.

Retinal laser photocoagulation is an effective treatment for underlying ischemic retinal pathology. Photocoagulation inhibits hypoxic process and VEGF release by leading damage of ischemic retinal tissue. Thus, it provides regression of neovascularization at iris and anterior chamber angle.⁸ However, it caused permanent visual field defects and reduction in color vision and contrast sensitivity.⁹ This brings forward the problem encountered in our patient. When assessing progression in neovascular glaucoma by visual field test, it should be kept in mind that PRP will lead peripheral defect in visual field.

It was shown that VEGF concentration is increased in both humor aqueous and vitreous.¹⁰ This indicates the role of VEGF in development of neovascularization in both anterior and posterior segment. In the literature, it was shown that intravitreal and intracameral bevacizumab

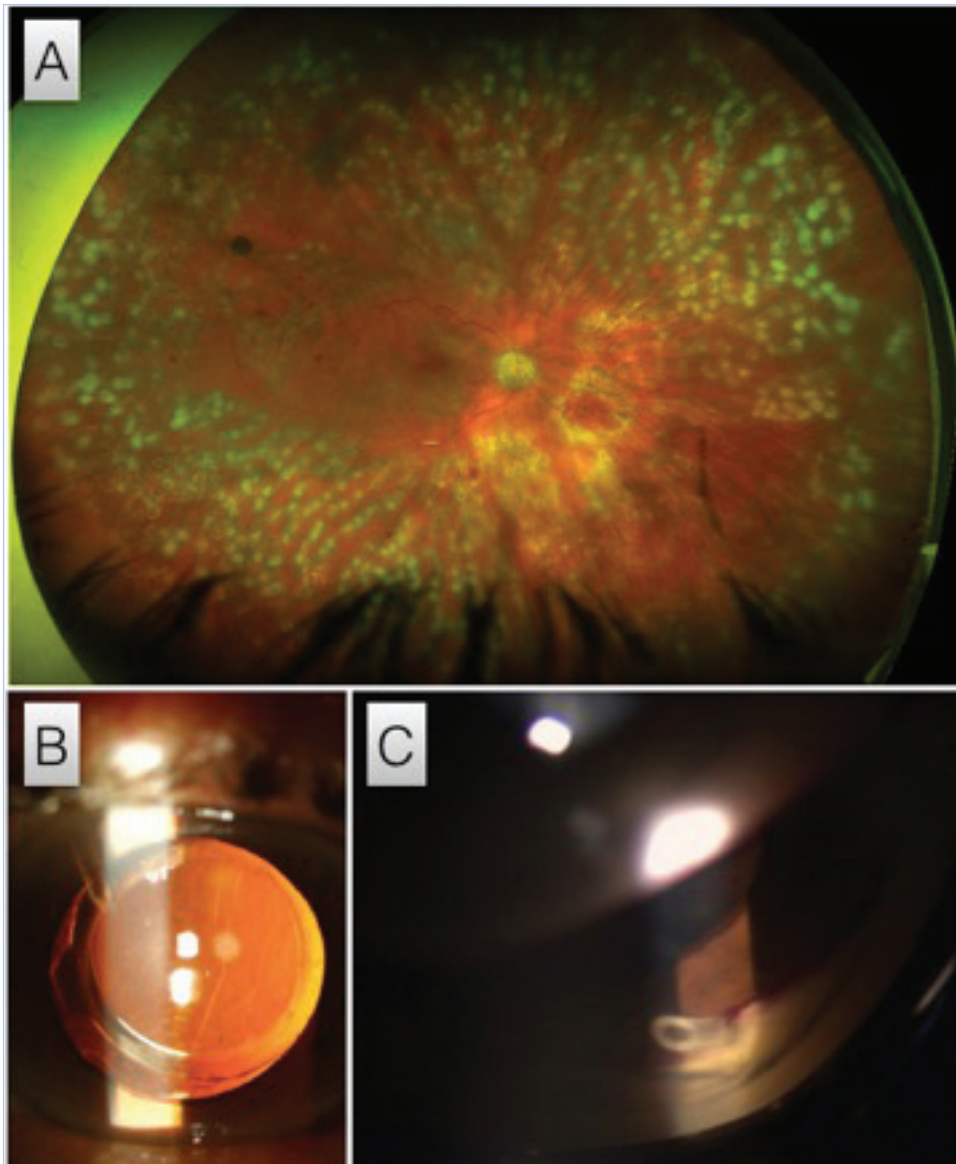


Figure 2: A. Wide-angled image of retina underwent PRP; B-C. Images of Ahmed valve tube implant in the anterior chamber and iridocorneal angle (respectively).

injections have beneficial effect in NVG.¹¹⁻¹³ There is relatively limited data regarding aflibercept use in the treatment of neovascular glaucoma. SoHoo et al. reported that intravitreal aflibercept injection led rapid regression of anterior segment neovascularization in 4 patients with NVG and that IOP was stable or decreased in all patients during 52-weeks follow-up.⁶ In our patient, intravitreal and intracameral aflibercept injection resulted in rapid regression in anterior segment neovascularization. Although anti-VEGF injection alone is associated with regression in anterior segment neovascularization, it seems to be inadequate to achieve long-term IOP regulation since underlying pathological process is ongoing. Ha et al. reported that 73% of patients with NVG underwent intracameral bevacizumab injection required IOP lowering surgery and that high baseline IOP, angle neovascularization and PRP failure are determinants of surgery.¹⁴

There is no consensus on optimal surgical approach in neovascular glaucoma. However, filtering trabeculectomy has limited surgical success. In particular, intraoperative hemorrhage and postoperative fibrovascular membrane formation are limiting factors. Glaucoma drainage implants have become first alternative in NVG surgery due to their effectiveness and lower postoperative complication rate. In addition, bevacizumab are used before glaucoma drainage implants insertion in patients with NVG.¹⁵ Preoperative intraocular anti-VEGF injection can prevent complications such as intraoperative and postoperative hemorrhage by decreasing neovascularization. In the systematic review comparing patients underwent Ahmed valve tube implantations with or without bevacizumab, Hwang et al. suggested that adjuvant bevacizumab injection is more effective in lowering IOP compared to surgery alone with lower incidence of complications secondary to hemorrhage such as hyphema.¹⁶

In conclusion, there is no standard protocol for management of patients with NVG. However, timely interventions should be performed due to aggressive course of disease. Early diagnosis and adequate PRP with intravitreal and/or intracameral anti-VEGF injections are major steps in management of NVG. However, glaucoma drainage implants as IOP lowering surgery may result in good outcomes in refractory NVG with progression.

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