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Rapid Response Of Treatment Resistant Polypoidal Choroidal Vasculopathy To Aflibercept Treatment

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ABSTACT:
Background: Polypoidal chorodial vasculopathy (PCV) is a disorder characterized by multiple, recurrent hemorrhagic exudative pigmented epithelium detachments and shows resistance to anti- photodynamic therapy (PDT) and anti-vascular endothelial growth factor (VEGF) treatment. In this case report, a rapid response to aflibercept treatment is presented.

Case report: An anti-VEGF resistant PCV case showed rapid response to switching from bevacizumab to aflibercept in his right eye, and to primary treatment in left eye.

Conclusion: Aflibercept can be more effective than other anti-VEGF agents and PDT in the treatment of PCV. Monthly aflibercept injection may be required rather than bimonthly regimen in resistant PCV cases.

KEY WORDS: Polypoidal choridal vasculopathy, aflibercept

Polypoidal chorodial vasculopathy (PCV) is a disorder characterized by multiple, recurrent hemorrhagic exudative pigmented epithelium detachments (PED). It is controversial whether it is a distinct disorder, or a subtype of age related macular degeneration (AMD). When it was first described, it was thought to be an isolated choroidal vascular anomaly of posterior fundus. Lately it was defined as a type of choroidal neovascularization [1]. Nevertheless, PCV has different natural history and treatment response characteristics from exudative AMD. Presence of a polypoidal branching vascular network in the inner choroid causes the disorder. Treatment is with photodynamic therapy (PDT) or anti-vascular endothelial growth factor (VEGF) injections. In this report, a PCV case with PED, having a rapid response to switching from bevacizumab to aflibercept, is presented.

CASE REPORT

A 77 years old male presented with blurring of vision in his right eye. He had iodine allergy, hypertension, and bilateral cataract surgery in his past medical history. Best corrected visual acuity (BCVA) was 4/10 in his right, and 7/10 in the left eye. Intraocular pressure (IOP) of right eye was 14, and the left was 16 mmHg. In the slit lamp examination of anterior segment, both eyes were pseudophacic with a slight posterior capsular opacification in the left eye. Fundus examination revealed a PED and sub-retinal fluid in right eye, and normal view of posterior pole in left eye. Optical coherence tomography (OCT) showed two macular PED areas with an overlying sub-retinal fluid in the right eye. OCT view of left eye showed no pathology except for a tiny pigmented epithelium irregularity.(Fig 1A and 1B) Fundus fluorescein angiography (FFA) showed right late hyperfluorence due to leakage in the right eye.

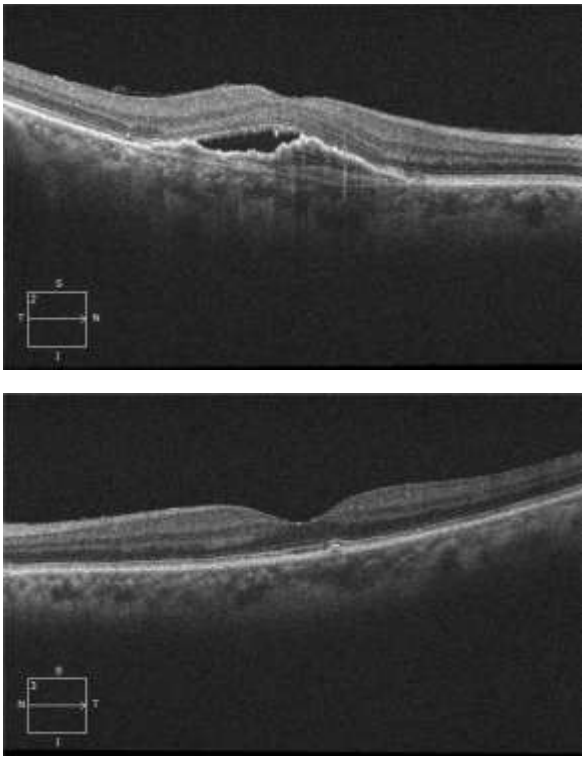

Fig. 1A, 1B: Baseline OCT views of right and left eye.

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Monthly intra-vitreal bevacizumab (IVB) injections were planned for the right eye. After three injections, minimal improvement was observed in the the right eye with no BCVA change.(Fig 2A, 2B) However, a sudden large serous PED occurred in the left eye with a significant BCVA decrease to 2/10. OCT and FFA images are shown in figure 3A, 3B.

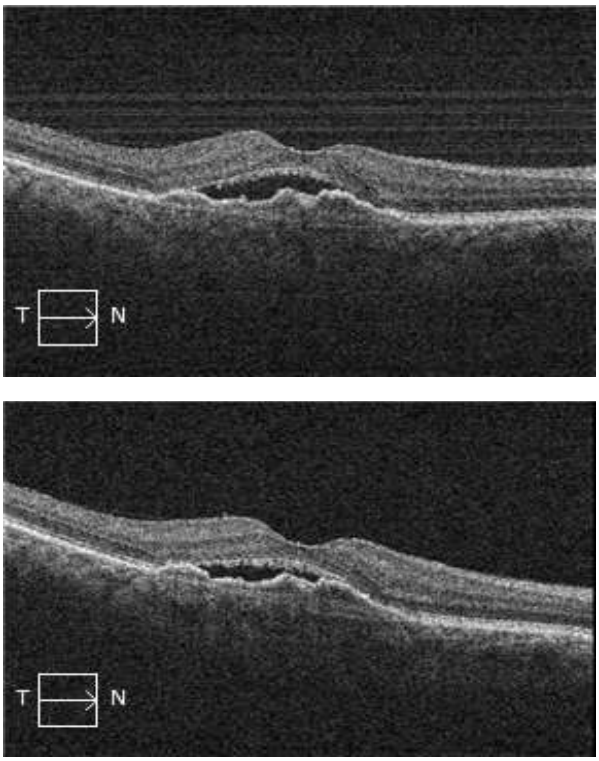

Fig 2A, 2B: OCT views of right eye at baseline and after three injections of bevacizumab.

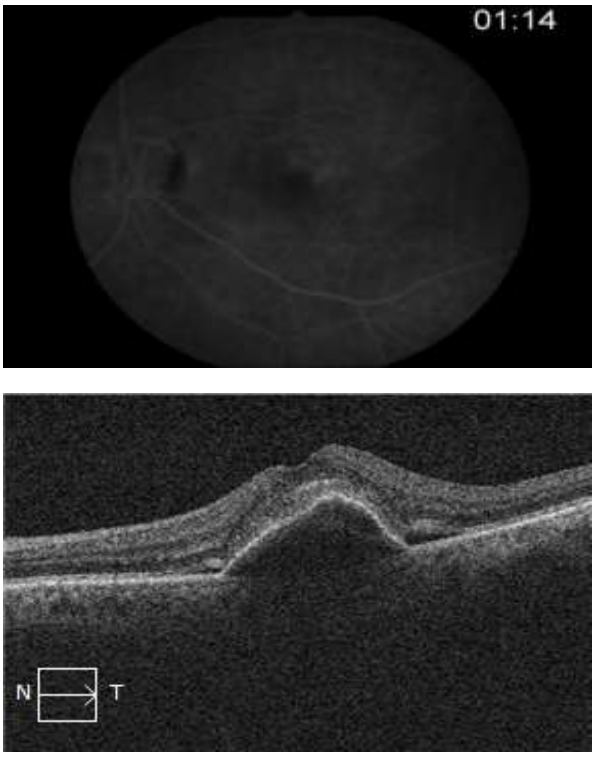

Fig 3A, 3B: FFA and OCT view of left sudden macular PED.

Atypical progression with sudden PED without AMD findings such as drusens in the left eye, multiple treatment resistant PEDs in the right eye, FFA and OCT findings brought the diagnosis to PCV, but this could not be confirmed with indocyanine green angiography (ICG) because of the iodine allergy.

The treatment was switched to bilaterally aflibercept injections. In the right eye, sub-retinal fluid was completely resolved and the PEDs were shrunk on the tenth day of first aflibercept injection (Fig 4A, 4B). After three aflibercept injections left eye revealed a significant PED shrink (Fig 5A, 5B) and BCVA reached to 7/10 in both eyes. Right eye got stable with a BCVA 6/10 with five injections and no need thereafter. Left eye showed a more resistant response and aflibercept treatment is going on to maintain stability with a BCVA of 6/10 while this report is being prepared. An attempt switching to bimonthly regimen failed because of PED dimension increase in left eye.

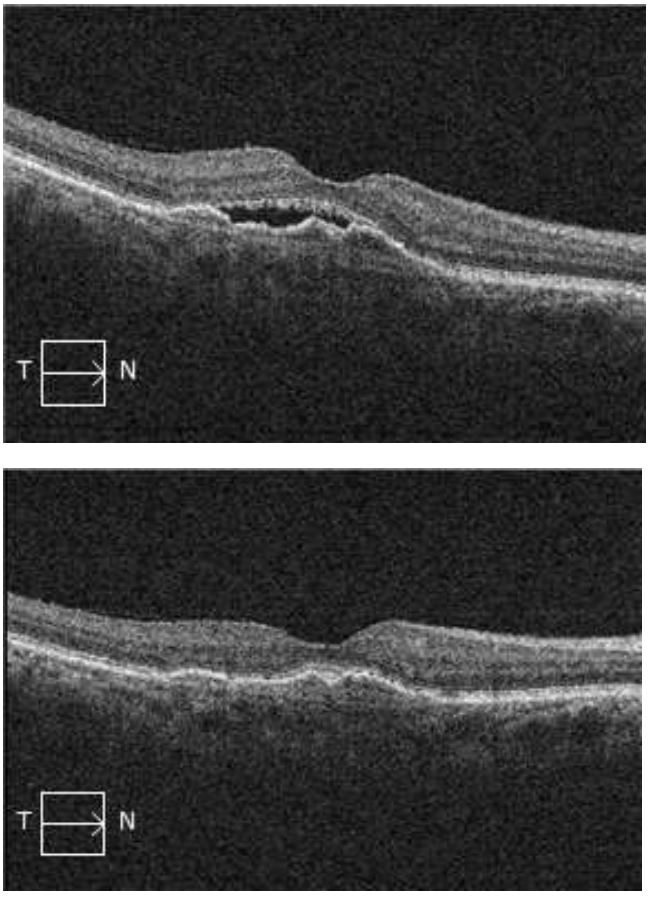

Fig 4A, 4B: Before and ten days after right aflibercept injection.

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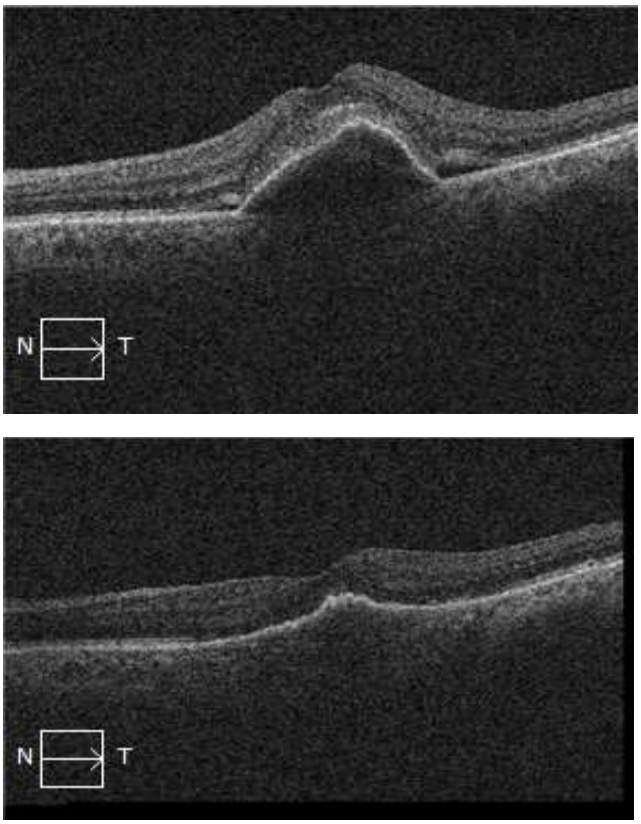

Fig 5A, 5B: Before and after three aflibercept injections.

DISCUSSION

The etiology of PCV, also known posterior uveal bleeding syndrome, is not clearly determined as in the case of AMD. There are similarities between two entity but, ethnicity, natural course and treatment response show differences. The most well known genetic loci associated with AMD are CFH and ARMS2/HTRA1. Only variants rs10490924 of ARMS2/HTRA1 genetic locus implicate a genetic and biological difference between PCV and AMD [2]. Differential diagnosis may be difficult because of interlaced relationship of these entities. The main pathology in PCV is an abnormal vascular network comprised of polypoidal lesions in the inner choroid. It is more prevalent in blacks and Asians compared to neovascular AMD and more common in women than men (5:1). Presentation is at late middle age with sudden unilateral visual impairment. The disease is often bilateral but asymmetrical in severity. Polypoidal lesions are frequently visible as orange nodules beneath the RPE in the peripapillary or macular area. Multiple recurrent serous PED results in leakage, bleeding, and visual impairment. FFA frequently shows a predominantly classic CNV like image. ICGA is essential in the diagnosis of PCV. Hyperfluorescent nodules with surrounding hypofluorescence appear in the early phase, then the choroidal polyps starts leaking. OCT shows sharply elevated PED with or without connecting lower PEDs, which is termed 'tomographic notch sign' [3]. Polypoidal lesions are usually cited at the external surface of higher PEDs (Fig 3B). Branching vascular network separates RPE from inner choroid under the lower PED and this OCT finding is defined as the 'double layer sign' (Fig 1A).

Treatment options are anti-VEGF therapy or PDT. Extrafoveal PCV lesions can be alternatively treated with argon laser photocoagulation. Some reports suggest that PCV has a better response to PDT than AMD [4-6] whereas a multicenter randomized controlled trial (LAPTOP study) reported that intravitreal ranibizumab (IVR) has a better visual improvement than PDT in PCV patients [7]. According to a multicenter randomized controlled trial (EVEREST study), all of the treatment options including PDT, IVR and combination therapy (PDT + IVR) resulted in improvements in VA in eyes with PCV [8]. In addition, PDT and combination therapy was more successful in complete polyp regression (70%) than IVR (30%). Some recent studies report that intavitreal aflibercept injection (IAI) is more effective than PDT and IVR and can be an option for resistant cases [9].

Although we could not confirm the diagnosis with ICGA because of iodine allergy, the clinical course, OCT and FFA findings strongly suggested the diagnosis of PCV in the presenting case. A sudden PED occurred in the left eye without prior findings, while the right eye was showing a resistant nature to monthly IVBs. Switching to bilateral IAIs resulted in immediate improvement in BCVA and PED dimensions of both eyes, and the stabilization of this improvement was achieved in six months. Aflibercept seems more effective than other treatment options in such treatment resistant disorders as PCV and PED. This might be due to anti-plasental growth factor effect and stronger affinity of aflibercept to VEGF. Also, aflibercept may have a better efficacy under the RPE than other anti-VEGF agents Left eye's PED was much higher than right eye's and more resistant to IAI. An attempt switching to bimonthly regimen failed because of PED dimension increase in left eye. More frequent injections may achieve more resolution of big PEDs which can be a subject of a future randomized controlled trial.

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