Spontaneous formation and closure of full thickness macular hole after treatment with anti-vascular endothelial growth factor therapy in polypoidal choroidal vasculopathy

Abhishek Sethia, Jay Sheth, Mahesh Gopalakrishnan, Giridhar Anantharaman

Full-thickness macular hole (FTMH) formation in Polypoidal choroidal vasculopathy (PCV) after intravitreal anti-vascular endothelial growth factor (anti-VEGF) treatment is a rare complication. Spontaneous closure of FTMH following anti-VEGF therapy has not been described in PCV till date. We present a case of Asian woman with PCV who developed a FTMH following treatment with intra-vitreal anti-VEGF injections which subsequently closed spontaneously on further course of treatment.

Key words: Full-thickness macular hole, intra-vitreal anti-vascular endothelial growth factor, polypoidal choroidal vasculopathy

Polypoidal choroidal vasculopathy (PCV), is a distinctive form of choroidal neovascular membrane (CNVM) seen commonly in Asian population. It preferentially presents as multiple recurrent serosanguinous detachments of neurosensory retina and is characterized by a branching vascular network terminating in polyp-like lesions beneath the retinal pigment epithelium (RPE).[1]

Spontaneous massive sub-macular hemorrhage (SMH) from rupture of thin walled choroidal vessel is not an infrequent presentation of PCV, requiring intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy with or without intra-vitreal gas injection and tissue plasminogen activator (tPA).[2] Management of PCV with anti-VEGF therapy is associated with complications such as RPE rips and rarely full thickness macular hole (FTMH) development.[3] We present a rare case of Asian woman with PCV who developed a FTMH following treatment with intra-vitreal anti-VEGF injections and which subsequently closed spontaneously on further course of treatment with anti-VEGF.

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Case Report

A 63-year-old pseudophakic female of Asian origin presented with sudden loss of vision in left eye (LE) for 3 days (CF 2M) and long standing decreased vision (HM+) in right eye (RE). Fundus examination showed scarred CNVM in RE with presence of significant exudative maculopathy and nasal exudative detachment in LE [Fig. 1a]. A provisional diagnosis of PCV was made and she underwent two monthly injection of intra-vitreal bevacizumab (IVB) in LE. Complete resolution of sub-retinal fluid [Fig. 1c and d] was noted at two months with improvement in BCVA to 6/18. She underwent an ICGA [Fig. 1b], which confirmed the diagnosis of PCV with an abnormal branching vascular network (BVN) and focal laser was performed for extrafoveal polyps. At 28 months from baseline, she presented with SMH [Fig. 2a] and drop in BCVA to 6/24. Spectral domain-optical coherence tomography (SD-OCT) shows hemorrhagic notched pigment epithelial detachment (PED), hyper-reflective shallow-irregular PED (Double-layer sign; DLS) and lamellar macular hole (LMH) [Fig. 3a]. Following this she received monthly injection of IVB. After second dose of IVB, her BCVA dropped to 6/36. On SD-OCT, there was a reduction in height of PED, resolution of sub-retinal fluid (SRF), but the LMH was converted into a FTMH [Figs. 2b and 3b]. Subsequently, she was periodically observed, and was noted to have recurrence of hemorrhagic PED [Fig. 3c] at 41 months from baseline for which she underwent two more monthly injection of IVB. Following this, her BCVA was maintained at 6/36, with resolution of hemorrhage clinically and presence of trace SRF

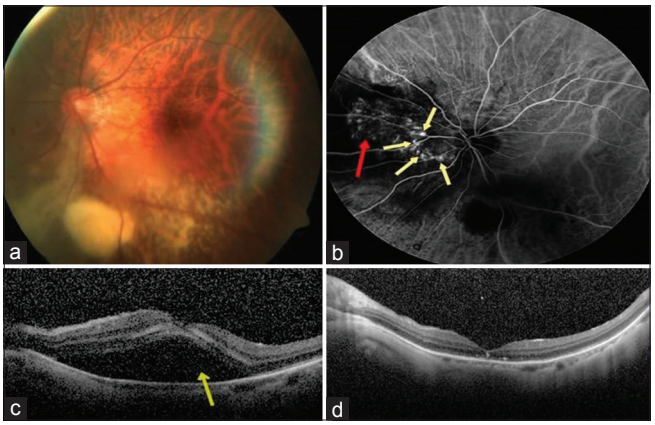

Figure 1: (a) Color photograph (baseline) showing exudative changes at inferior and nasal retina (b) ICGA Shows Cluster of nodular polyp nasal to disc at peripapillary area (yellow arrow) with large branch vascular network (red arrow). (c) SD-OCT at foveal sections how sub macular detachment (yellow arrow) which resolved after treatment with anti-VEGF (d)

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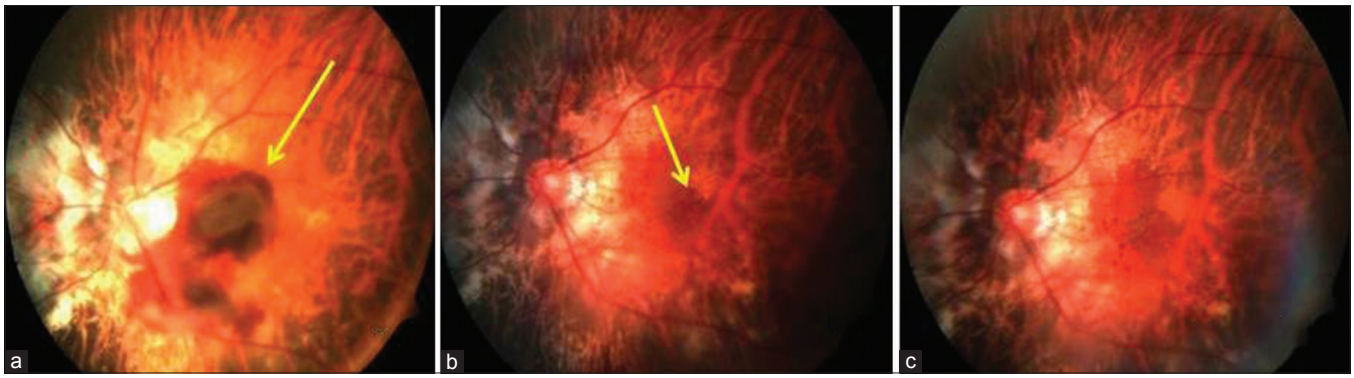

Figure 2: (a) Color photograph (28 months) shows appearance of hemorrhage at macula (yellow arrow). (b) After treatment with anti-VEGF complete resolution of hemorrhage with formation of full thickness macular hole. (c) After 2 more anti-VEGF closure of FTMH occurs at final follow-up

on SD-OCT. Furthermore, we also observed spontaneous closure of the FTMH [Figs. 2c and 3d].

Discussion

The choice of treatment in PCV depends on location of the polypoidal network, extent of network and associated clinical features, which primarily involves intra-vitreal anti-VEGF therapy with or without photodynamic therapy and thermal laser.[1] We present a rare case of Asian woman having PCV who developed a FTMH following treatment with intravitreal anti-VEGF injections which spontaneously closed on further course of treatment with anti-VEGF.

VEGF is significantly increased in eyes with PCV[4] and treatment with intra-vitreal anti-VEGF has been the standard treatment of choroidal neovascularization (CNV) secondary to age-related macular degeneration (ARMD) as well as PCV.[5] So the same treatment has been used in our case to treat exudative maculopathy and SMH due to PCV.

Baskaran P *et al*. reported that SMH can damage the relatively thin fovea resulting in atrophy, or very rarely, development of FTMH. The presence of blood at base of MH, bridge of remnant retinal tissue, and break through vitreous hemorrhage are indirect evidence for that.[2] MH development following subretinal hemorrhage in ruptured retinal arterial macroaneurysm (RAM) was reported by Sagara N *et al*.[6] MH formation after SMH has been reported in a 75-year-old female with ARMD.[7] All above studies support that presence of SMH can cause FTMH as seen in our case.

However, Cho JH *et al*. have reported MH following intra-vitreal Ranibizumab in PCV.[4] Although macular hole is not a complication of PCV itself, it is likely to be because of interactions between the neovascular tissue complex and anti-VEGF agents. Anti-VEGF agents may cause formation of macular hole by modulating the activity of the choroidal neovascularization and inducing contraction of the vascular membrane, leading to exacerbation of the tangential traction on the overlying retina.[8] Raiji VR *et al*. have also reported FTMH development overlying PED after treatment with anti-VEGF agent and have suggested pushing or stretching forces of choroidal neovascular complex as an additional mechanism for MH development.[9] Thus, shearing force associated with contraction of the polypoidal choroidal vessels and decrease in height of PED after anti-VEGF on the overlying retina might also influence the development of the MH in our case.

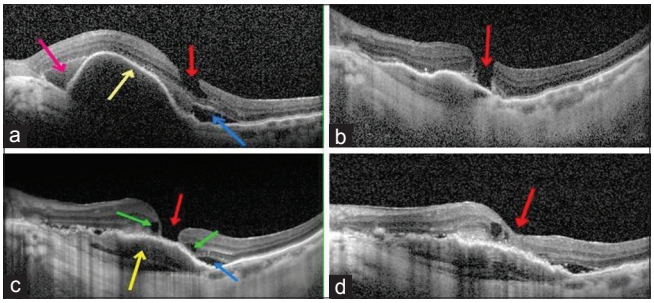

Figure 3: (a) SD-OCT at foveal section (28 month) showing large hemorrhagic notched PED (yellow arrow) nasal to fovea, sub retinal hyper reflectivity (pink arrow), SRF (blue arrow) with LMH (red arrow). (b) Decrease in height of hemorrhagic PED, resolution of sub retinal hyperreflectivity and SRF with conversion of LMH into FTMH (red arrow) after anti-VEGF treatment. (c) Increase in height of PED, reappearance of sub retina hyper reflectivity, SRF and IRF during follow-up (41 months). (d) With further treatment, spontaneous closure of FTMH (red arrow) with thin ERM, persistence of FVPED and trace SRF at foveal section

Hence, MH seems to be potential rare sequelae after intra-vitreal anti-VEGF injection and should be suspected for patients who do not show an improvement or who worsen after intra-vitreal anti-VEGF therapy.

Additionally, changes in PED and centripetal contraction of thin ERM after anti-VEGF therapy seemed to release the mechanical stress on the retina. This can potentially allow approximation of the MH edges and closure of the hole in our case report. Storch MW *et al*. reported a case of MH closure after intra-vitreal Bevacizumab therapy for an underlying PED due to exudative AMD.[10] Spontaneous closure of FTMH in PCV has not been described in literature.

In conclusion our case report is complementary to Cho *et al*., describing FTMH development following intra-vitreal Ranibizumab therapy in PCV. In addition, our case report is unique since it describes development of FTMH following intra-vitreal Bevacizumab for the first time in literature. Furthermore, this is a singular case to illustrate spontaneous formation as well as spontaneous closure of FTMH secondary to intra-vitreal anti-VEGF therapy for PCV.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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