Original Research Article

Vitrectomy for Breakthrough Bleeding in Age Related Macular Degeneration and Polypoidal Choroidal Vasculopathy in a Malaysian Hospital

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Abstract

This study aimed to review the risk factors and clinical outcomes of patients undergoing pars planar vitrectomy (PPV) for breakthrough bleeding (BTB) from age related macular degeneration (AMD) and polypoidal choroidal vasculopathy (PCV). We performed a retrospective review of medical records of 346 patients operated by the vitreoretinal unit at Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Kuala Lumpur, Malaysia from January 2008 - June 2011. We found eight eyes of 8 patients with AMD/IPCV-related BTB who underwent PPV. Mean age of patients was 64.4 years (range 41-80 years) with 5 males. Five were Chinese. Duration of symptoms ranged from days to months. Four patients were on anti-coagulants. Two had history of prior photodynamic therapy. There were five cases of PCV, of which three were macular in location. All three cases of AMD were macular. Intraoperative intravitreal ranibizumab injection was given in three cases and two had combined vitrectomy and cataract extraction. All cases reported improvement in visual acuity with four cases achieving 6/60 or better post operatively including two cases of extramacular PCV achieving 6/9 vision. Mean follow-up was 60 weeks. Postoperative complications included retinal tear and detachment in one case, reattached on reoperation. Six patients had a history of hypertension including one individual with stroke. Our small series indicates a predominance of Chinese individuals with BTB. Usage of anticoagulants and hypertension may be a predisposing factor. Better visual prognosis occurs with extramacular lesions which tend to be of PCV type.

Keywords: Age-related macular degeneration, breakthrough haemorrhage, polypoidal choroidal vasculopathy, vitrectomy, indocyanine green angiography

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Date of submission: 12 June, 2012 Date of acceptance: 25 July, 2012

Introduction

Age related macular degeneration (AMD) is one of the most common causes of reduced visual acuity in the aged population. Exudative AMD is characterized by the presence of subretinal neovascularisation with subretinal haemorrhages, exudation and pigment epithelial detachments. Recently, a disease that has clinical features similar to AMD has been found to have a higher prevalence in Asian populations, namely polypoidal choroidal vasculopathy (PCV) (1). Unlike cataract and glaucoma in which there are effective treatments which can completely cure or control the disease, AMD and PCV remain diseases that carry heavy financial burdens for those afflicted and may result in persistent, poor central vision despite treatment.

Subretinal haemorrhage following choroidal neovascular membrane secondary to age-related macular degeneration or idiopathic polypoidal choroidal vasculopathy (PCV) is an important sight-threatening condition (1). A massive intraocular haemorrhage in the course of age-related macular degeneration (AMD) is a devastating event which often requires immediate surgical intervention. It can

also be a diagnostic and treatment dilemma. There is evidence that anticoagulant therapy prescribed for vascular or cardiac indications plays a role in the development of a massive haemorrhage (2-4).

The aim of this retrospective review was to review the ocular and systemic risk factors and clinical outcomes of patients undergoing pars planar vitrectomy (PPV) for breakthrough bleeding (BTB) from age related macular degeneration (AMD) and polypoidal choroidal vasculopathy (PCV).

Materials and methods

A retrospective review of 346 patients operated by the vitreoretinal unit in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) in Kuala Lumpur from January 2008 - June 2011 was conducted to detect all cases of vitreous haemorrhage secondary to breakthrough bleeding (BTB) from AMD or PCV which underwent pars planar vitrectomy for clearance of the haemorrhage. The study was conducted in accordance with the Declaration of Helsinki. All patients had signed an informed consent form prior to vitrectomy surgery. Pars planar vitrectomy was performed by one surgeon and was either 20G or 23G pars planar vitrectomy using the Millenium™ (Bausch and Lomb, London, UK) or Accurus™ (Alcon laboratories, Texas, USA) vitrectomy machines. Patients underwent subsequent fundus fluorescein and indocyanine green angiography with Heidelberg Retinal Angiogram™ (Heidelberg Engineering, USA) if angiography had not been performed prior to the bleed or for better localization of the membrane or polyp or if the lesions looked active and were not fibrotic. The patient medical records were reviewed to collect information on the demographics, the fundus photography and the angiography confirming diagnosis of AMD and PCV. The data was analysed by SPSS version 16.

Results

Eight eyes of 8 patients with AMD/PCV-related BTB who underwent PPV were included. Table 1 shows the demographics and clinical data of the patients. The mean age of patients was 64.4 years (range 41-80 years). Males just outnumbered females. The majority of patients were Chinese (n=5).

Photodynamic therapy (PDT) was performed previously in two eyes including one eye with previous PDT and anti-VEGF. Five cases out of the eight had components of idiopathic polypoidal choroidal vasculopathy (PCV) and three of them were macular in location. (Patient 6, Figure 1) Three cases with features of AMD were all macular in location and had fibrotic elements. (Table 1) (Patient 5, Figure 2 and Patient 7, Figure 3) Only one case of PCV with BTB was in fibrotic stage. (Patient 2, Figure 4) Four cases of PCV were in the active stage. Small gauge (23G) vitrectomy was used in all cases except one. Two cases were combined with phacoemulsification. Vision at presentation was poor in all cases (counting finger or worse). The vision in all patients improved after vitrectomy. However, only half achieved 6/60 or better vision. Two patients achieved vision better than 6/12 who were the two patients with extramacular PCV. (Patient 3, Figure 5) Mean follow up was 60 weeks (range 4-28 months).

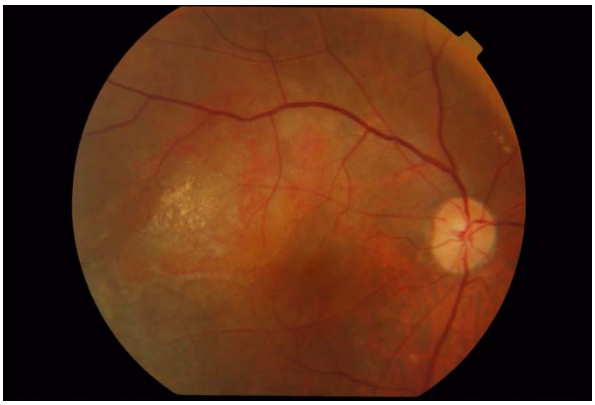

Figure 1: Fundus photograph of the right eye of Patient 6 showing Exudative AMD involving the right fundus as evidenced by subretinal hard exudation and haemorrhagic pigment epithelial detachment.

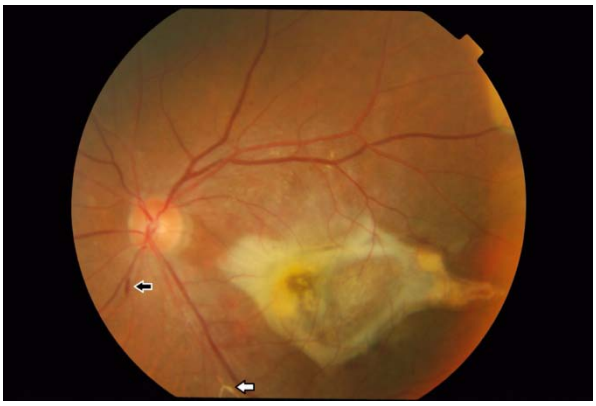

Figure 2: Left fundus photograph of Patient 5 showing extensive subretinal fibrosis in a submacular location with altered blood. Other interesting features in the photograph include the presence of atherosclerosis in the inferotemporal arteriole (small white arrow). There is also AV nipping and arteriolar narrowing consistent with Grade 2 hypertensive retinopathy and a flame shaped haemorrhage (small dark arrow)

Table 1: Shows the demographics and clinical features of the patients

Patient No	Age (yrs at diagnosis)/ Gender/ Ethnicity	Vision at presentation (affected eye)	Duration of symptoms	Duration of follow-up (weeks)	Treatments prior to BTB	Vitreoretinal procedure	Causative Lesion	Location	Stage	Systemic disease	Post-operative vision	Anticoagulant usage	Complications
1	75/F/C	PL	5 months	214	Nil	PPV/ PEA/ IOL	AMD	submacular	fibrosis	DM with mild DR/IHD/HPT	CF	warfarin	
2	52/F/C	HM	2 days	132	Nil	PPV/SF6	PCV	submacular	fibrosis	NIL	CF	NIL	Retinal tear, cataract
3	41/F/O	HM	1week	19	Nil	PPV/ SF6	PCV	juxta- foveal	active	NIL	6/9	NIL	Retinal tear
4	58/M/M	HM	1 month	47	PDT	PPV/ ranibizumab	PCV	Temporal extramacular	Pulsating (active)	DM with mild DR/HPT	6/9	NIL	Cataract
5	80/M/C	HM	2 weeks	19	Nil	PPV	AMD	submacular	fibrosis	DM with mild DR/IHD	CF	ticlopidine	
6	74/M/C	PL	1 week	15	PDT/ ranibizumab	PPV	PCV	submacular	Polyps (active)	Stroke	6/36	aspirin	
7	70/M/I	HM	2 week	16	Nil	PPV/ ranibizumab	AMD	submacular	fibrosis	IHD	CF	clopidogrel	
8	65/M/C	HM	1month	16	Nil	PPV/ PEA/ IOL/ ranibizumab	PCV	submacular	active	NIL	6/60	NIL	
Key:	Gender: M-male; F-female/ Ethnicity: M-Malay; C-Chinese; I-Indian; O-Others (Indonesian)	HM – hand motion; PL – perception to light			PDT-photodynamic therapy	PPV-23G pars planar vitrectomy; *PPV–20G PPV; PEA-phacoemulsification; IOL–intraocular lens implantation; SF6–sulphur hexafluoride gas	PCV–polypoidal choroidal vasculopathy; AMD – age related macular degeneration			DM–diabetes mellitus; DR –diabetic retinopathy; IHD–ischaemic heart disease			

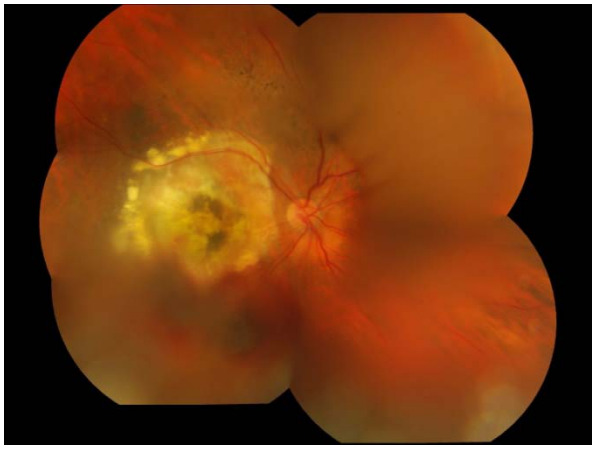

Figure 3: Right fundus composite photograph showing extensive submacular scarring in patient 7 in association with subretinal exudation and haemorrhage inferior to the arcades indicating still active disease components.

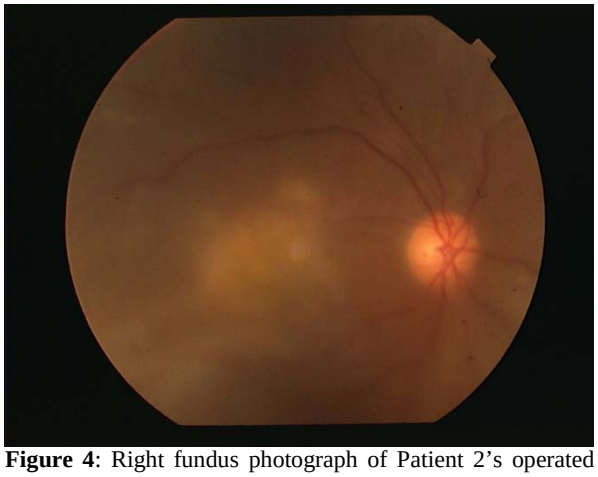

Figure 4: Right fundus photograph of Patient 2's operated eye with subretinal altered blood and scarring following vitrectomy and silicone oil for PCV at the macula.

Four patients were observed following the BTB and did not receive any treatment until their last review with stable visions. Patient 6 underwent indocyanine green angiography 1 week following vitrectomy which revealed an extensive cluster of polyps, branching vascular network and feeder vessel (Patient 7, Figure 6). He received PDT and intravitreal ranibizumab 0.5 mg/ 0.05 ml injection and was stable until final review. Patient 4 with extramacular PCV on ICGA (Patient 6, Figure 7) was treated with laser photocoagulation. One patient defaulted 1 month after vitrectomy. One patient underwent angiography (Patient 8) but declined further treatment.

Discussion

Spontaneous vitreous haemorrhage in elderly patients with no prior history of eye disease is a diagnostic and

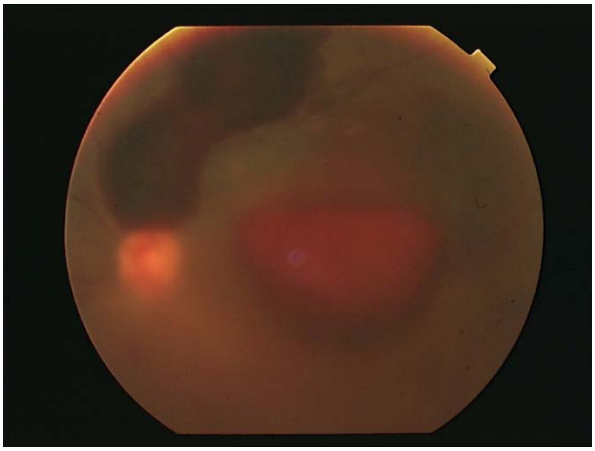

Figure 5: Fundus photograph of Patient 3's left eye showing the fresh and dense premacular (subhyaloid haemorrhage) with darker subretinal bleed involving the superior fundus just above the disc. The subretinal blood arose from a cluster of polyps (PCV) just near the disc sparing the fovea. Hence post-operative vision was good at 6/9.

treatment dilemma. The differential diagnoses include ischaemic retinal conditions with neovascularisation such as vein occlusion or diabetic retinopathy, retinal tear or rhegmatogenous retinal detachment, posterior vitreous detachment and AMD or PCV. Interestingly, BTB necessitating vitrectomy was performed in a mere 2.3% of vitrectomy surgeries at our centre suggesting an overall low rate of breakthrough bleeding in all forms of AMD or PCV which eventually require vitrectomy.

The large number of PCV lesions found in this study (half) is reflective of the Asian parentage of the subjects (5). PCV accounts for about ¼ to ½ of cases manifesting as exudative AMD in Asia (5,6) compared to approximately 10% of the Caucasian population (6).

BTB is often related to PCV lesions which are prone to sudden torrential bleeds. The average age of onset of PCV is 65 years (7). The mean age of this small local series was 64.4 years with a slight male preponderance similar to the findings of Uyama M et al[7] and A K H Kwok et al (8). In this case series of patients with BTB, there was a large number of Chinese highlighting a higher predisposition to BTB secondary to AMD or PCV in Chinese individuals (5,6). Furthermore, this group is disproportionate to the ethnic distribution of the surrounding population which has a Malay majority.

Seventy percent of the lesions in this case series are located in the macula. In the cases due to AMD neovascular membranes, the lesions were invariably at the macula as in other series (8). In contrast, PCV lesions

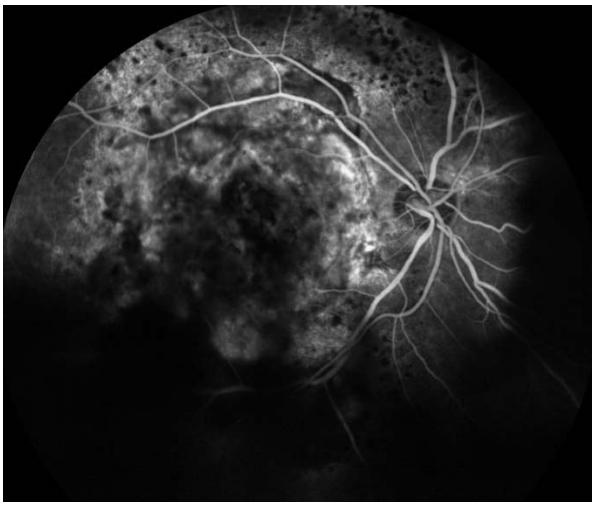

Figure 6: The right fundus indocyanine green angiogram of Patient 7 shows no active lesions and mainly subretinal exudative scarring.

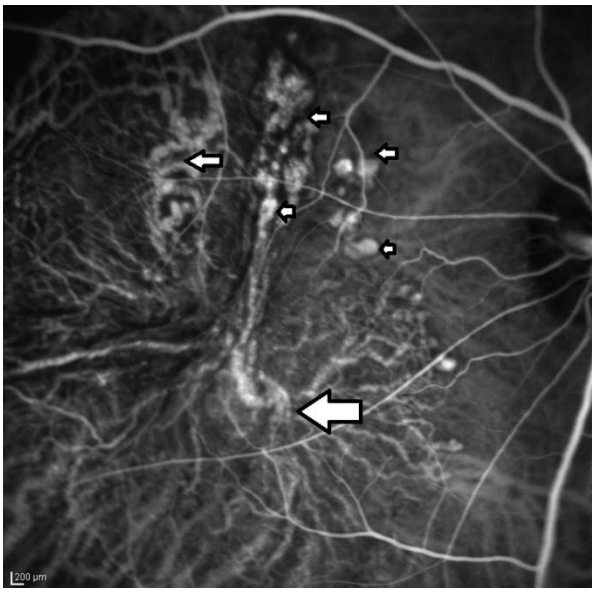

Figure 7: Indocyanine green angiogram of Patient 6's right eye showing a cluster of large polyps (small arrows, not all are marked) and large, wide caliber of branching vascular network (medium arrow) associated with a large feeder vessel (large arrow). Without vitrectomy, such good view for angiography and ultimately targeted therapy would have been impossible.

can be peripapillary, at the macula or in the periphery with a majority at the periphery. Interestingly, a proportion of PCV lesions were located outside the macula and these lesions had the best visual prognosis in our series because the macula was spared.

Other interesting features of the study group included the heterogenous but common usage of anticoagulant (up to half). Usage of anticoagulants or antithrombotics clearly predispose them to serious haemorrhagic complications including BTB. Studies strongly support this observation (2,3,4). Anticoagulant medication probably poses a more significant risk in the development of a massive intraocular haemorrhage in patients with exudative AMD, compared to those on antiplatelet medication (2) but we had at least one patient on aspirin and one on ticlopidine at the time of BTB. Kiernan DF et al found an annual incidence of vitreous haemorrhage in Exudative AMD of 0.1% in those who are taking anticoagulants and antiplatelets agents, and 2.5 times less in those who are not on anti coagulants (0.04%) (4).

In our case series, two patients had had previous PDT. PDT for eyes with a large PCV lesions may be another risk for serious haemorrhagic ocular complications (9). In fact, up to 30% of PCV lesions which had received PDT subsequently bled subretinally and of these, up to 20% had vitreous haemorrhages (9). The risk of BTB seemed to be related to the size of area of branching vascular network with larger networks at higher risk of BTB.

El Baba et al. found a positive history of systemic hypertension and cardiovascular diseases in 40% of patients with AMD (3). The occurrence of hypertension is no surprise in an aged population with AMD. However, the high proportion of hypertension in three quarters of our group of patients requiring vitrectomy for BTB suggests an association of hypertension with BTB.

Vitrectomy is beneficial for improving vision in cases of breakthrough vitreous haemorrhage. The functional outcome in our patients with BTB from AMD and PCV is acceptable where half of them achieved 6/60 or better. All eyes post operatively had anatomical success and good functional success in macula sparing lesions. Edward Roufail et al 2008, found that surgical and functional outcome in combined cataract and BTB was poor in AMD most likely due to the advanced stage and location of lesions (10). Submacular fibrosis was observed in patients with low post-operative visual acuity and limited visual gain. It is possible that bleeding from submacular networks or polyps promoted fibrosis and healing of the inciting lesions leading to fibrotic stage AMD and PCV.

The visual outcome in PCV seems better compared to AMD because of bleeding from extramacular sites. The same findings were noted by Jung Jae Ho et al in their retrospective review, which found that functional outcomes of vitrectomy for vitreous haemorrhage

associated with AMD were inferior to outcomes of the PCV group (11).

This study sets the scene for further investigation involving a large cohort of AMD/ PCV patients followed over time to detect risk factors for bleeding. Nonetheless, treatment for BTB requires vitrectomy to improve view for further investigation and treatment of the underlying polyp, branching vascular network or choroidal neovascularisation which should not be different from the usual approach.

Conclusion

Vitrectomy for BTB in AMD/PCV is successful in improving functional outcomes in only half of those undergoing surgery despite the excellent anatomical outcomes. Hence our observations suggest that systemic hypertension in AMD and PCV patients, particularly in those with a single remaining good eye, be well controlled to reduce the risk of BTB. We also suggest judicious usage of anticoagulants of any kind in these patients to prevent BTB. This requires communication between physician and ophthalmologist for the well-being and quality of life of elderly patients. Chinese patients have a genetic predisposition to BTB. Counselling of patients with AMD or PCV should include the risk of BTB.

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