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Case Report

Marked Choroidal Thinning Observed after Intravitreal Brolucizumab Injection

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Keywords

Case report · Brolucizumab · Intravitreal injection · Intraocular inflammation · Choroidal thinning

Abstract

Introduction: Here, we report a case of severe intraocular inflammation (IOI) and prominent choroidal thinning following the initial intravitreal brolucizumab injection (IVBr). ***Case Presentation:*** The patient was a 75-year-old Japanese man with type 2 age-related macular degeneration of both eyes. Until 2015, he had undergone two intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections and two photodynamic therapies in his right eye. His decimal best-corrected visual acuity (BCVA) was 0.1 in the right eye and 0.1 in the left eye. Central choroidal thickness (CCT) measured 240 μm in his right eye. IVBr was administered to the right eye. The patient reported pain in the right eye 23 days after the injection. On day 26, panuveitis and retinal vasculitis were observed in the right eye. CCT measured 436 μm. On the same day, a sub-tenon triamcinolone injection was administered. On day 42, retinal inflammation remained at a similar level. The CCT decreased to 164 μm. On day 68, the intraocular pressure (IOP) in the right eye increased to 39 mm Hg, and IOI persisted. On day 89, the patient's eye pain disappeared, and the IOP decreased to 13 mm Hg. On day 225, the IOI and symptoms were completely resolved. The decimal BCVA was 0.04 in the right eye, and CCT measured 84 μm. ***Conclusion:*** Brolucizumab is a highly effective anti-VEGF drug; however, it has the potential to induce inflammation in tissues adjacent to the retina and may occasionally cause irreversible sequelae.

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Introduction

Brolucizumab is a novel anti-vascular endothelial growth factor (anti-VEGF) drug used to treat neovascular age-related macular degeneration (nAMD). Brolucizumab is non-inferior to aflibercept for improving and maintaining visual acuity in eyes with nAMD and is more effective for intraretinal and subretinal fluid and subretinal pigment epithelium fluid [1, 2]. However, cases of intraocular inflammation (IOI), such as uveitis and retinal vasculitis, have been reported with intravitreal brolucizumab injections (IVBr) [2–11].

Choroidal thinning caused by IVBr has also been reported [9–13]. However, to our knowledge, no reported cases exist of severe choroidal thinning caused by IOI after IVBr. Herein, we report a case of severe IOI and prominent choroidal thinning following the initial IVBr. The CARE Checklist has been completed by the authors for this case report, attached as supplementary material (for all online suppl. material, see https://doi.org/10.1159/000534817).

Case Report

The patient was a 75-year-old Japanese man with type 2 nAMD in both eyes. He had no significant medical history except for hypertension and diabetes. Having been a smoker for 40 years, he has now successfully ceased smoking. The patient did not take any oral medication. Until 2015, he had undergone two intravitreal anti-VEGF injections and two photodynamic therapies in his right eye. In his left eye, he received 11 intravitreal anti-VEGF injections and three photodynamic therapies and also underwent vitrectomy and submacular washout for subretinal hemorrhage. He had a cataract in his right eye and underwent intraocular lens implantation in his left eye.

Injections were discontinued in both eyes after 2015 and were monitored. However, in April 2021, recurrent subretinal hemorrhage was observed in both eyes. The fundus photographs and optical coherence tomography findings are shown in Figure 1. His decimal best-corrected visual acuity measured 0.1 in both the right and left eyes. Intraocular pressure (IOP) was 13 and 17 mm Hg in the right and left eyes, respectively. Central choroidal thickness (CCT) measured 240 μm in his right eye.

The patient expressed a desire for treatment of the right eye only; therefore, IVBr was administered to the right eye. Eleven days after the injection, conjunctival congestion was observed in the right eye; however, no anterior chamber inflammation or retinal vasculitis was observed.

On day 23, the patient experienced pain in the right eye. On day 26, panuveitis and retinal vasculitis were observed on the inferior side of the fundus of the right eye. CCT measured 436 μm. Fundus photographs and optical coherence tomography findings are shown in Figure 2. On the same day, a sub-tenon triamcinolone injection was administered, and 0.1% fluorometholone eye drops 4 times a day were initiated in the right eye.

On day 42 following the injection, the patient continued to experience eye pain, and inflammation in the retina remained at a similar level. The CCT decreased to 164 μm. Oral analgesics were prescribed.

On day 68, the IOP in the right eye increased to 39 mm Hg, and IOI persisted. Therefore, treatment with 0.1% betamethasone eye drops four times a day was initiated along with tafluprost and dorzolamide eye drops. On day 89, the patient's eye pain disappeared, and the IOP decreased to 13 mm Hg. The dose of 0.1% betamethasone was then gradually decreased.

By day 225, IOI and associated symptoms had fully subsided, leading to the discontinuation of all eye drops. His decimal best-corrected visual acuity was 0.04 in the right eye

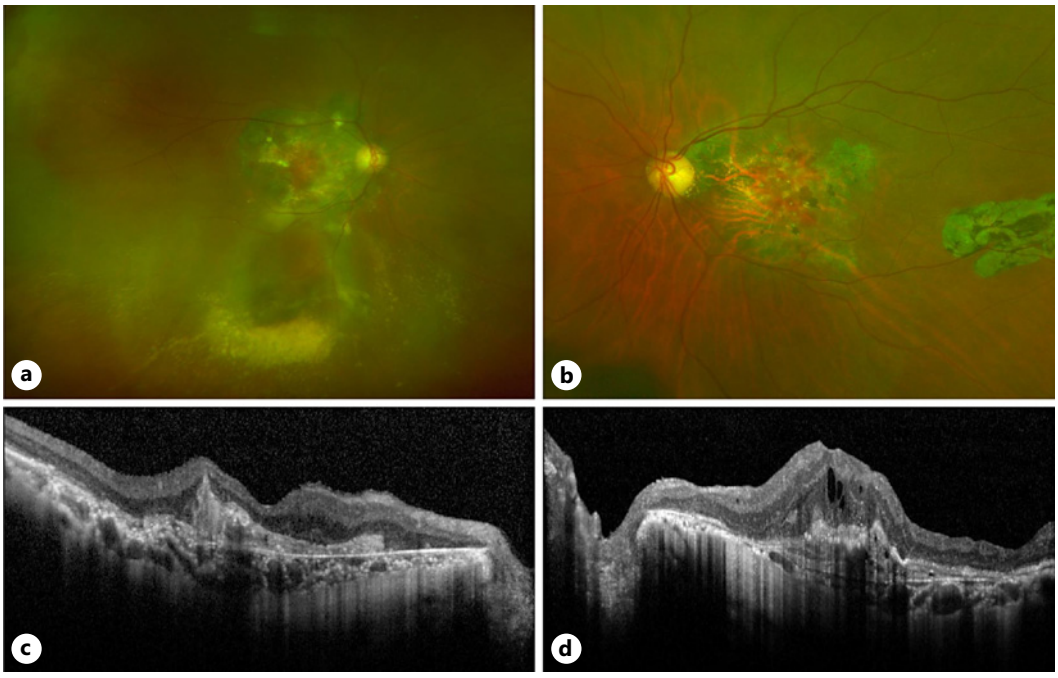

Fig. 1. Fundus photographs and OCT of both eyes before IVBr. **a** Fundus photograph of the right eye shows macula atrophy and subretinal hard exudate at the inferior retina due to subretinal hemorrhage. **b** Fundus photograph of the left eye shows macula atrophy and slight subretinal hemorrhage. **c** OCT of the right eye shows type 2 nAMD. **d** OCT of the left eye shows type 2 nAMD and slight intraretinal fluid. IVBr, intravitreal brolucizumab injection; OCT, optical coherence tomography; nAMD, neovascular age-related macular degeneration.

and 0.1 in the left eye. IOP was 12 and 15 mm Hg in the right and left eyes, respectively. White sheathing of the retinal artery on the inferior side persisted. The CCT was 84 μm in the right eye. The progression of CCT is shown in Figure 3.

Discussion

Here, we report a case of severe IOI and subsequent marked choroidal thinning following the initial IVBr. Several reports have documented IOI associated with brolucizumab, with reported frequencies ranging from 4.6 to 22.1% [2, 5–11]. According to reports, the Japanese may have a higher incidence of IOI [5, 7–11]. Most reported cases of IOI have focused on anterior chamber inflammation, retinal vasculitis, and retinal vascular occlusion, with no reports specifically addressing the choroid.

Furthermore, macular atrophy in AMD is associated with visual prognosis and reduced choroidal thickness [14]. Therefore, choroidal thickness should be monitored during AMD treatment. Reports on brolucizumab and choroidal thickness indicate a 14–25% reduction in CCT after IVBr [9, 10, 12, 13]. In this case, choroidal thinning was 65%, surpassing the severity level typically encountered in such instances.

Barchichat et al. [15] reported a case in which bilateral blindness occurred after two IVBr. Magnetic resonance imaging with fat suppression revealed high signal intensity in the choroid, choroidal detachment, and high signal intensity around the optic nerve, suggesting that brolucizumab can cause vasculitis in the retina and adjacent tissues. In this case, transient choroidal thickening was observed at the onset of IOI, followed by thinning, suggesting the possibility of

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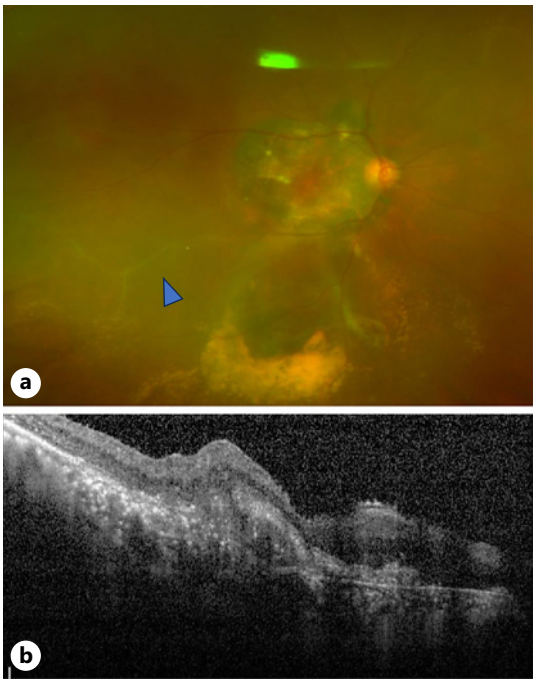

Fig. 2. Fundus photograph and OCT of the right eye at the onset of IOI caused by IVBr. **a** Fundus photograph shows retinal vasculitis at the inferior retina (arrowheads). **b** OCT is blurry and shows choroid thickening. OCT, optical coherence tomography; IOI, intraocular inflammation; IVBr, intravitreal brolucizumab injection.

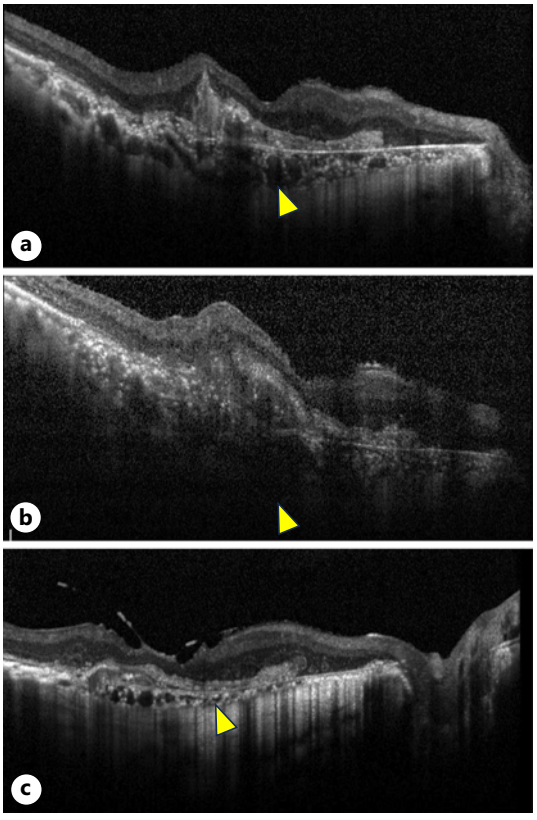

Fig. 3. OCT of the right eye before IVBr, at the onset of IOI, and 225 days after injection. **a** OCT before IVBr. CCT was 240 µm (arrowheads). **b** OCT at the onset of IOI. CCT was 436 µm. **c** OCT 225 days after IVBr. CCT was 84 µm. OCT, optical coherence tomography; IOI, intraocular inflammation; IVBr, intravitreal brolucizumab injection; CCT, central choroidal thickness.

occlusive vasculitis in the choroid adjacent to the retina. Severe eye pain may also be attributed to the spread of scleral inflammation. Alternatively, ocular arterial occlusion due to vitreous injection of anti-VEGF drugs has also been reported [16], and choroidal thinning and eye pain may result from ocular ischemia syndrome caused by inflammation and occlusion of ocular arteries. If this is the case, anti-inflammatory treatment should include systemic administration of oral medication or intravenous infusion alongside sub-tenon triamcinolone injection.

This case report has a major limitation, as it is just 1 case, suggesting the possibility that brolucizumab could cause inflammation in the retina and adjacent tissues. Although establishing a causal relationship between brolucizumab treatment and choroidal thinning is challenging, further accumulation of similar cases is warranted to elucidate the pathophysiology of IOI.

In conclusion, brolucizumab is a highly effective anti-VEGF drug; however, it has the potential to induce inflammation in tissues adjacent to the retina and may occasionally cause irreversible sequelae. Choroidal thinning can lead to macular atrophy and irreversible visual impairments.

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Statement of Ethics

The Ethics Committee of Shinseikai Toyama Hospital waived the need for approval for this study, which involved a retrospective review of medical records. This study adhered to the tenets of the Declaration of Helsinki 1964. Written informed consent was obtained from the patient for the publication of this case report and the accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Yoshiki Ueta collected the clinical data. Yoshiki Ueta analyzed the findings and provided critical suggestions. Yoshiki Ueta contributed to the original draft preparation. Ryoma Kamada, Yuji Watanabe, and Nobuya Tanaka reviewed and edited the manuscript. All agree to be accountable for all aspects of this study. All authors approved the final version of the manuscript for publication.

Data Availability Statement

All data analyzed in this study are included in this article. Further inquiries can be directed to the corresponding author.

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