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Case report

Management of recalcitrant polypoidal choroidal vasculopathy by feeder vessel laser photocoagulation

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ABSTRACT

Purpose: To describe management of residual branch vascular network (BVN) in polypoidal choroidal vasculopathy (PCV) by thermal laser photocoagulation of feeder vessel.

Observations: Case report of sixty-four year old female with polypoidal choroidal vaculopathy (PCV) with moderate response to seven doses of intravitreal ranibizumab, six doses of intravitreal bevacizumab and one session of photodynamic therapy (PDT). The patient has resolved polyps but persistence of disease activity due to residual BVN and large pigment epithelial detachment (PED). Patient underwent thermal laser photocoagulation of feeder vessel of BVN identified on indocyanine green angiography (ICGA). There was complete resolution of residual BVN and large PED, which was confirmed on ICGA.

Conclusions and Importance: Recalcitrant cases of PCV without polyps but having BVN with feeder vessel can be managed by ICGA guided thermal laser photocoagulation. The case report illustrates the importance of utilizing multimodal imaging such as video indocyanine green angiography (ICGA) for identification of feeder vessel and its deployment for optimal management of refractory PCV.

1. Introduction

Polypoidal Choroidal Vasculopathy (PCV) is a clinical entity first described by Yannuzzi et al. in 1982,[1] characterized by subretinal polypoidal vascular lesions associated with serous and hemorrhagic pigment epithelial detachments (PED). With advancement in retinal imaging and formulation of new diagnostic criteria, PCV is being increasingly recognized as an important cause of exudative maculopathy in Asian eyes. Multiple studies have documented the prevalence of PCV amongst patients diagnosed with neovascular age related macular degeneration to be as high as 24.5%[2] –54.7%[3] in Chinese and Japanese population respectively, 49% in the Taiwanese[4] and 24.6% in the Korean populations[5] compared to 4% to 9.8%in Caucasians.[5–7]

Clinically the classical features of PCV include presence of sub-retinal reddish orange nodules and serosanguineous maculopathy, with the exudation being disproportionately larger than the size of lesion. Other findings include hemorrhagic pigment epithelial detachment, submacular hemorrhage and neurosensory retinal detachment in the peripapillary or macular retina.[8] According to current recommendations, indocyanine green angiography (ICGA) is the gold standard for detection and evaluation of PCV.[9] Existing treatment modalities for PCV include photodynamic therapy (PDT), anti-vascular endothelial growth factor (anti-VEGF) agents and thermal laser (TL). However, none of these treatment modalities, either singularly or in combination, may achieve complete regression of disease activity. This calls for continual assessment of each patient with application of multimodal imaging to individualize the treatment strategy. The choice of specific treatment modality and prognosis depends upon multiple factors such as the location and size of PCV lesion, presence or absence of polyp with residual abnormal vascular network (AVN), amount of submacular hemorrhage, presence or absence of leakage on fundus fluorescein angiography (FFA), visual acuity, and so on.

We report a case of recalcitrant PCV non-responsive to standard anti-VEGF therapyadd, in whom regression of disease activity was achieved by indocyanine green angiography (ICGA) guided thermal laser photocoagulation of feeder vessel.

2. Case report

A sixty-four year old lady of Asian origin presented to our clinic in August 2013 with complaint of metamorphopsia in right eye of one week duration. At presentation, her best-corrected visual acuity (BCVA) was 6/9, N8 with presence of a massive sub-foveal serous pigment epithelial detachment (PED) and shallow serous macular detachment (SMD) which was confirmed on spectral-domain optical coherence tomography (SD-OCT) (Fig. 1B) (Spectralis HRA + OCT, Heidelberg

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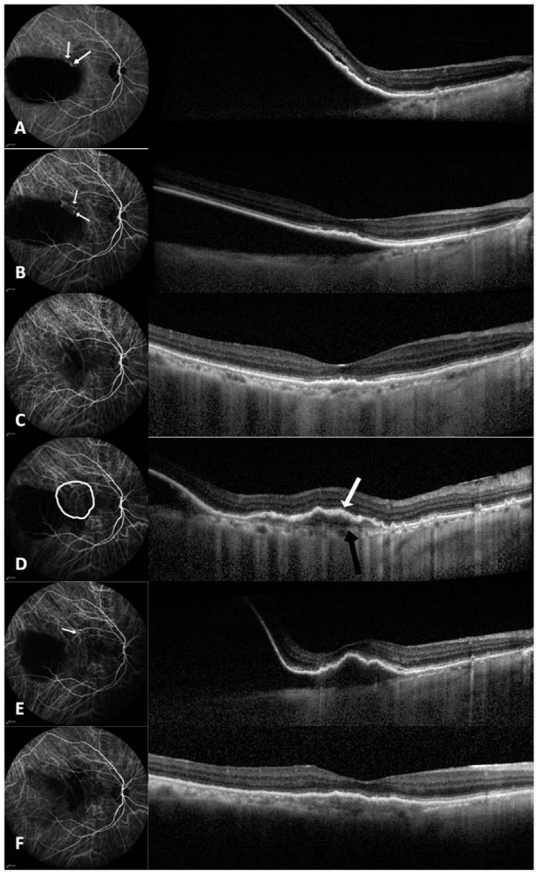

Fig. 1. Sequential imaging of progression and management of right eye of the patient on spectral-domain optical coherence tomography (SD-OCT) and indocyanine green angiography (ICGA). **1A, 1B.** Baseline ICGA showing cluster of polyps on ICGA (White arrows, 1A) at the superonasal margin of large hypofluorescent area corresponding to huge serous pigment epithelial detachment (PED) on SD-OCT. **2A, 2B.** Reduction in PED height on SD-OCT but persistence of polyps on ICGA (White arrows, 2A) after patient underwent seven doses of intravitreal ranibizumab and two doses of intravitreal bevacizumab. **3A, 3B.** Complete resolution of polyps and PED on ICGA and SD-OCT respectively after single session of full fluence photodynamic therapy (PDT). **4A, 4B.** Recurrence of PCV with presence of branch vascular network (BVN) on ICGA (White circle, 4A) but absence of polyps. SD-OCT showing characteristic "Double-layer sign" formed by shallow undulated RPE (White arrow) above and intact Bruch's membrane (Black arrow) below with moderate hyperreflectivity interspersed between them. **5A, 5B.** Persistence of BVN (White circle) with feeder vessel (White arrow) on ICGA and PED on SD-OCT. **6A, 6B.** Feeder vessel photocoagulation was executed with intravitreal bevacizumab following which there was complete resolution of BVN on ICGA.

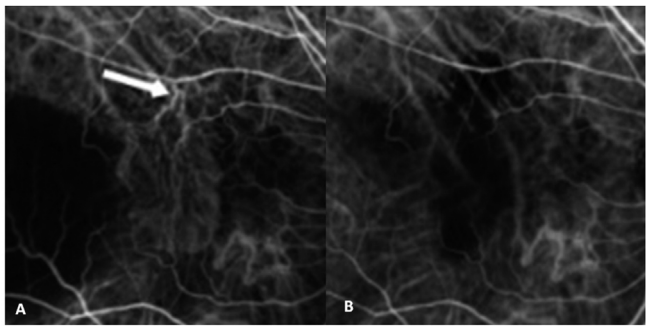

Fig. 2. Indocyanine green angiography (ICGA) images showing large branch vascular network (BVN) with feeder vessel (White arrow) (2A) and complete resolution of entire BVN after thermal laser photocoagulation (2B).

Engineering, Heidelberg, Germany). Indocyanine green angiography (ICGA) showed blocked fluorescence corresponding to the PED and presence of nodular hyperfluorescence at the nasal margin of PED

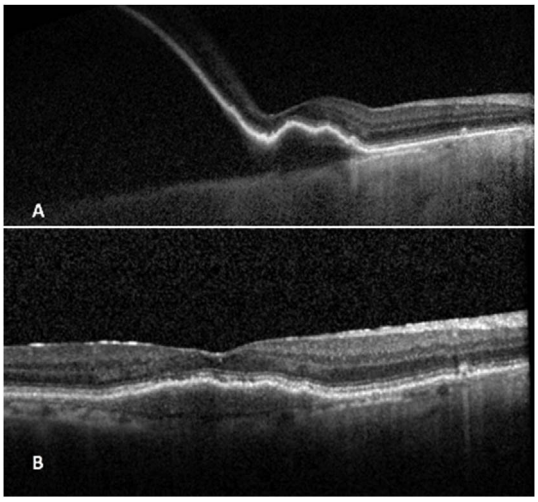

Fig. 3. A: SD-OCT image prior to thermal laser photocoagulation demonstrating presence of huge serous pigment epithelial detachment (PED) while Fig. 3B shows complete resolution of PED with minimal irregular RPE elevation 12 months post thermal laser photocoagulation.

confirming the presence of Extrafoveal polyps (Fig. 1A). In view of presence of massive PED and good visual acuity, PDT was deferred and subsequently, patient underwent seven doses of intravitreal ranibizumab and two doses of intravitreal bevacizumab, with modest response in form of slow progressive reduction in PED height, but there was persistence of polyps on ICGA (Fig. 2A and B). Once the height of PED reduced appreciably, PDT was deemed to be safe and hence patient underwent a session of full-fluence PDT. The patient responded drastically and there was complete resolution of PED and SMD which was confirmed on ICGA (Fig. 3A and B). However, six months later, the patient presented with recurrence of PED. Repeat dynamic ICGA done showed absence of polyp but presence of large branch vascular network (BVN) with feeder vessel. There was presence of double-layer sign (DLS) corresponding to the location of BVN. Since the patient had good visual acuity (6/9) in absence of polyp, she underwent three doses of intravitreal bevacizumab with minimal response. Dynamic ICGA was repeated again, which showed persistent BVN with feeder vessel. Since the location of the feeder vessel was extrafoveal, we performed ICGA guided thermal laser photocoagulation (power 150 mW, duration 0.1 ms, spot size 100 μm) in combination with intravitreal bevacizumab. The patient responded dramatically with complete resolution of PED, DLS and SMD on SD-OCT. Likewise, ICGA too demonstrated absence of the large BVN network with disappearance of large hypofluorescent area corresponding to PED. Fig. 2 shows a detailed view of ICGA before and after laser photocoagulation of the feeder vessel. The patient's final BCVA improved to 6/6, N6. The patient has been followed-up regularly for over 12 months with stable visual acuity and no recurrence (Fig. 3).

3. Discussion

Management of PCV remains to be a conundrum for practicing retinal physician due to its variable clinical presentation and response to therapy. Although international guidelines have been proposed for systematic evaluation and management of PCV, they are based on the literature present upto March 2012.[8] The treatment of PCV is primarily based on its location, and whether it is active or inactive. Inactive PCV can be safely monitored and observed.[9] For active lesions, the options available include PDT, anti-VEGF therapy and thermal laser photocoagulation. Landmark trials for management of PCV, including the EVEREST study,[9] the LAPTOP study[10] and the FUJISAN trial,[11] have compared the efficacy of anti-VEGF agent ranibizumab, either as

monotherapy or in combination with PDT. With polyp closure rate and improvement in visual acuity being the primary end points of treatment, these three landmark trials ascertained the role of combination therapy of full-fluence PDT (greater polyp closure rate) with anti-VEGF agents (better visual outcomes) in initiating therapy for this disease entity. In the EVEREST study, the reported polyp closure rate of PDT with or without ranibizumab therapy was 77.8% and 71.4% respectively.[9]

Since the guidelines have been published, the armamentarium of retinal imaging has grown exponentially. These include advancements in spectral domain optical coherence tomography (SD-OCT) and utilization of video/dynamic ICGA for optimal management of PCV·PCV being primarily a choroidal pathology, is best visualized and characterized by ICGA. ICGA permits better identification and demarcation of the entire lesion. Characteristically, the early phase of ICGA (First 1 minute) reveals a distinct pattern of vessels within the choroid which is known as the abnormal vascular network (AVN).[12] Nodular hyperfluoresence within the first 6 minutes of ICGA, which ascertains presence of polyps, are seen at the terminal ends of the AVN. This is indicative that the entire PCV lesion is a type 1 neovascularization comprising of abnormal vascular network that forms the primary neovascular tissue complex with the polyps purely being an abnormal aneurysmal dilatation at their terminal end. Knowledge of these facts is essential because they help us guide further treatment strategy in the form of continuation with anti-VEGF agents with/without PDT or switching over to a different treatment modality vis-à-vis thermal laser photocoagulation of feeder vessel. In principle, if a feeder vessel is visualized at an extra-foveal location, its treatment by thermal laser should eventually lead to collapse of the entire network of vessels with associated polyps, culminating in resolution of disease activity. This can be achieved only by performing a dynamic ICGA and plays a vital role in cessation of disease activity, thereby reducing the burden of anti-VEGF injections and PDT.

AVN is classified into two varieties: First, a branching vascular network (BVN) in which a feeder vessel can be recognized on ICGA, which fills the entire network of vessels.[9,12] This is best evaluated by performing a video ICGA within the first 30 s in which the feeder vessel can be visualized distinctively which fills the entire vascular network. The second variety of AVN includes the interconnecting channels (IC) in which there are absence of any feeder vessel.

In cases where the feeder vessel to a BVN can be demonstrated on video ICGA, TL to the vessel may help achieve resolution of BVN and subsequently disease activity. Traditionally, thermal laser (TL) photocoagulation has been advocated only for extra-foveal, peripapillary and peripheral PCV as the major concern with TL are chorio-retinal scarring, scotoma and choroidal neovascular membrane formation. It utilizes 532-green argon laser parameters of 100 μm–200 μm spot size and duration of 200–300 ms.[13] The target is to achieve a greyish or moderately white lesion and these should be titrated according to the blanching starting with low energy. Similar parameters may be utilized for treating of feeder vessel in a confluent manner.

Feeder vessel photocoagulation has been tried for management of Wet AMD in the past. However, it is no longer recommended by the American Academy of Ophthalmology practice guidelines since it was associated with high rates of complications including CNVM formation from breaks in the Bruchs membrane and formation of retinal breaks. Theoretically, chances of development of these complications are possible even in PCV patients who may be treated with thermal laser. Nonetheless, the probability of these complications, especially the choroidal complications are higher in Wet AMD since is associated with choroidal thinning which begets choroidal ischemia and subsequent CNVM formation. In contrast, PCV belongs to the pachychoroid disease spectrum which is associated with choroidal thickening. Hence, one of the key pathways in CNVM formation, which is ischemia, is negated in these patients. So theoretically, thermal laser may be relatively safer in PCV patients. However, long-term follow-up of these patients is essential to assess potential complications associated with this treatment modality. Additionally, it is important to note that this modality can be contemplated in refractory cases with clear angiographic evidence of feeder vessel.

Another key issue in management of type CNVM remains differentiating Wet AMD from PCV and it is here that multimodal imaging plays a key role. In the EVEREST trial,[9] which is the landmark trial for management of PCV, they used 3 specific criteria to define the polyps of PCV – nodular hyperfluorescence on stereoscopic ICGA (91.8%), hypofluorescent halo around the nodule (68.9%), pulsation during dynamic ICGA (6.6%). The EVEREST criteria was tested over a large number (241 eyes) of exudative maculopathy cases, of which 131 were PCV cases and 110 typical Wet AMD cases with fundus camera based ICGA.[14] The single criteria of focal subretinal hyperfluorescence on ICGA for a diagnosis of PCV had a sensitivity of 85.3% and a specificity of 80.9%.

Based on current scientific evidence based guidelines for clinical diagnosis and management of PCV by the Expert PCV panel,[8] a polyp is defined as *"Early nodular hypercyanescence arising from choroidal circulation noted within the first 6 minutes of ICG dye injection"*. Here we would like to highlight that in our case report, we undoubtedly demonstrate nodular hypercyanescent on the ICGA images (Fig. 1:1A and 1:2B) which appears within the first six minutes. Moreover, if we carefully look at those ICGA images, we have illustrated a bunch of nodular hypercyanescent lesions which undeniably confirms a diagnosis of PCV. To the best of our knowledge, such a cluster of nodular hypercyascent lesions have not been described in relation to either Wet AMD or even RAP based on current literature.

With regards to the BVN, the evidence based guidelines define it as *"Abnormal vascular network appearing within 1 minute of dye injection in the presence of feeder vessel"*. Also, corresponding OCT demonstrates a shallow irregular PED which is referred to as the double-layer sign (DLS). In our case, similarly, we demonstrate the network of branching vessels with a feeder (Fig. 1:4A and 2A) and correspondingly also illustrate the DLS on SD-OCT. Also, the patient did not have any other features of Wet AMD, including presence of drusen in either eye. Few other features in our case which are highly characteristic of PCV include lack of response to intravitreal anti-VEGF therapy. Although this is present even in cases of wet AMD, it is seen more in PCV mainly because on immunohistology in PCV, the vascular endothelial cells were negative for vascular endothelial growth factor (VEGF) which is not so in wet AMD.[15] Another distinctive feature of PCV includes an excellent response to photodynamic therapy (PDT). This is because it is primarily a pachychoroid disease and hence the good response. In our case, we have shown dramatic response to PDT whereby there was complete resolution of PED and SMD on SD-OCT and disappearance of all nodular hypercyanescent lesion on ICGA (Fig. 2A,B and 3A,B). Thus the multimodal imaging features of nodular hypercyanescence and branching vascular network on ICGA, DLS on SD-OCT, lack of any clinical features of wet AMD, lack of response to anti-VEGF therapy and drastic response to PDT indisputably clinches a diagnosis of PCV.

Monés et al.[16] have reported management of subfoveal PCV refractory to anti-VEGF and PDT by feeder vessel laser photocoagulation. Our case is complementary to that described by Monés et al. in that there is complete resolution of PCV once the feeder vessel was photocoagulated. In addition, our report is exclusive since it describes management of recalcitrant PCV in whom although the polyps have regressed completely following PDT, still the residual large BVN was a constant source of disease activity. Given the fact that many authors have described residual BVN as source of persistent fluid in PCV,[17,18] management of such obstinate cases by thermal laser photocoagulation of feeder vessel, if located extra-foveally, can be strongly considered.

4. Conclusion

Thermal laser continues to be an effective and relatively inexpensive

treatment modality as compared to PDT. Many patients of PCV continue to receive multiple doses of anti-VEGF therapy with variable response since ICGA, especially dynamic ICGA, is seldom performed in clinical practice. Our case report emphasizes on performing a dynamic ICGA for identification of feeder vessel of AVN and its management by thermal laser photocoagulation in cases with resolved polyps but persisting disease activity for achieving long-term disease inactivity. This modality can be safely considered if a feeder vessel can be clearly identified in an extrafoveal location.

Patient consent

Obtained.

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Conflicts of interest

The following authors have no financial disclosures: JS, AG, SC, MG.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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