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Polypoidal Choroidal Vasculopathy and its effect after four months of treatment outcome- Case Report

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Abstract: A 42-year-old female presented with moderate Non-proliferative diabetic retinopathy (NPDR) in both eyes, and the left eye hadpolypoidal choroidal Vasculopathy (PCV). The Optical coherence tomography (OCT) report of the left eye shows Pigment Epithelial Detachment (PED) with heterogeneous hyperreflectivity, which indicates the presence of polyps along with subretinal fluid collection. Initially, the patient was treated with an anti-VEGF injection of Ranibizumab. Afterward, there was no significant improvement in polyps regression and visual improvement.Then, three months of repeated anti-VEGF injections of Brolucizumab were given as a treatment. After the follow-up with the patient, Oct reports show that there was a resolved subretinal fluid, and the size of the polyps also reduced, with a marked visual outcome obtained.This case shows that treatment for PCV with an anti-VEGF injection of Brolucizumab gave better results in the polyp regression and showed good visual improvement.

Keywords: Polypoidal choroidal vasculopathy, Polyps regression, Brolucizumab, Anti-VEGF injection, Intravitreal injection.

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INTRODUCTION

Neovascular age-related macular degeneration (nAMD) possesses a distinct form referred to as polypoidal choroidal vasculopathy (PCV). This condition is marked by polypoidal lesions that develop from a branching neovascular network (BNN) beneath the retinal pigment epithelium (RPE). This abnormal vascular growth can lead to vision impairment and is an important consideration in the management of age-related macular degeneration [1]. Clinically, it is characterized by significant serosanguineous detachments in both the retinal pigment epithelium and the neurosensory layer. When considering a diagnosis, it's important to differentiate it from other conditions such asneovascular age-related macular degeneration and similar disorders [2].

The inner choroidal vessels exhibit defects in their lining, which is attributed to a reduction in pericytes and a thinning of the endothelial cells. As a result, the affected vessels become prone to bulging, leading to the formation of polypoidal protrusions [3]. The clinical features of Polypoidal Choroidal Vasculopathy (PCV) include dilated choroidal vascular channels that terminate in polyps, which manifest as orange bulging lesions in the macular and peripapillary regions. These lesions can be subtle and may not be easily detected unless the vascular components are sufficiently large and the overlying retina appears flat. PCV is often associated with serous and serosanguineous pigment epithelial detachments (PEDs), and micro-tears can occasionally occur at the edges of these PEDs. The recurrent traits of the illness are usually indicated by the appearance of intraretinal and subretinal lipid formations. Studies suggest that 23% to 55% of cases may also present with drusen. Over time, the extent of fibrous scarring tends to be minimal and is primarily influenced by any associated hemorrhagic complications [2].

It has been reported that Polypoidal Choroidal Vasculopathy (PCV) accounts for approximately 27.0% to 41.3% of cases of neovascular age-related macular degeneration (nAMD) within the Asian population. Specifically, in Korean patients diagnosed with nAMD, the prevalence of PCV ranges from 24.6% to 36.3%.1 While Polypoidal Choroidal Vasculopathy (PCV) generally has a more favorable natural progression and prognosis compared to typical neovascular age-related macular degeneration (nAMD), it can occasionally result in significant complications. These include extensive subretinal hemorrhage, breakthrough vitreous

hemorrhage, and geographic retinal pigment epithelium (RPE) atrophy. Such complications can lead to lasting and severe visual impairment [4]. Systemic risk factors play a significant role in various health conditions. In the case of Polycythemia Vera (PCV), cardiovascular abnormalities have been linked to the disorder. Research indicates that approximately 41% to 45% of individuals diagnosed with PCV also experience systemic hypertension. This correlation highlights the importance of monitoring cardiovascular health in patients with PCV [5]. Diabetes mellitus (DM) has a stronger association with choroidal neovascularization in age-related macular degeneration (CNV-AMD) compared to polypoidal choroidal vasculopathy (PCV). This difference may be attributed to elevated levels of vascular endothelial growth factor (VEGF) in individuals with uncontrolled diabetes, indicating that high VEGF levels do not always cause PCV, even if neovascular age-related macular degeneration (nAMD) is prevalent among diabetic people. Interestingly, studies indicate that the aqueous concentration of VEGF is lower in PCV cases than in those with nAMD [6-8].

Anti-vascular endothelial growth factor (anti-VEGF) therapies, either as monotherapy or in combination with photodynamic therapy (PDT), have become standard treatments for polypoidal choroidal vasculopathy (PCV). A variety of anti-VEGF agents are currently utilized for managing PCV, including bevacizumab (Avastin, Genentech Inc.), ranibizumab (Lucentis, Genentech Inc.), aflibercept (Eylea, Regeneron Pharmaceuticals Inc.), and brolucizumab (Beovu, Novartis AG).

Among these, brolucizumab received approval from the U.S. Food and Drug Administration in October 2019. It is a high-affinity monoclonal antibody specifically designed to inhibit VEGF-A. With a relatively low molecular weight of 26 kDa compared to other anti-VEGF agents, brolucizumab allows for higher concentrations per injection. This characteristic contributes to its increased duration of action and effective tissue penetration, making it a promising option in the treatment of PCV [9].

The Hawk and Harrier phase 3 clinical studies have shown that brolucizumab is non-inferior to aflibercept in enhancing visual outcomes, while also demonstrating enhanced anatomical advantages from the optimal reduction of subretinal pigment epithelial fluid, intraretinal fluid (IRF), and subretinal fluid (SRF). Despite these positive results, it is important to note that brolucizumab injections can occasionally lead to Idiopathic Orbital Inflammation (IOI), which may manifest as vitritis, retinal artery occlusion, or occlusive retinal vasculitis, potentially resulting in significant visual impairment. This particular case study sheds light on the effectiveness of brolucizumab in promoting the regression of polyps and diminishing subretinal fluid accumulation in a patient diagnosed with polypoidal choroidal vasculopathy (PCV).

CASE SUMMARY

A 42-year-old female patient came for an eye examination with complaints of a sudden, painless decrease in vision in her left eye for 2 weeks. She had comorbidities like diabetic mellitus and hypertension for 8 years, not on regular medications. Her recent investigation revealed a post-prandial blood sugar value (PPBS) of 365 mg/dl and blood pressure (BP) of 140/90 mm/Hg. Her past ocular history showed that she had undergone cataract surgery 2 years ago. Her right eye vision was good, and she was not wearing any spectacles. Her past ocular history indicated her fundus diagnosis of Moderate Non-proliferative diabetic retinopathy in both eyes and advised strict Diabetic and Hypertension control.

She had undergone a thorough eye examination, and the findings show that the Right eye had PCIOL and the Left eye had Early lens changes. Her intra-ocular pressure was 16 mmHg and 15 mmHg, respectively, with both eyes, which is normal. We tested visual acuity, which is right eye BCVA at 6/9 with astigmatism at 1.50*90 and left eye BCVA at 6/60. There was no improvement with the glass and no improvement with the Pinhole. Now, her fundus showed that there was Polypoidal Choroidal Vasculopathy (PCV) in the left eye, associated with Moderate NPDR in both eyes. Her Optical Coherence Tomography report (Fig. 1) of the Left eye showed Polypoidal Choroidal Vasculopathy, and the signs include PED, polyp protrusion, and sub-retinal fluid collection.

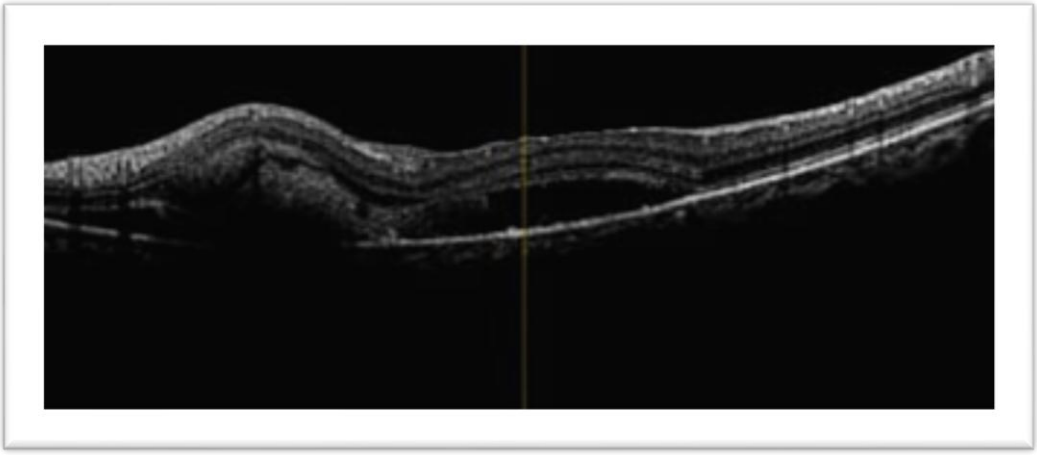

Fig.1: OCT of the Left eye shows a Polyp, PED, and SRF

We planned to start treatment with Anti-VEGF injection Ranibizumab as an initial course of treatment. After injection, she was followed up closely and found no improvement with the polyp regression, and she doesn't have any significant visual outcome. The BCVA of Left eye remains same as before like 6/60, No Improvement with Glass (NIG), No Improvement with Pinhole (NIP).

After two months, we decided to go with anti-VEGF injection Brolucizumab, which was more effective and has a low molecular weight (26 kDa) compared to other anti-VEGF agents. This promotes longer duration of action, better molar concentration per injection, and efficient tissue penetration.

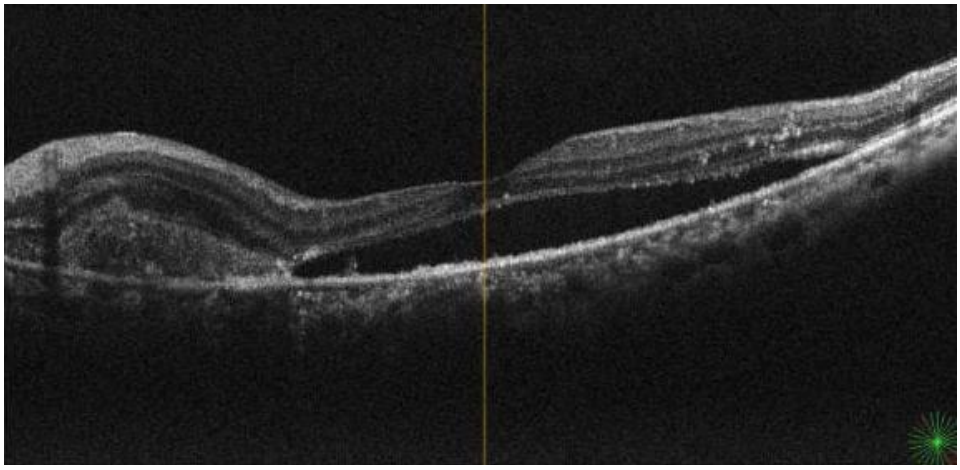

Fig. 2 OCT of the Left eye shows minimal regression of the polyp.

After loading the Injection Brolucizumab, we found the effective reduction of subretinal fluid and showed some changes in regression of the polyp in PCV (Fig. 2). The expected visual outcome was improved from 6/60 to 6/18. Inj Brolucizumab was more effective than the other anti-VEGF injections and showed significant improvement with the first dose itself.

Weekly follow-up was done with the patient and monitoring the visual outcome, and was under observation for any other complications, like checking for the occurrence of brolucizumab-related IOI. The patient was prescribed prophylactic steroid eye drops (1% prednisolone acetate) for 1 week to prevent brolucizumab-related IOI and was discontinued if IOI was not confirmed after a 1-week follow-up.

The patient was treated with three monthly Brolucizumab injections. After the loading injections, follow-up visits were scheduled every 1 to 2 months, according to the eye consultant's decision.

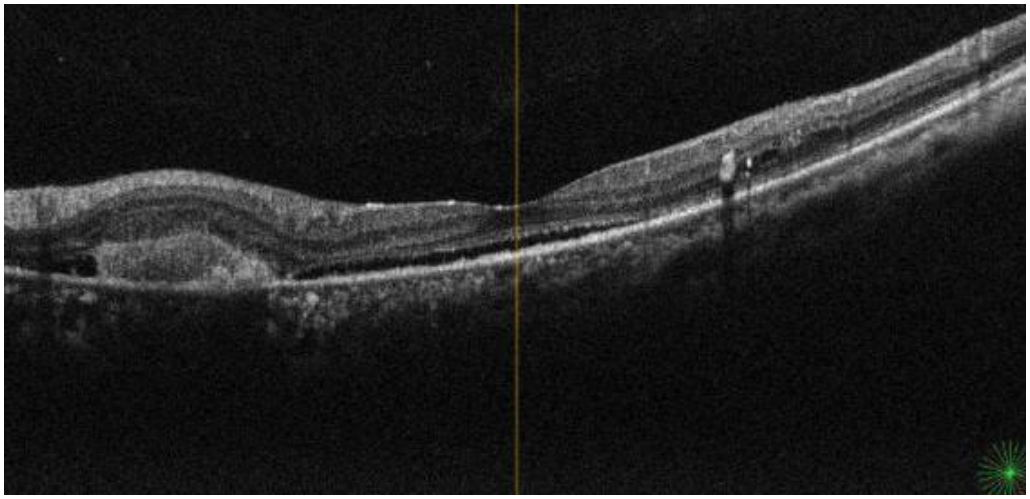

Fig. 3 OCT of the Left eye shows minimal polyp and well-reduced SRF

After loading three settings of Anti-VEGF injections of Brolucizumab, we asked the patient to come for every monthly follow-up visit. OCT report of the Left eye (Fig. 3) showed significant regression of polyp and well reduction of sub-retinal fluid shown in the left eye. Few atrophy changes were observed in the choroidal region. We evaluated the visual outcome. Visual outcomes remain stable, as in the first follow-up. Left eye BCVA remained 6/18 NIG, NIP. The patient was asked to come after one month for the next follow-up.

Nearly four months after the first injection was given last follow-up was done. OCT report of the Left eye (Fig. 4) showed almost complete polyp regression with very minimal residual polyp remaining. A well-recovered sub-retinal fluid collection and PED got attached to the neurosensory retina.

Even though the polyp got regressed and subretinal fluid got drained, there arose significant geographical choroidal atrophy changes which led to some visual impairment, and couldn't get a full visual outcome over BCVA of 6/18. After loading three Brolucizumab injections, the Left eye BCVA remains unchanged and stable at 6/18. Changes in geographical atrophy hindered the improvement of further results.

After the third injection was loaded, the patient had anterior uveitis, aqueous flares, and redness in her Left eye, and treatment was done under steroid cover. As we expected, this may be one of the complications of Brolucizumab anti-VEGF injection, which may produce IOI after injection. Due to anterior uveitis, the patient had some iris pigmentation on the corneal endothelial layer and an irregular pupillary margin in the left eye.

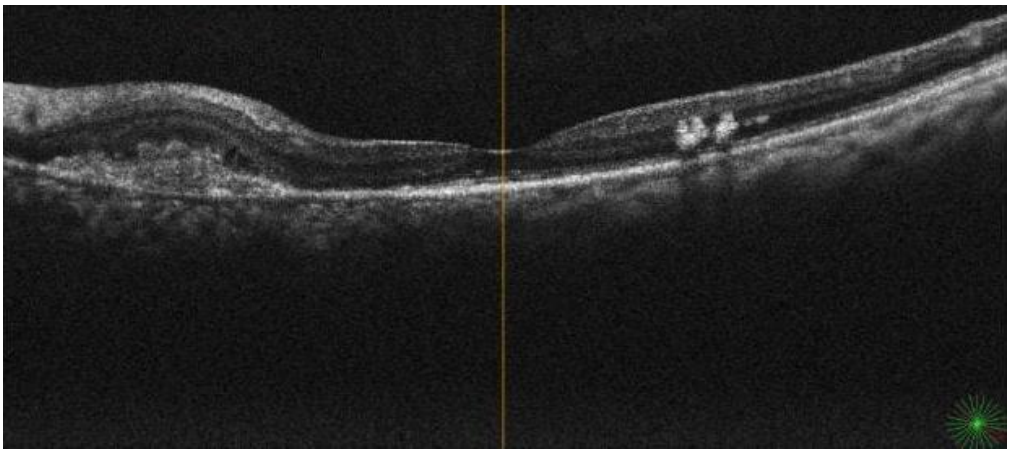

Fig. 4 OCT of the left eye shows that completely regressed, and without SRF

DISCUSSION

Sakurada Y, Yoneyama S, Imasawa M, *et al*. [6] studies show that DM and Hypertension (HTN) were the risk factors for this particular case associated with Moderate nonproliferative diabetic retinopathy. The patient did not have proper medication for the systemic illness, which led to Polypoidal choroidal vasculopathy (PCV). Anti-VEGF injection ranibizumab is widely used to treat nAMD and PCV patients, but in this particular case, Brolucizumab injection provides a better outcome compared to ranibizumab. According to Nguyen QD, Das A, Do DV, *et al*., [9] Brolucizumab administered to patients demonstrated better tissue penetration and sustained effectiveness over a longer duration.

According to the statement in Hawk and Harrier, brolucizumab was able to reduce PEDs and sub-RPE fluid thickness more than aflibercept [12].

As per the statement of Ciardella, A. P., Donsoff, I. M., Huang, *et al*. [13] Typically, PDT or combination therapy is recommended for PCV patients. Gomi, F., & Tano, Y., *et al*. [14] studies also show that PDT was one of the effective treatments for polypoidal choroidal vasculopathy. Lindeke-Myers, A., Kokame, G. T., *et al*. [15] studies show that PCV is successfully treated with monotherapy without combination therapy. In this specific case, we used monotherapy with an anti-VEGF injection of brolucizumab instead of combination therapy with PDT plus an anti-VEGF injection, since the patient did not experience any major bleeding that would cause significant visual impairment, and considering the high cost associated with the combination therapy.
According to Dugel PU, Koh A, Ogura Y, *et al*., [11] clinical studies reported the incidence of anterior uveitis and IOI after brolucizumab anti-VEGF injection. Similarly, our patient experienced the same complication, which was managed with steroids.Anti-VEGF injection of brolucizumab provided a better visual outcome for the patient, who was extremely happy with the treatment, and OCT reports showed regression of the polyp and disappearance of subretinal fluid collection.The patient was advised to maintain strict control of diabetic conditions and hypertension. They were also advised to use appropriate medication for these issues. Additionally, the patient was encouraged to follow up bi-monthly.

CONCLUSION

Anti-VEGF monocular therapy is particularly effective in cases with significant exudation and polyps that exhibit small protrusions or are currently inactive. Brolucizumab is a newer anti-VEGF molecule with a good response rate in patients with Polypoidal Choroidal Vasculopathy. It is more effective than ranibizumab. Though it has limited complications like uveitis and IOI, it is easily manageable. When we weigh the pros and cons, it has more advantages, better visual improvement, and good patient outcomes.

After four months of close follow-up and treatment, the patient experienced positive visual outcomes compared to their initial condition. However, the emergence of geographic atrophy has hindered the achievement of the desired visual results. This development is a known occurrence in cases of Polypoidal Choroidal Vasculopathy (PCV). The patient has been advised to continue with regular follow-ups in the future to monitor their condition. It is crucial to prioritize the effective management of diabetes and hypertension to improve the visual prognosis for patients. Active control of these conditions plays a significant role in safeguarding and enhancing visual health.

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ACRONYMS

- PCV - Polypoidal Choroidal Vasculopathy
- DM - Diabetes Mellitus
- OCT - Optical Coherence Tomography
- PED- Pigment Epithelial Detachment
- VEGF- Vascular Endothelial Growth Factor
- nAMD- Neovascular Age-Related Macular Degeneration
- BNN-Branching Neovascular Network
- CNV - Choroidal Neovascularization
- IR - Intra-Retinal Fluid
- SRF - Subretinal Fluid
- IOI -Idiopathic Orbital Inflammation
- PCIOL - Posterior Chamber Intra Ocular Lens
- BCVA -Best Corrected Visual Acuity
- NIG -No Improvement with Glass
- BP -Blood Pressure
- NIP -No Improvement with Pinhole
- PDT - Photodynamic Therapy
- HTN - Hypertension

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