• Clinical Research •

Long-term observation of vitrectomy without subretinal hemorrhage management for massive vitreous hemorrhage secondary to polypoidal choroidal vasculopathy

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Received: 2018-12-10 Accepted: 2019-06-25

Abstract

• AIM: To describe the long-term observation of vitrectomy without subretinal hemorrhage (SRH) management for massive vitreous hemorrhage (VH) secondary to polypoidal choroidal vasculopathy (PCV).

• METHODS: This is a retrospective, consecutive case series. A total of 86 eyes of 86 patients with >14d of massive VH associated with PCV were included. All patients underwent vitrectomy without SRH management, followed by intravitreal ranibizumab injections and/or photodynamic therapy (PDT) as needed. The main outcome measures were best-corrected visual acuity (BCVA), postoperative adverse events and the recurrence of VH.

• RESULTS: The average follow-up period was 25.5±9.2mo (range 12-35mo). Mean BCVA at baseline (2.16±0.39 logMAR) had improved significantly, both 3mo after surgery (1.42±0.66 logMAR, *P*<0.001) and by the last visit (1.23±0.74 logMAR, *P*<0.001). The common postoperative complications included macular subretinal fibrosis in 14 eyes (16.3%) and ciliary body detachment in 4 eyes (4.7%). Nineteen eyes (22.1%) received following treatment with ranibizumab injections without/with PDT, and 15 (17.4%) were resolved. Four eyes (4.7%) had recurrent hemorrhage during the follow-up period. In multiple regression analysis, thicker SRH (beta=0.33, *P*=0.025) in the preoperative B-scan and the presence of foveal subretinal fibrosis (beta=0.28, *P*=0.018) in the follow up were associated with poor postoperative BCVA.

• CONCLUSION: Vitrectomy without SRH management for massive VH secondary to PCV improved/stabilized visual function in the long-term observation. Eyes presenting with thicker SRH preoperatively and forming foveal subretinal fibrosis in the follow-up period tended to have worse BCVA.

• KEYWORDS: polypoidal choroidal vasculopathy; vitreous hemorrhage; vitrectomy; visual acuity

DOI:10.18240/ijo.2019.12.07

Citation: Li ZX, Hu YJ, Atik A, Lu L, Hu J. Long-term observation of vitrectomy without subretinal hemorrhage management for massive vitreous hemorrhage secondary to polypoidal choroidal vasculopathy. *Int J Ophthalmol* 2019;12(12):1859-1864

INTRODUCTION

Polypoidal choroidal vasculopathy (PCV) is a choroidal vascular abnormality characterized by a branching, polypoidal, vascular network with choroidal lesions. PCV causes pigment epithelial and neurosensory retinal detachment, a recurring problem associated with subretinal leakage and hemorrhage[1-6]. In those diagnosed with PCV, vitreous hemorrhage (VH) occurs in 19.9%; and among patients at first PCV diagnosis, 4.5% present with VH[7].

The mechanism that allows a subretinal hemorrhage (SRH) to cloud the vitreous has remained enigmatic[8-10]. If SRH is thick, the patient is at risk for VH, which often results in a poor prognosis for central visual acuity[11-13].

Vitrectomy with or without subretinal manipulation were the main surgical methods for PCV complicated by VH. However, little information concerning associated surgery outcomes has been reported and the attempt to define an ideal treatment has been inconclusive[14-15]. In fact, the VH is mainly caused by the breakthrough of SRH and there is no consensus on the management of chronic SRH. The long-term observation of relative surgical interventions in such condition will help ophthalmologists develop treatment strategy. However, the

information is limited. Thus, the purpose of this study was to report the long-term observation of a large sample of patients treated with vitrectomy without SRH management for VH secondary to PCV.

SUBJECTS AND METHODS

Ethical Approval The study followed the guidelines of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board of Zhongshan Ophthalmic Center and written informed consent was obtained from all subjects.

The medical records of patients with PCV-related VH were reviewed retrospectively in Zhongshan Ophthalmic Center in Guangzhou city of China. Analysis was performed on 86 consecutive patients (86 eyes) who were presented with PCV secondary to VH, between August 10, 2012 and October 31, 2017. Patients were treated with a 3-port pars plana vitrectomy (PPV), using a standard 23-gauge sutureless system. The inclusion criteria were as follows: 1) Vision deterioration because of massive VH, defined as dense VH with complete obscured fundus by slit lamp examination after full mydriasis; 2) Diagnoses of PCV made either preoperatively or postoperatively, based on the results of fundus examination, optical coherence tomography (OCT), fundus fluorescein angiography (FFA) and indocyanine green angiography (ICGA). PCV was defined as the presence of a branching vascular network with polypoidal or aneurysmal structures at any visits as determined by ICGA, and/or the presence of elevated orange-red lesions observed at fundus examination during the operation, and/or multiple sero-sanguinous retinal pigment epithelium detachments, and/or double-layer sign or thumb-like polyps on OCT[16-17]; 3) The absence of other ocular diseases that affect visual acuity (*i.e.,* age related macular degeneration, retinal vein occlusion, diabetic retinopathy, choroidal melanoma, retinal detachment and retinal vasculitis). Patients with VH secondary to other eye diseases, any severe systemic diseases and any retinal tears with ultrasound preoperatively have been excluded.

All patients underwent a comprehensive ophthalmologic examination, including a test of best-corrected visual acuity (BCVA), slit-lamp microscope examination, ultrasound biomicroscopy (UBM) and B-scan ultrasonography. Preoperative data included BCVA, duration of symptoms, and the characteristics of VH. Postoperative BCVA, fundus photography, spectral-domain OCT (SD-OCT; Heidelberg, Germany), FFA and ICGA were also obtained.

All patients underwent a 23-gauge PPV, under local or general anesthesia, without subretinal manipulation. The surgical procedure consisted of a core and peripheral vitrectomy. If a retinal tear was observed during the operation, endophotocoagulation was used to create chorioretinal adhesions and silicone oil used for an intraocular tamponade. For those without retinal tears, vitrectomy was performed without external indentation, SRH management, or intraocular tamponade.

Following treatment was done if lesion activity was supposed to be present as follows: early-stage intense saccular hyperfluorescence and late-stage leakage/staining of the polypoidal lesions and accumulation of fluid in ICGA[18]. Intravitreal ranibizumab (0.5 mg/0.05 mL; Lucentis; Genentech, Inc) alone or combined with photodynamic therapy (PDT) were applied to these eyes postoperatively.

BCVA was measured by a standard Snellen visual acuity chart and converted to a logarithm of minimal angle of resolution (logMAR) scale for statistical analysis. Visual acuity was described as improved or worsened if there was a change of more than two Snellen lines, and stable if within two lines from baseline. According to previous methods[19-20], no light perception was set at 2.9 logMAR, light perception at 2.6 logMAR, hand movements at 2.3 logMAR, and counting fingers (CF) at 1.85 logMAR.

Statistical Analysis The Mann-Whitney *U* test was used for comparison of preoperative, 3mo after surgery, and final postoperative BCVAs. Univariate and multiple regression analyses were performed to explore the association between BCVA at final visit with age, gender, history of diabetes mellitus, history of hypertension, duration of symptom, area of SRH, and thickness of SRH and foveal subretinal fibrosis. A *P* value of 0.05 or less was considered statistically significant. All statistical analyses were performed using SPSS for Windows version 17.0 (SPSS, Inc, Chicago, Illinois, USA).

RESULTS

Eighty-six consecutively treated eyes of 86 patients were included in this study. The baseline demographic data of subjects and ocular characteristics are shown in Table 1. Nine eyes (10.5%) had received previous treatments for PCV, including intravitreal ranibizumab in 7 eyes (8.2%) and PDT in 2 eyes (2.3%). The other 77 eyes (89.5%) had VH as their initial presenting feature, which had an undefined diagnosis before undergoing 23-gauge PPV and were diagnosed postoperatively (Figure 1). The average duration from the onset of visual symptoms to the first visit was 72.2±53.8d (range 20-270d). B-scan showed VH in all eyes, extensive SRH in 54 eyes (62.8%) with mean thickness of 4.61±1.70 mm and suspected mass lesion in 10 eyes (11.6%). UBM examination showed no abnormalities preoperatively.

Eighty-four eyes (97.7%) without a retinal tear received 23-gauge vitrectomy; and 2 (2.3%) underwent vitrectomy combined with endophotocoagulation and silicone oil tamponade, when a retinal tear was observed during the operation. The yellowish thick organized SRH companied by reddish-brown

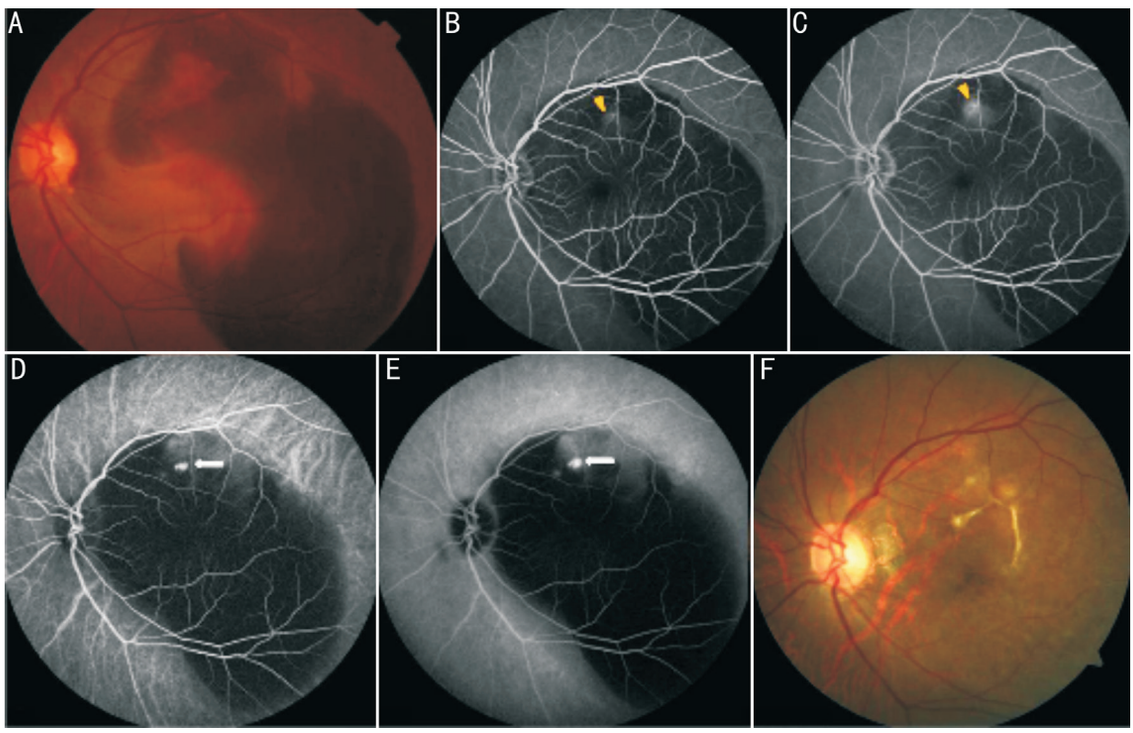

Figure 1 Submacular hemorrhage due to PCV after vitrectomy A: Fundus photography shows the dense SRH with CF/50 cm vision; B, C: FFA 1wk after vitrectomy shows blockage from the hemorrhage; and the late frame of the angiogram demonstrates hyperfluorescence from the abnormal choroidal vessel; D, E: ICGA shows partial polypoidal-shaped lesions on the edge of the hemorrhage; F: The SRH resolved and mild subretinal fibrosis was observed 1y after vitrectomy with 0.3 logMAR vision.

Table 1 Demographics and clinical characteristics of patients with massive VH secondary to PCV treated by 23-gauge PPV

Parameters	Values
Age (y)	
Mean (SD)	59.9 (8.1)
Range	39-87
Gender, *n* (%)	
Male	56 (65.1)
Female	30 (34.9)
Hypertension, *n* (%)	
No	54 (62.8)
Yes	32 (37.2)
Diabetes mellitus, *n* (%)	
No	79 (91.9)
Yes	7 (8.1)
PCV lesion, *n* (%)	
Monocular	77 (89.5)
Binocular	9 (10.5)
Duration of VH (d)	
Mean (SD)	72.2 (53.8)
Range	20-270
Follow-up time (mo)	
Mean (SD)	25.5 (9.2)
Range	12-35

SD: Standard deviation.

SRH on the border was observed in 79 eyes (91.9%) and macular subretinal fibrosis was found in 7 eyes (8.1%) during the surgery. The average size of the SRH was 28.9 disc areas (range 8.2 to 86.7 disc areas), based on fundus photography one week after surgery. The submacular hemorrhage was absorbed in 3.7±1.6mo (range 1-7mo) and SRH was almost automatically absorbed clearly in 6.9±3.4mo (range 4-11mo).

The mean follow-up time was 25.5±9.2mo (range 12-35mo). During the follow-up period, 15 eyes (17.4%) received phacoemulsification and intraocular lens implantation at a follow-up visit. At the final visit, subretinal fibrosis in the posterior pole area were found in 14 eyes (16.3%). Among these eyes, 6 (7.0%) involved the fovea. Ciliary body detachment developed in 4 eyes (4.7%) at one week after the operation but fortunately, this resolved itself within 4 to 12wk without specific treatment. There were no other complications including tractional retinal/choroidal detachment, glaucoma, or endophthalmitis.

Nineteen eyes (22.1%) needed postoperative management of active PCV. Intravitreal ranibizumab was injected into 15 eyes (17.4%), 4 (4.7%) received combined treatment with PDT. The average number of intravitreal ranibizumab injections was 1.81±0.93 (range 1 to 3 injections). Four eyes (4.7%) had recurrent VH in the follow-up period. One of them received 3 ranibizumab injections and the other underwent the combined treatment (intravitreal ranibizumab and PDT).

At baseline, 78 eyes (90.7%) had visual acuity ranging from CF to no light perception. Mean preoperative BCVA was 2.16±0.39 (logMAR; range, 1.2-2.9); while postoperatively, visual acuity improved to 1.42±0.66 (P<0.001; range 0.1-2.9) 3mo after vitrectomy and 1.23±0.74 (P<0.001; range 0.2-3.2) at the final visit. BCVA improved in 54 (62.8%) of the 86 eyes, remained unchanged in 28 eyes (32.5%), and aggravated in 4 eyes (4.7%) at the finial visit caused by recurrent VH.

In univariate regression analysis, thicker SRH in the B-scan preoperatively (P<0.001) and subretinal fibrosis involving fovea (P<0.001) at the final visit were predictors for worse BCVA at the final visit, which was consistent with previous studies[11-13]. At no time-point did visual outcomes appear to correlate with age (P=0.165), gender (P=0.536), history of diabetic mellitus (P=0.219), history of hypertension (P=0.382), hemorrhage duration (P=0.750) or area of SRH (P=0.849).

In multiple regression analysis, increased thickness of SRH (beta=0.33, P=0.025) in the B-scan before surgery and the presence of foveal subretinal fibrosis (beta=0.28, P=0.018) predicted the worse postoperative BCVA.

DISCUSSION

PCV is considered a posterior uveal bleeding syndrome, and often results in a large, thick VH. Various vitrectomy-based methods are used to manage severe hemorrhagic complications caused by PCV but many complications have been reported with vitrectomy combined with retinotomy. Abdel-Meguid *et al*[21] reported postoperative complications among 39 eyes with SRH that underwent PPV with retinotomy. In their study, 10 eyes (25.6%) had proliferative vitreoretinopathy leading to postoperative retinal detachment; and 11 eyes (28.2%) had postoperative hypotony (intraocular pressure less than 8 mm Hg). Choi *et al*[22] reported similar outcomes: among 17 eyes that underwent large/small retinotomies for SRH management, retinal detachment occurred in two eyes (11.8%).

For SRH related to PCV, reports on vitrectomy with subretinal tissue plasminogen activator (tPA) injection are conflicting. In a sample of 15 eyes, Kimura *et al*[23] reported encouraging results of complication-free surgeries. However, compared to our subjects, their study had patients with smaller/thinner SRHs (mean 5.7±4.9 disc diameters) with shorter symptom duration (mean 9.5±4.5d) and with less follow-up time (mean 9.4±3.1mo). Another large, retrospective review of submacular hemorrhage treated with vitrectomy combined with subretinal tPA injection found partial or no hemorrhage displacement in 18 eyes (18%), rhegmatogenous retinal detachment in 4 eyes (4%), VH in 2 eyes (2%), and recurrent SRH in 6 eyes (6%)[24]. The differing results among these studies were primarily the result of variations in the amount of time elapsed between onset and treatment, the area and thickness of SRH, and whether the fovea were involved.

In our study, the mean interval from symptom onset to the first visit were quite long (72.2±53.8d) and the SRH was larger, thicker and organized. Thicker SRH is associated with increased iron, hemosiderin and fibrin deposition is toxic to photoreceptors, large clot retraction could sheer and damage photoreceptors and a large physical separation of the photoreceptors from the RPE in this stage usually causes atrophy and disciform scar formation. The SRH in our series also encircled the optic nerve and adhered to the underlying retinal pigment epithelium or subretinal surface. Such cases were frequently excluded from studies of SRH management with subretinal tPA injection[23-25]. The blood does not liquefy with conventional doses of tPA in these cases and the dose of tPA needed in this situation is far more than the recommended maximum of 50 μg. In addition, a compulsory physical separation of the photoreceptors from the RPE in this stage can cause atrophy and disciform scar formation. Thus, it is too early to consider subretinal tPA injection as the gold-standard treatment for organized SRH.

Previous studies have shown that, during the chronic stage (>14d) of massive of SRH, BCVA was not better than the CF even after surgery[26-27]. Nevertheless, some studies demonstrated more favorable visual outcomes of vitrectomy without SRH management, but the validity was limited by their small sizes and short follow up period[14,16]. We found that BCVA improved significantly, both at 3mo after surgery and at the final visit, consistent with studies on vitrectomy for VH secondary to PCV[14-16]. Narayanan *et al*[16] investigated outcomes of PPV without drainage of SRH in 27 eyes with PCV and their findings showed that 57.1% of eyes had improved BCVAs by two or more Snellen lines postoperatively. Serious postoperative complications included retinal tear/detachment (n=5, 17.9%) and choroidal detachment (n=1, 3.6%). Other complications included macular subretinal fibrosis, organized dehemoglobinized blood and recurrent VH. These results are in accordance with our study. In our study, 90.7% of eyes included had shown severe vision loss (CF to no light perception), whereas 54 (62.8%) of the included 86 eyes had improved visual acuity by two Snellen lines. We did not have any incidence of choroidal detachment, iatrogenic retinal tear or retinal detachment. The ciliary body detachment that occurred in 4 eyes (4.7%), resolved itself without specific treatment within 3mo. We speculated that the low retinal complication rate in our study was associated with carefully removal of the vitreous cortex and prohibition of external indentation to avoid iatrogenic retinal tears, especially in the uplift areas with SRH.

There is limited data on recurrence rate of VH after vitrectomy in PCV. Narayanan *et al*[16] noted recurrence rate of VH was 10.7% in 28 eyes. However, in our study, only 4 out of 86 eyes

(4.7%) had recurrent VH during the follow-up period. This high recurrence rate in the earlier study was mostly because of relatively high rate of retinal tear (17.8%), as organized hemorrhage underneath and around retinal tear would decrease the effect of retinal photocoagulation and SRH would cloud the media of vitreous cavity through the retinal tear even after vitrectomy. In addition, the destruction of abnormal vessels during the course of hemorrhage breakthrough from polypoidal structures was also an explanation for the low recurrence rate of PCV-related VH in our study.

Our study was limited by its lack of a comparison group and thus difficult to underline the difference of impacts of this surgical procedure with those of other management. Despite this and its retrospective nature, we believe it offers important implications for treatment. A prospective, randomized controlled clinical study is needed to fully clarify the impact of this surgical procedure.

In conclusion, this study reports the long-term outcomes in a large series of patients with massive VH secondary to PCV treated by PPV without SRH management and demonstrated vitrectomy without SRH management for such patients had favorable visual outcome and less complications even after a long follow-up period. As treatment for patients with VH secondary to PCV and chronic stage of SRH was not well documented, our study provides a feasible method for the management of such patients. Certainly, in the future, a randomized controlled study with the surgical procedures of PPV and SRH management would bring better understanding for the management of such condition.

ACKNOWLEDGEMENTS

Authors' contributions: Li ZX, Hu YJ, Hu J and Lu L were involved in the concept, design and conduct of the study. Li ZX, Hu YJ contributed to the acquisition, analysis and wrote the paper. Atik A involved in the analysis of data. All authors revised and edited the manuscript.

Foundations: Supported by the National Natural Science Foundation of China (No.81271009); the Science and Technology Planning Project of Guangdong Province, China (No.2017A030303016).

Conflicts of Interest: Li ZX, None; **Hu YJ,** None; **Atik A,** None; **Lu L,** None; **Hu J,** None.

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