

Clinical Features and Surgical Outcomes of Subretinal Proliferation in Proliferative Diabetic Retinopathy

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Research article

Keywords: Subretinal proliferation, Proliferative diabetic retinopathy, Tractional retinal detachment, Vitrectomy

Posted Date: August 20th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-49211/v1>

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Abstract

Background: To investigate the clinical characteristics, treatments and prognosis of subretinal proliferation (SRP) in patients with proliferative diabetic retinopathy (PDR).

Methods: 154 patients (182 eyes) who received vitrectomy for PDR were retrospectively reviewed. Patients with SRP were enrolled as the study group, and those without SRP served as the control group. The following data were collected from their medical records: demographics, systemic and ophthalmologic findings, and treatment given specifically for SRP. The main outcome measures included the visual acuity, funduscopy examination and final anatomic success. The association between SRP and other systemic involvement of PDR was also analyzed.

Results: There were 9 eyes (9 patients) in the study group and 145 eyes (145 patients) in the control group. The average fasting blood glucose was 11.48 ± 3.52 mmol/L and 8.72 ± 3.05 mmol/L, respectively ($P = .048$). The study group had a significantly higher proportion of tractional retinal detachment (TRD) ($P < .0001$) and a significantly lower proportion of vitreous hemorrhage (VH) ($P = .0006$). The rate of silicone oil usage was higher in the study group ($P < .0001$). No retinal break was found preoperatively or intraoperatively. Only one eye (11.1%) had undergone subretinal band removal procedure intraoperatively, and the final anatomical success rate was 100%.

Conclusion: SRP in PDR was associated with higher blood sugar levels and TRD. The retina could reattach successfully after vitrectomy without removal or transection of the subretinal bands in most eyes.

Background

Proliferative diabetic retinopathy (PDR) is one of the leading causes of blindness worldwide[1]. It is characterized by neovascularization originating from the retina and optic disc as a severe complication of diabetes mellitus (DM). The new vessels often grow along the vitreoretinal interface and sometimes into the vitreous, leading to vitreous hemorrhage (VH), epiretinal fibrovascular membranes (FVMs) and subsequent tractional or combined tractional-rhegmatogenous retinal detachment, for which surgical intervention is indicated to avoid severe vision loss[2]. The formation of epiretinal FVMs is a proliferative process on the inner surface of the retina, which is frequently found in PDR, whereas proliferation on the retrolental surface is less common[3]. Subretinal proliferations (SRPs) are also known as subretinal strands, subretinal membranes, retrolental membranes, or subretinal fibrosis. SRP occurs with long-standing exudative, traction, or rhegmatogenous retinal detachments but is most common in eyes with rhegmatogenous retinal detachment (RRD) complicated by proliferative vitreoretinopathy (PVR)[4, 5]. Several studies have reported the pathogenesis, clinical features and surgical management of SRP in PVR[6–10]. However, to the best of our knowledge, SRP in PDR has not been described in the literature. Therefore, the purpose of this study was to describe the clinical characteristics of SRP in PDR and to investigate its clinical treatments and prognosis.

Methods

Patients and study design

This retrospective observational study was approved by the institutional review board (IRB) of Peking Union Medical College Hospital. All data with patient-specific information were masked and deidentified prior to analysis. Written informed consent was not required by the IRB but participants who did not grant authorization to use their medical records for the research were excluded from analyses. This study was performed according to the tenets of the Declaration of Helsinki.

We reviewed ophthalmological records of PDR patients who were treated with pars plana vitrectomy (PPV) in Peking Union Medical College Hospital by one experienced surgeon (RPD.) between January 1, 2018 and December 31, 2019. All patients received vitrectomy because of reduced visual acuity principally from nonclearing VH, fibrovascular proliferation affecting the macula, or tractional retinal detachment (TRD). Among all these PDR patients, those who presented with SRP were enrolled as the study group, and those who exhibited no SRP served as the control group. Exclusion criteria included (1) previous eye diseases such as RRD, uveitis, endophthalmitis, choroidal melanoma, Coats disease, or penetrating ocular trauma; (2) prior intraocular surgery such as cataract surgery, glaucoma surgery, vitrectomy or scleral buckling.

Surgical Methods

All patients underwent standard 23-gauge or 25-gauge three-port PPV with the Constellation Vitrectomy System (Alcon Labs, Fort Worth, TX, USA) under topical or general anesthesia. In patients with cataract, phacoemulsification with intraocular lens (IOL) implantation was performed immediately before vitrectomy. Procedures such as fibrovascular membrane dissection, endolaser photocoagulation, drainage of the subretinal fluid (SRF) through an artificial retinal hole, and air-fluid exchange were performed as needed. The decision to remove the subretinal membrane was made intraoperatively if the subretinal tissue prevented proper flattening of the retina or if it caused distortion of the macula after drainage of the SRF. The membranes were removed by making a small incision in the detached retina and grasping the membrane with special forceps. Retinal tamponade was performed with gas or silicone oil as required. The silicone oil was removed 3–6 months after the initial procedure to avoid complications such as emulsification or secondary ocular hypertension. No additional buckling was performed in any of our cases.

Collections Of Clinical Data

The demographic and clinical information (such as age, gender, and ocular and systemic examination results) of the included patients was extracted from medical records. Systemic conditions including DM type (insulin-dependent DM [IDDM] or non-insulin-dependent DM [NIDDM]), hypertension, cardiovascular disease, renal disease, and preoperative blood test results were collected. The systolic and diastolic pressures measured on the day of admission for the operation were recorded. The laboratory data consisted of complete blood counts, urinalysis, coagulation function, creatinine and fasting blood glucose (FBG). Ophthalmological data collected from the charts included the study eye, presence of VH, presence and extent of retinal detachment (RD), presence of retinal breaks, presence of epiretinal FVMs, characteristics of SRP, prior panretinal photocoagulation (PRP) or intravitreal injection (IVI) of anti-VEGF drugs, peeling of epiretinal FVMs, removal or transection of SRP, gas or silicone oil infusion, anatomic outcome of surgery, and pre- and postoperative best corrected visual acuity (BCVA). Anatomical success was defined as total retinal reattachment after vitrectomy without silicone oil tamponade or after silicone-oil-removal surgery. Patients were followed every 3 months until the ocular condition was stable after the final surgery.

Statistical analysis

For statistical analysis, visual acuity levels for individual patients reported as the Snellen acuity or decimal acuity scores were converted to logarithm of the minimum angle of resolution (logMAR) scores using standard calculations[11]. The LogMAR values of 2.0, 2.4, 2.7, and 3.0 were substituted for visual acuity (VA) levels reported as “count fingers,” “hand movements,” “light perception,” and “no light perception,” respectively[12]. The mean VA (and standard deviation) at baseline and follow-up and changes in VA were calculated using the logMAR scores.

Descriptive statistics were applied to summarize the location and scale of factors; 95% confidence interval (CI) was constructed with *P*-values, which served as signal detection rather than hypothesis testing. For continuous variables such as age and blood pressure, the CI was based on the normal approximation, whereas the *P*-value was obtained from *t*-statistics. For binary variables such as gender and chronic cardiovascular disease, the CI was based on the likelihood scoring, considering that extreme estimates (0% or 100%) and imbalance (9 vs. 145) could lead to boundary and coverage issues using the Wald (approximation) CI. A pseudo-*P*-value was generated using the mid-*P* method; therefore, it was rare but possible to have an inconsistent interpretation between the score CI and mid-*P* *P*-value.

Results

Among 182 eyes of 154 PDR patients evaluated, 9 eyes of 9 patients were diagnosed with SRP and were enrolled into the study group. Two of the 9 patients also had undergone vitrectomy in the contralateral eye without SRP. Of another 145 patients, 26 patients had undergone vitrectomy in both eyes, from which we randomly chose one eye as the control eye. In total, 145 eyes of 145 patients served as the control group. The overall prevalence of SRP was 5.84%. The clinical characteristics of the two groups are summarized in Table 1.

Table 1

Demographic data and ocular findings in the PDR patients with subretinal proliferation group (the study group) and the PDR patients without subretinal proliferation group (the control group)

Clinical features	Study eyes (n = 9), n (%),	Control eyes (n = 145), n (%),	P-value
	mean ± SD	mean ± SD	
Age (years)	48.78 ± 11.24	53.34 ± 10.79	0.267
Gender (female)	6 (66.67)	72 (49.66)	0.116
DM type (NIDDM)	9 (100)	132 (91.03)	0.164
Duration of DM (years)	11.11 ± 6.85	12.58 ± 7.48	0.550
Hypertension	3 (33.33)	77 (53.10)	0.082
Duration of hypertension (years)	0.83 ± 1.70	4.21 ± 7.28	0.0003
Systolic blood pressure (mmHg)	126.0 ± 15.19	132.42 ± 20.99	0.258
Diastolic blood pressure (mmHg)	77.67 ± 7.53	77.12 ± 12.48	0.845
Coronary artery disease	2 (22.22)	10 (6.90)	0.113
Renal disease	3 (33.33)	46 (31.72)	0.455
Glucose (mmol/L)	11.48 ± 3.52	8.72 ± 3.05	0.048
Creatinine (μmol/L)	69.44 ± 36.63	112.09 ± 134.90	0.016
Fibrinogen (g/L)	3.47 ± 0.48	3.58 ± 0.95	0.562
Preoperative PRP	2 (22.22)	44 (30.34)	0.269
Preoperative anti-VEGF	7 (77.78)	116 (80.00)	0.432
Vitreous hemorrhage	4 (44.44)	132 (91.03)	0.0006
Tractional RD	9 (100.00)	62 (42.76)	< 0.0001
Silicone oil tamponade	9 (100.00)	63 (43.45)	< 0.0001
Preoperative BCVA (LogMAR)	1.43 ± 0.52	1.83 ± 0.63	0.056
Postoperative BCVA (LogMAR)	1.90 ± 0.47	1.50 ± 0.68	0.036
Change in BCVA (LogMAR)	0.47 ± 0.59	-0.33 ± 0.81	0.003
<i>BCVA</i> best corrected visual acuity, <i>DM</i> diabetes mellitus, <i>NIDDM</i> noninsulin dependent diabetes mellitus, <i>PRP</i> panretinal photocoagulation, <i>RD</i> retinal detachment, <i>VEGF</i> vascular endothelial growth factors			

The average age of the two groups was 48.78 ± 11.24 years and 53.34 ± 10.79 years, respectively ($P = .267$). There were 6 female (66.7%) and 3 male patients in the study group and 72 female (49.7%) and 73 male patients in the control group ($P = .116$). The DM type was similar in the two groups (100.0% NIDDM in the study group vs. 91.0% NIDDM in the control group, $P = .164$). The mean duration from the diagnosis of DM to operation was 11.11 ± 6.85 years in the study group and 12.58 ± 7.48 in the control group ($P = .550$). The average FBG was 11.48 ± 3.52 mmol/L and 8.72 ± 3.05 mmol/L, respectively ($P = .048$). The prevalence of hypertension, cardiovascular disease and renal disease showed no significant difference between the two groups except for a longer duration of hypertension in the control group. The average creatinine level was also higher in the control group, while the fibrinogen level was similar in the two groups.

The mean LogMAR of BCVA before the operation was 1.43 ± 0.52 in the study group and 1.83 ± 0.63 in the control group ($P = .056$). Previous IV-anti-VEGF and PRP were performed in 77.8% and 22.2% of the cases, respectively, in the study group; the proportions were 80.0% and 30.3%, respectively, in the control group. The surgical indication in the study group was mainly TRD (100.0%), while VH was more prevalent in the control group (91.0%). Due to the recent lack of inert gases in China, we performed silicone oil tamponade in more serious cases. The rate of silicone oil usage was higher in the study group (100% vs. 43.45% in the control group, $P < .0001$). In the control group, the LogMAR of BCVA significantly improved from 1.83 ± 0.63 at baseline to 1.50 ± 0.68 at 1 week after operation. The LogMAR of BCVA decreased from 1.43 ± 0.52 at baseline to 1.90 ± 0.47 at 1 week in the study group; however, several months after the silicone-oil-removal surgery, it improved to 1.03 ± 0.44. The detailed examination data and operative methods are listed in Table 1.

Among the 9 eyes that had SRP, 4 were right eyes and 5 were left eyes. Four eyes had VH, while all 9 eyes had TRD. Epiretinal FVMs were detected in all eyes (Fig. 1). No retinal break was noted in any eye. RD involved one quadrant in 1 eye (11.1%), two quadrants in 3 eyes (33.3%), and three quadrants in 1 eye (11.1%), and total RD was found in 4 eyes (44.4%) (Fig. 1). Seven eyes had only one subretinal band each (77.8%) (Fig. 1–2), while 1 eye had two subretinal bands (11.1%) (Fig. 3), and 1 eye had three subretinal bands (11.1%) (Fig. 4). Seven eyes had linear-shaped bands (77.8%), which were mainly located in the midperiphery and parallel to the borderline between the detached and unaffected retina. One eye had bands with many branches (11.1%), and one eye had both linear-shaped bands and branching bands (11.1%) (Fig. 3). Both of the branching bands were located at the posterior pole; one was right beneath the macula, and one was near the optic disc. Seven eyes had undergone previous anti-VEGF treatment (77.8%), while only 2 eyes had undergone previous PRP (22.2%). All eyes received PPV with silicone oil tamponade (100%). Only one eye (11.1%) had undergone a subretinal band removal or transection procedure intraoperatively (Fig. 5). Silicone oil was removed 3–6 months after the initial vitrectomy in all eyes. Phacoemulsification with IOL implantation was

performed simultaneously during the silicone-oil-removal surgery in two eyes (22.2%). All cases had a follow-up of at least 6 months after the final surgery. The median time of follow-up was 12 months, ranging from 6 months to 18 months. All eyes achieved reattachment after the silicone-oil-removal surgery without any severe complications. Table 2 shows the characteristics of these patients.

Table 2
Characteristics of nine PDR patients with subretinal proliferation

Pt No.	Gender	Age (yr)	Laterality	Baseline BCVA	VH	Extent of RD	Extent of SRP	Shape of SRP	Retinal break	Pre-OP IVI Anti-VEGF	Pre-OP PRP	Removal of SRP	Intra-OP SO	BC aft PP
1	F	50's-60's	OD	HM	N	Total	Inferotemporal	Linear	N	Y	N	N	Y	CF
2	M	50's-60's	OS	20/250	Y	Inferior and temporal	Inferotemporal	Linear	N	Y	Y	N	Y	HM
3	F	30's-40's	OD	20/500	N	Total	Temporal	Linear	N	Y	N	N	Y	20.
4	M	60's-70's	OD	20/100	N	Superior, inferior and nasal	Inferonasal	Linear	N	N	N	N	Y	20.
5	F	30's-40's	OS	20/2000	Y	Nasal and para-inferotemporal arcade	Macular and nasal	Branched and linear	N	Y	N	N	Y	CF
6	F	40's-50's	OD	20/1000	N	Posterior	Peripapillary	Branched	N	Y	N	N	Y	HM
7	F	50's-60's	OS	20/400	N	Total	Superior, inferior and nasal	Linear	N	Y	N	N	Y	HM
8	F	40's-50's	OS	20/400	Y	Inferior and temporal	Inferior	Linear	N	Y	Y	N	Y	20.
9	M	40's-50's	OS	20/200	Y	Total	Inferonasal	Linear	N	N	N	Y	Y	20.

BCVA best corrected visual acuity, *CF* counting fingers, *F* female, *HM* hand movement, *IVI* intravitreal injection, *m* months, *M* male, *N* no, *OCT* optical coherence tomography, *OS* left eye, *PHACO* phacoemulsification, *PPV* pars plana vitrectomy, *PRP* panretinal photocoagulation, *Pt* patient, *RD* retinal detachment, *SO* silicone oil, *SRP* subretinal proliferation, *VEGF* vascular endothelial growth factors, *VH* vitreous hemorrhage, *w* week, *Y* yes, *yr* years old

* The follow-up duration was the follow-up length after the silicone oil removal surgery.

Significant associations between clinical factors and SRP in PDR are presented in Table 1 for the categorical and continuous variables. Factors found to be significantly ($P < .05$) related to SRP in PDR were higher FBG level, TRD and silicone oil tamponade.

Discussion

SRP is mainly known as a complication of RRD and is part of the spectrum of PVR. It has been reported in 3–15.5% of eyes with uncomplicated RRD and in 47% of eyes with RRD associated with PVR[4, 5, 13]. SRP may also occur in several uveitis syndromes[14, 15], choroidal melanoma[16], and Coats disease[17]. However, to the best of our knowledge, our study is the first to report SRP in PDR.

Although subretinal fibrosis in diabetic macular edema (DME) has been reported in the literature before[18], that fibrosis is completely different from the SRP we reported in the present study. Subretinal fibrosis is an elevated mound or a flat sheet of gray or white tissue located deep to the retina at or near the center of the macula. Subretinal fibrosis always develops after very severe, hard exudate and has no association with RD[18]. Clinicopathologic studies have shown that the accumulation of hard exudate in the outer retina in juxtaposition to the retinal pigment epithelium (RPE) is associated with focal metaplasia of the RPE, leading to fibrotic scar formation. The optical coherence tomography (OCT) findings revealed that the fibrosis appears to have replaced at least a portion of the outer retina, suggesting that the fibrosis may be "intraretinal" rather than "subretinal"[19].

In our study, all PDR patients with SRP had epiretinal FVMs and TRD. We did not find any retinal breaks preoperatively or intraoperatively. Our observation suggested that RRD was not likely the main mechanism in PDR patients with SRP. In RRD, liquefied vitreous flows through the retinal breaks into the subretinal space and forms SRP. SRP may result in breakdown of the blood-retina barrier, and some serum components that stimulate the proliferation of RPE cells and retinal glial cells may penetrate the blood-ocular barrier, such as fibronectin, platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), epidermal growth factor (EGF), glial maturation factor, glial growth factor, IL-1, glial growth-promoting peptides, and thrombin[20]. In addition, once the neural retina has separated from the RPE, increased distance to the choroidal blood supply and reduced oxygen flux from the choroid to the inner segments lead to a loss of photoreceptor outer segments and, furthermore, to a proliferation of glial cells[21]. Ultimately, SRP develops. In our study, though all PDR patients with SRP had non-RRD, they may have had a similar pathogenesis. Our observation suggested that the FBG level was higher in the study group, which indicates that the blood-retina barrier may be poorer in the study group. The analysis of various indications for vitrectomy revealed that TRD was more likely and VH was less likely to be seen in the study group than in the control group, implying rapid progression of vitreoretinopathy in the study group once retinal neovascularization

with VH occurred. Following the advance of TRD, long-standing accumulation of the SRF, which also contains some growth factors, could continuously stimulate RPE cells and glial cells, leading to SRP.

In a previous study, RRD of long duration, atrophic retinal breaks, young age, and greater number of detached quadrants were identified as factors significantly associated with SRP[5]. Wallyn and Hilton reported that the incidence of SRP was associated with the duration of RRD, ranging from 0.8% in cases with a duration < 1 month to 22% in cases with more than 2 years[13]. In our investigation, we found that the study group had a significantly higher rate of TRD and a lower rate of VH. Furthermore, the severity of VH in the study group was much lower compared with the control group. These results may be explained by the longer course of PDR and more advanced PDR in the study group. This severity was also reflected by the higher percentage of eyes requiring silicone oil tamponade in the study group. On the other hand, the BCVA was significantly poorer in the study group at 1 week after operation, which can also reflect the severity of the study group. The systemic risk factors of developing SRP in PDR have also been studied. The prevalence of hypertension, cardiovascular disease and nephropathy showed no significant difference between the two groups except for a longer duration of hypertension in the control group. The average creatinine was also higher in the control group. These results may suggest rapid progression of vitreoretinopathy in the study group, even earlier than the onset of nephropathy and hypertension. Both the preoperative IV-anti-VEGF and PRP rates were similar in the two groups, which suggests that the SRP in PDR had no association with anti-VEGF injection or PRP.

We observed that 77.8% of the eyes had only linear-shaped subretinal bands. Previous laboratory works have demonstrated that most cells exhibit polarity. Cells need a surface to grow on, and they usually settle onto a surface with a specific polarity[22]. The subretinal space is a hostile environment for cells to proliferate under normal conditions. After detachment, the subretinal space converts into a tissue culture system, where the RPE cell-derived macrophages originally settle onto the back surface of the retina and then multiply[23]. Some cells transform into fibroblasts, which in turn produce collagen. This process creates a surface that can be populated by additional cells[24, 25]. As the cells proliferate around this material, they form a circular pattern and a linear band. The glial cells undergo a similar process. They can transform into myofibrocytes after long-standing RD. Once stabilized, the attached cells also begin to synthesize collagen and create the proliferation surface[26, 27]. Finally, the linear-shaped band forms. In our study, the linear-shaped subretinal bands were mainly located in the midperiphery, and the direction of the subretinal bands was parallel to the borderline between the detached and unaffected retina. This finding may indicate that the RPE-derived cells and glial cells that compose the subretinal bands tend to accumulate along the borderline and proliferate. We also found that 22.8% of the eyes had branching subretinal bands, both of which were located at the posterior pole. This condition may be explained by the TRD at the posterior pole having relatively irregular borderlines; therefore, the cells could proliferate in multiple directions. The case with the band near the optic disc had posterior TRD. However, in another case with both a branching SRP beneath the macula and a long linear SRP at the nasal area, we found RD extending from the para-inferotemporal arcade to the nasal area without involving the macula. We presumed that in this case, the TRD involved the macula at the beginning, and the submacular fluid absorbed gradually over time for some reason, leaving only the branching SRP beneath the macula. The mechanism underlying the development of spontaneous macular reattachment in this case presumably involved the occurrence of posterior vitreous detachment[28].

Previous studies have evaluated different surgical management strategies for SRP in PVR, including PPV and scleral buckling surgery[6, 8, 9, 29, 30]. PPV is needed for eyes with posterior and extensive anterior epiretinal proliferation in order to remove the contractile membranes and release the retinal traction. Lewis et al. reported that only 28% of subretinal strands require removal or transection therapy during vitrectomy and the patients who do not require removal or transection surgery have a relatively better visual prognosis[4]. Many PVR patients with only SRP and no preretinal membrane can be treated successfully by scleral buckling surgery. Wallyn and Hilton reported a retinal reattachment rate of 95% with scleral buckling surgery in 20 eyes with pure SRP[13]. Yao et al. reported that single scleral buckling surgery anatomical success was 90% in 40 eyes with RRD and SRP[29]. Ghasemi Falavarjani K et al. reported that the single surgery anatomical success rate was 88.7% in 44 eyes with RRD associated with SRP[9]. Some earlier studies classified SRP following RRD into two main types[31]. The first type tends to form diffuse cell sheets that do not interfere with RD, and the retina may be reattached with scleral buckling procedures alone in the absence of contractile epiretinal proliferation[32]. The second type embodies taut membranes or bands, which raise the neuroretina and impede RD surgery[4]. Laboratory investigations found that the first type is usually composed of glial cells and contains little or no extracellular material. Glial membranes are thin, and therefore, they rarely cause structural changes requiring surgical intervention. In contrast, the second type is composed of up to 95% RPE-derived cells, while the extracellular component includes fibrin and collagen types I to IV[31]. In our study, eight eyes (88.9%) in the study group underwent PPV without a subretinal band removal or transection procedure. We only performed retinotomy and SRP removal in one eye (11.1%), since the subretinal band prevented retinal flattening after drainage of the SRF. The SRP removed from this eye contained a lot of pigment, which indicates that this SRP is more likely to be the second type. The retina was attached in all eyes after the silicon-oil-removal surgery, even in the eyes with submacular bands. This result may indicate that most SRPs in PDR do not interfere with conventional RD maneuvers. Therefore, we speculate that glial cells are the main component of most subretinal bands in PDR, which may also contain some RPE-derived cells.

Our study has several limitations. The sample size was relatively small and imbalanced across groups. Statistically nonsignificant findings may be attributable to the sample size. Additionally, the study was retrospective and uncontrolled. The data of systemic conditions such as HbA1c, long-term blood sugar, blood pressure and renal function data were incomplete. The follow-up time was also not uniform and varied broadly among the patients. Since only one eye had undergone SRP removal and no pathological examination was performed, we cannot determine the exact pathological composition of SRP in PDR. Further evaluation and observation over a longer period as well as pathological study are required. Despite these limitations, this is the first report analyzing the clinical manifestations and surgical results of PDR patients with SRPs.

Conclusion

This study showed that SRP in PDR was associated with higher blood sugar levels and TRD. SRP had no association with preoperative anti-VEGF injection or PRP. The retina could reattach successfully after PPV without removal or transection of the subretinal bands in most eyes. Moreover, the visual outcomes were generally favorable with the current treatment. However, an adequate analysis would require a prospective study and a longer follow-up.

Abbreviations

BCVA

best corrected visual acuity; CI:confidence interval; CF:counting fingers; DM:diabetes mellitus; DME:diabetic macular edema; EGF:epidermal growth factor; FBG:fasting blood glucose; FGF:fibroblast growth factor; FVMs:epiretinal fibrovascular membranes; HbA1C:hemoglobin A1C; HM:hand movement; IDDM:insulin dependent diabetes mellitus; IOL:intraocular lens; IVI:intravitreal injection; NIDDM:noninsulin dependent diabetes mellitus; OCT:optical coherence tomography; PDGF:platelet-derived growth factor; PDR:proliferative diabetic retinopathy; PHACO:phacoemulsification; PPV:pars plana vitrectomy; PRP:panretinal photocoagulation; PVR:proliferative vitreoretinopathy; RD:retinal detachment; RPE:retinal pigment epithelium; RRD:rhegmatogenous retinal detachment; SO:silicone oil; SRF:subretinal fluid; SRP:subretinal proliferation; TRD:tractional retinal detachment; VA:visual acuity; VEGF:vascular endothelial growth factors; VH:vitreous hemorrhage.

Declarations

Ethics approval and consent to participate

This study adhered to the tenets of the Declaration of Helsinki, and was approved by the Institutional Review Board of Peking Union Medical College Hospital. Informed consent was waived by Institutional Review Board of Peking Union Medical College Hospital because this is a retrospective study that does not include data that can identify patients.

Consent for publication

Not applicable.

Availability of data and materials

The data of the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by The Non-profit Central Research Institute Fund of Chinese Academy of Medical Sciences (2018PT32029).

Authors' contributions

Design and conduct of the study (R.P.D., C.W., Y.X.C.); Collection of data (C.W., X.Z., Z.C.); Analysis and interpretation of data (C.W., R.P.D.); Writing the article (C.W.); Critical revision of the article (R.P.D., Y.X.C.); Final approval of the article (C.W., R.P.D., Y.X.C., X.Z., Z.C.).

Acknowledgements

Not applicable.

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Figures

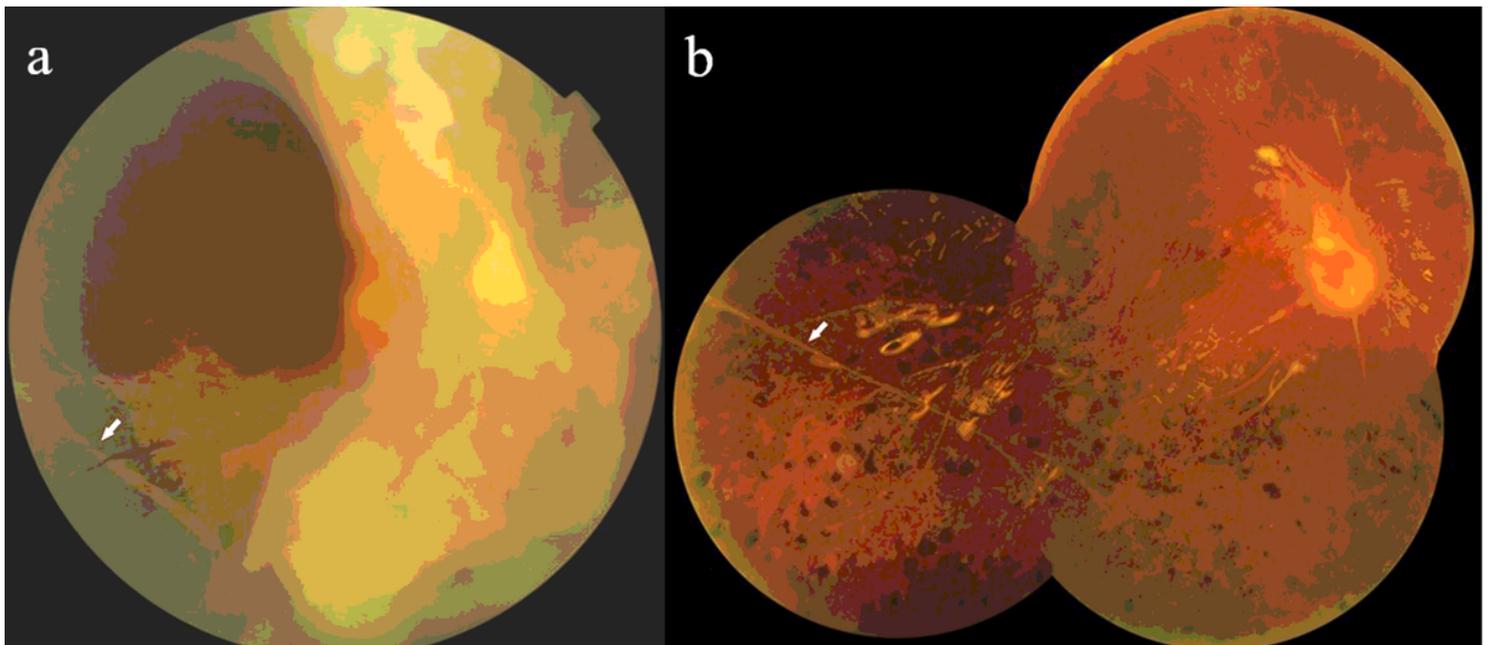


Figure 1

Fundus photographs of case 1. a. Preoperative fundus photograph showing total tractional retinal detachment (TRD) with extensive epiretinal fibrovascular membranes (FVMs) and inferotemporal linear subretinal proliferation (SRP) (arrow) in the right eye. b. One month after pars plana vitrectomy (PPV) with silicone oil tamponade: fundus photograph showing the attached retina with a linear SRP (arrow) at the inferotemporal area.

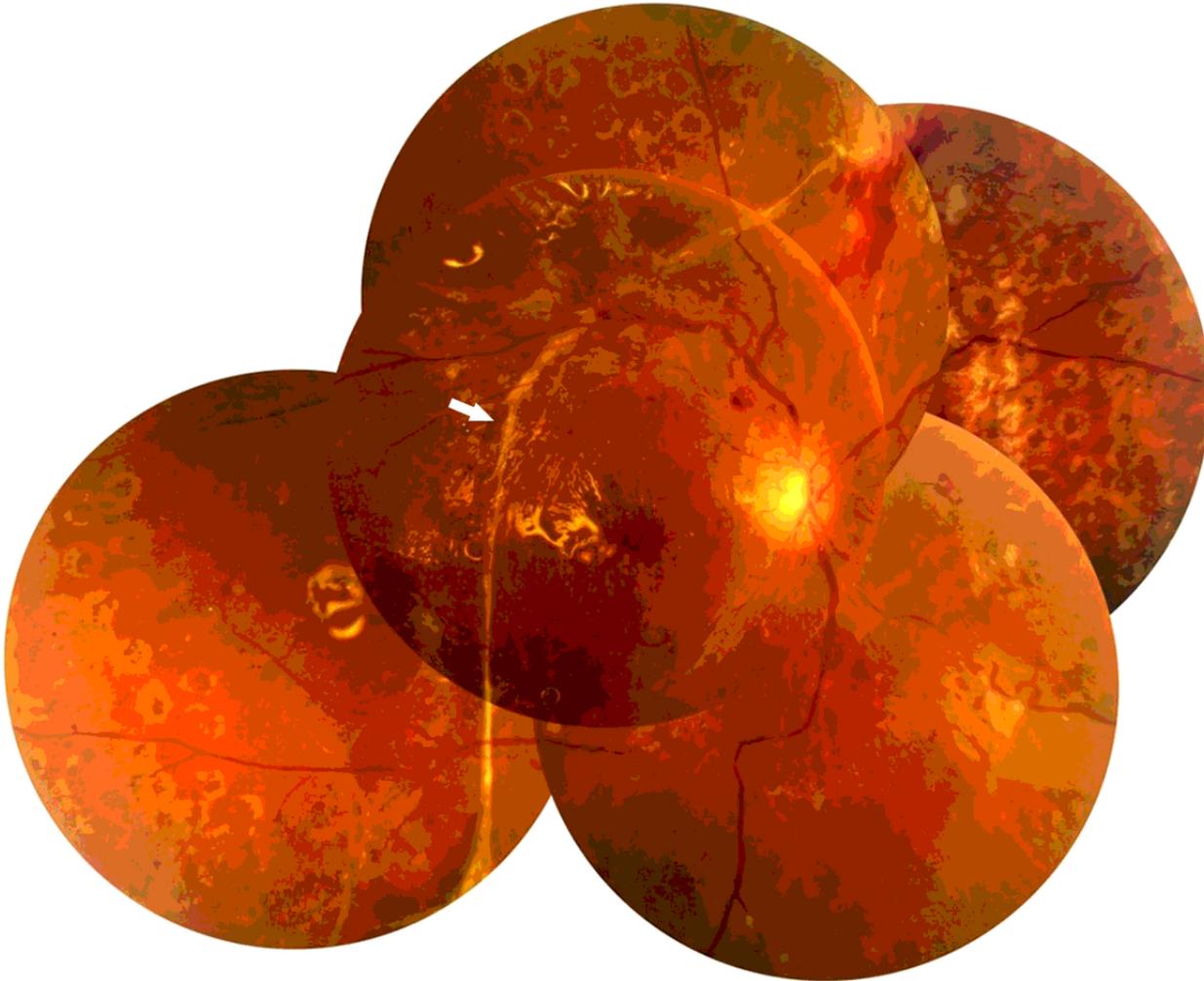


Figure 2
Fundus photograph of case 3. It shows a well-attached retina and temporal long linear subretinal proliferation (SRP) (arrow) 1 month after pars plana vitrectomy (PPV).

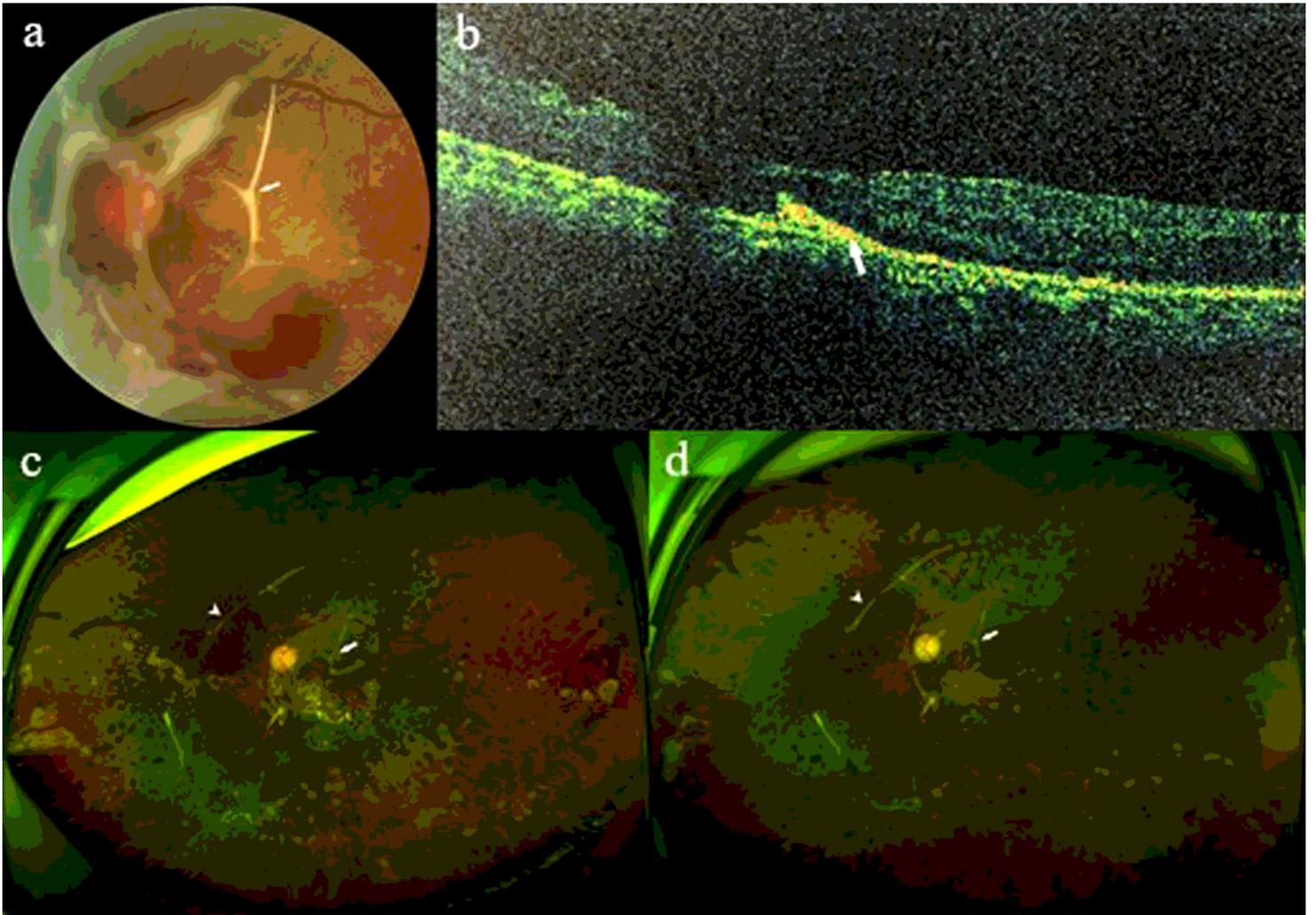


Figure 3

Fundus photographs of case 5. a. Preoperative fundus photograph showing tractional retinal detachment (TRD) from the para-inferotemporal arcade to nasal area with epiretinal fibrovascular membranes (FVMs) and submacular branching band (arrow) in the left eye. b. Preoperative spectral domain-optical coherence tomography (SD-OCT) demonstrated a hyperreflective subretinal band (arrow) with thinning of the outer retina. c. 3 months after pars plana vitrectomy (PPV) with silicone oil tamponade: ultrawide-field fundus photograph showing the attached retina with a branching subretinal proliferation (SRP) near the macula and papilla (arrow), and a long linear SRP at the nasal area (arrowhead), which had already existed before the surgery. d. 3 months after silicone oil removal surgery: ultrawide-field fundus photograph still showing the attached retina with a long, linear SRP at the nasal area (arrowhead) and a branching SRP near the macula and papilla (arrow).

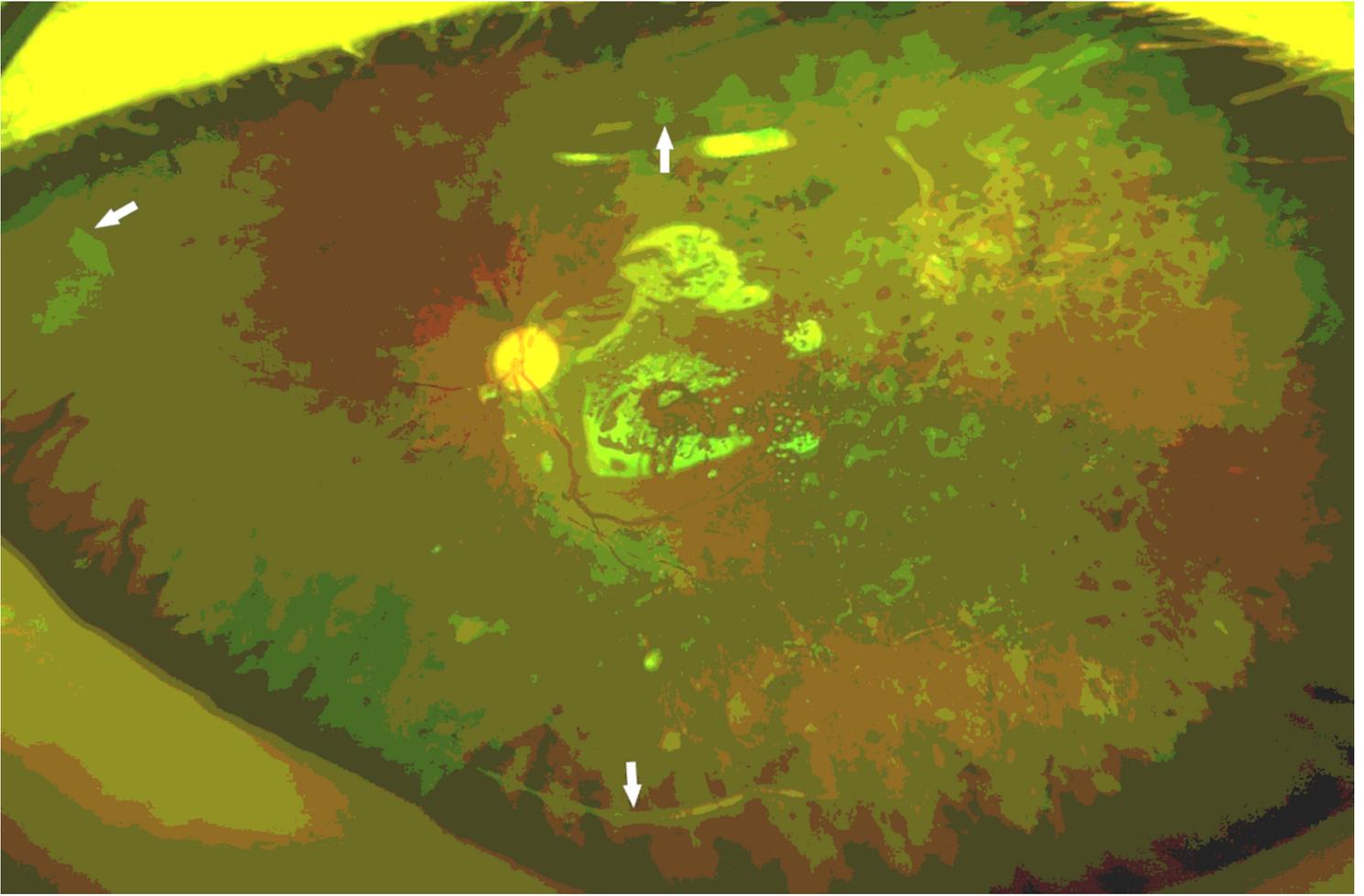


Figure 4
 Fundus photograph of case 7. 3 months after pars plana vitrectomy (PPV): ultraspectral fundus photograph showing the well-attached retina and 3 linear SRPs (arrow) separately located at the superior, inferior and nasal areas.

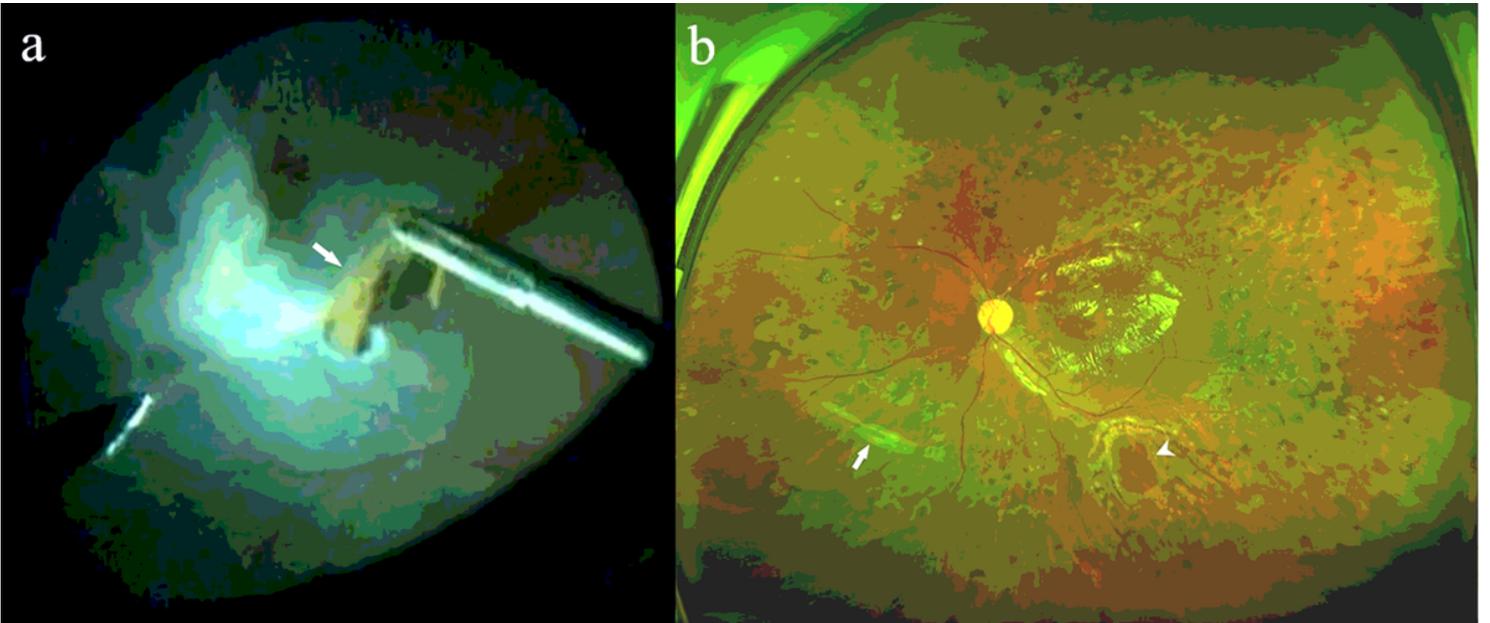


Figure 5
 Fundus photograph of case 9. a. Intraoperative photo showing the removal of the inferonasal subretinal proliferation (SRP) (arrow) through a small incision in the detached retina. Note that the SRP contains many pigments. b. Three months after pars plana vitrectomy (PPV), ultraspectral fundus photograph

demonstrating a well-attached retina and a trace of inferonasal linear SRP (arrow), which had been removed during the vitrectomy. The edge of the incision (arrowhead) is seen in the inferior area.