Case Report

Intravitreal aflibercept for rubeosis iridis secondary to proliferative diabetic retinopathy

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Abstract: The purpose of this article is to report a case with rubeosis iridis treated by intravitreal aflibercept. A 61-year-old man had iris neovascularization and scanty vitreous hemorrhage secondary to proliferative diabetic retinopathy in the right eye. Neither neovascularization of angle nor elevation of intraocular pressure was found. Single intravitreal aflibercept 2 mg injection was performed. Rubeosis iridis disappeared on the next day. Scattered retinal laser photocoagulation was added 1 week later. There was no recurrence after 3-month follow-up. Aflibercept may serve as another anti-vascular endothelial growth factor (anti-VEGF) for treating rubeosis iridis.

Keywords: Anti-vascular endothelial growth factor agent (anti-VEGF agent); intravitreal injection; aflibercept; rubeosis iridis; neovascularization of iris; proliferative diabetic retinopathy

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Introduction

Rubeosis iridis, also known as iris neovascularization, is caused by ocular ischemia in patients with proliferative diabetic retinopathy (1-3). Intravitreal anti-vascular endothelial growth factor (anti-VEGF), such as bevacizumab, ranibizumab, and pegaptanib, were reported to be beneficial for anterior segment neovascularization (4-7). Aflibercept, a new anti-VEGF, was not described for treating rubeosis iridis after reviewing the literature.

Case presentation

A 61-year-old man had diabetes mellitus under insulin control for 10 years. HbA1c level was between 7 to 8.5 mg/dL for these 3 years. He did not have other systemic disease. Pan-retinal argon laser photocoagulation was performed for proliferative diabetic retinopathy 3 years ago in both eyes. He underwent pars plana vitrectomy and silicone oil infusion for vitreous hemorrhage and tractional retinal detachment 2 years ago in the left. Neovascular glaucoma occurred subsequently, which caused phthisis bulbi and vision without light perception. The patient complained of right progressive blurred vision for 1 week 3 months ago. His corrected visual acuity was 20/30 in the right eye. Intraocular pressure and anterior segment were normal, except neovascularization around pupillary margin (*Figure 1A*). Mild nuclear sclerosis of lens was found. Neovascularization of angle was not demonstrated under gonioscopic examination. Spectral-domain optical coherence tomography revealed normal macular structure. Fundus examination showed scanty vitreous hemorrhage and laser spots scattering on mid-peripheral retina, without accompanying preretinal fibrosis. Iris neovascularization secondary to proliferative diabetic retinopathy was diagnosed.

After full explanation of benefit, risk, and off-label usage, the patient signed the informed consent. Single intravitreal aflibercept (2 mg/0.05 mL) was injected. Rubeosis iridis

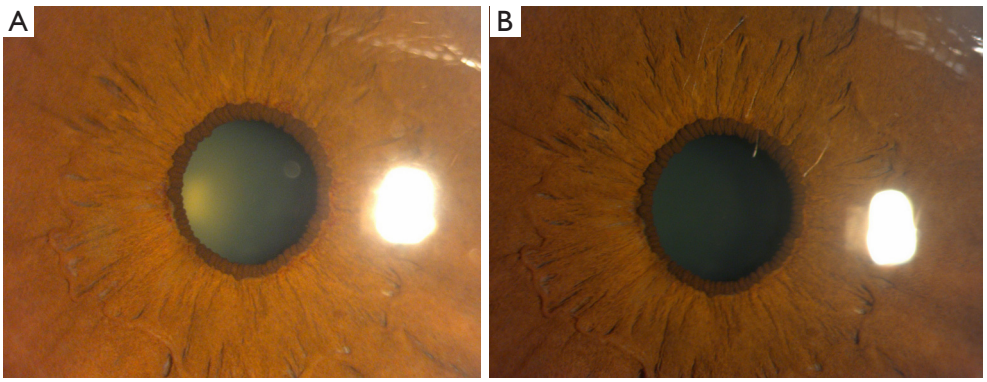

Figure 1 (A) Neovascularization found on the pupillary margin, especially on the superior, temporal, and nasal-inferior part in the right eye; (B) disappearance of neovascularization of iris on the next day following intravitreal aflibercept.

disappeared on the next day (*Figure 1B*). One week later, scattered retinal laser photocoagulation was added on the peripheral retina.

Vitreous hemorrhage gradually vanished without increasing preretinal fibrosis. Neovascularization of angle and iris was not found, along with improved corrected visual acuity to 20/25 3 months following the injection.

Discussion

In eyes with proliferative diabetic retinopathy, the elevated level of VEGF is found in response to retinal hypoxia (1). Higher VEGF concentration in vitreous cavity and aqueous humor is strongly associated with development of retinal and iris neovascularization (2,3). Rubeosis iridis may cause hyphema, which obstructing the visual axis and impairing vision. Iris neovascularization may extend to anterior chamber angle, resulting in neovascular glaucoma and subsequent optic nerve damage associated with visual field and acuity defect.

Pan-retinal laser photocoagulation can lower the severity of retinal ischemia, as the standard of care for management of rubeosis iridis secondary to proliferative diabetic retinopathy. Intravitreal injection anti-VEGF can serve as an adjunct or main treatment for anterior segment neovascularization. Bevacizumab is a full-length recombinant humanized monoclonal antibody directed against all isoforms of VEGF-A, the most important VEGF for pathologic angiogenesis. Bevacizumab used intravitreally resulted in regression of rubeosis iridis within several days (5). Ranibizumab is an antigen-binding fragment of monoclonal antibody against all isoforms of VEGF-A. Intravitreal ranibizumab was described to cause receding of iris neovascularization secondary to diabetic retinopathy (6). Pegaptanib is RNA aptamer to inhibit one isoform of VEGF-A, $VEGF_{165}$. Disappearance of iris neovascularization was also reported after intravitreal pegaptanib in diabetic patients (7). However, intravitreal anti-VEGF agents have temporary effects for controlling rubeosis iridis (8). Iris neovascularization may recur 2 to 4 months after anti-VEGF injection. Besides, anti-VEGF can cause tractional retinal detachment in cases with pre-existing preretinal fibrosis (8).

Aflibercept (Eylea™, Regeneron Pharmaceuticals, Inc., and Bayer Pharma AG, Berlin, Germany) is a decoy receptor fusion protein, composed of the second domain of human VEGF receptor 1 and the third domain of VEGF receptor 2, which are fused to the Fc domain of human IgG1 (9). Aflibercept can downregulate both VEGF-A, VEGF-B, and placental growth factor, which are synergistic for pathologic angiogenesis. The binding affinity of VEGF for this drug is higher than for ranibizumab and bevacizumab (10). Aflibercept displays a prolonged VEGF inhibition in comparison with the other VEGF-antagonists ranibizumab and bevacizumab in retinal pigment epithelium/choroid organ cultures (11). For diabetic patients, aflibercept have been proven to reduce macular edema and to restore visual acuity (12). Aflibercept was not described for treating rubeosis iridis secondary to diabetic retinopathy previously.

In our case with proliferative diabetic retinopathy, iris neovascularization can occur after incomplete pan-retinal laser photocoagulation. Intravitreal aflibercept caused rapid regression of iris neovascularization, preventing further deterioration to neovascular glaucoma or hyphema. Adding

scattering retinal laser photocoagulation was helpful to avoid recurrence of rubeosis iridis. Because there was no pre-existing preretinal fibrosis, aflibercept did not cause subsequent tractional retinal detachment in this diabetic patient.

In summary, we described a case with iris neovascularization secondary to proliferative diabetic retinopathy responding rapidly to intravitreal aflibercept. Aflibercept may serve as another anti-VEGF for treating rubeosis iridis.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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