RHEGMATOGENOUS RETINAL DETACHMENT IN CHOROIDAL MELANOMA: CLINICAL FEATURES AND SURGICAL OUTCOMES

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ABSTRACT

Purpose

To describe the clinical features, prognostic factors, safety and rate of success of surgery and visual outcomes in patients with rhegmatogenous retinal detachment (RRD) and choroidal melanoma (CM).

Methods

A retrospective, observational case-series of 21 patients with rhegmatogenous retinal detachment or combined tractional-rhegmatogenous retinal detachment in patients with choroidal melanoma over a period of 20 years.

Results

19 patients were included in the final analysis. The mean elevation of CM was 4.0 mm and the mean largest diameter was 11.0 mm. RRD occurred after the CM treatment in 14 eyes at a mean interval of 44.2 months. The RRD was macula-on RRD in 6 eyes, there was posterior vitreous detachment (PVD) in 15 and PVR in 7 eyes. BCVA at presentation was 0.71 logMAR and final was 1.5 logMAR (p=0.01). The primary surgical success rate was 59%. No intraocular or extraocular tumor dissemination occurred. Mean follow-up was 66 months.

Conclusion

RRD in patients with CM is uncommon but requires multidisciplinary management. Anatomical results are favourable but visual outcomes are poor due to a combination of factors related to melanoma treatment, macular retinal detachment and PVR. Vitrectomy as a surgical intervention for RRD in treated CM appears to be safe in terms tumour dissemination.

INTRODUCTION

The relationship between choroidal melanoma and serous retinal detachment has been widely described and it is a well-known risk factor for malignant transformation of choroidal nevus.[1-3] In addition, rhegmatogenous retinal detachment (RRD) and tractional retinal detachment (TRD) have been reported as a complication of different treatment modalities for choroidal melanoma.[4-8] The association between spontaneous rhegmatogenous retinal detachment (RRD) and choroidal melanoma (CM) and its surgical and visual outcomes have not been reported in detail.

In this study we analyzed the presenting features, clinical outcomes of patients who presented with rhegmatogenous retinal detachment with co-existing choroidal melanoma.

METHODS

A retrospective, observational, case-series of patients with diagnosis of RRD or combined TRD and RRD and CM over a period of 20 years from January 2002 to January 2022 at Moorfields Eye Hospital. An electronic database search was performed on Moorfields OpenEyes electronic health records. Variables analyzed included age, gender, past medical history, choroidal melanoma features, choroidal melanoma treatment, initial and final best corrected visual acuity (BCVA), RRD clinical features, rate of success of surgery and follow up. Patients were excluded from the analysis if there were incomplete notes (inaccessible legacy paper notes). The data was recorded onto a database (Excel®). All statistical analyses were performed using GraphPad Prism® 6.01. Test. P value of <0.05 was considered statistically significant for all tests.

The research protocol fulfilled the Declaration of Helsinki and it was registered with the audit number 1004 at Moorfields Eye Hospital.

RESULTS

Demographic features:

A total of 21 eyes of 21 patients with a diagnosis of RRD or combined TRD and RRD in patients with CM were identified. Two patients were excluded from the analysis because of incomplete clinical data, leaving a total of 19 eyes. The average age at diagnosis of RRD was 62 years (SD 13, range 20-80). Eleven patients (58%) were male and 8 (42%) female. Nine patients had systemic comorbidities, most commonly hypertension (5 patients). None of the patients had a previous ocular history.

Choroidal melanoma clinical features:

The mean elevation of CM was 4.0 mm (SD 1.7) (range 0.8-7.3 mm) and the mean widest diameter was 11.0 mm (SD 2.4) (range 7.3 -16.6 mm). Eighteen cases were classified as medium CM according with the COMS classification and 1 case as large CM. Eleven (56%) CM lesions were located in the mid-periphery and 8 (44%) at the posterior pole.

Retinal detachment clinical features:

Fifteen patients had RRD (79%) and 4 (21%) had combined RRD and TRD (as a consequence of radiation retinopathy). In 5 cases (26%), the RD developed before the CM treatment (Fig. 1, representative case). Of these, CM was noticed during the vitrectomy to repair the RD in 2 cases; both cases were bullous RRD covering the CM. In these patients no pre-operative ultrasound was performed.. In one eye a suspicious melanocytic lesion noted before surgery was later confirmed as CM. Four of the 5 patients with RRD and CM proceeded to have surgical intervention for the RRD prior to CM treatment that included vitrectomy in 3 cases and scleral buckle in 1 case. Remaining one patient with RRD and CM had their RRD surgery deferred until the radiation treatment was performed.

In 14 eyes (74%) the RD developed after the CM treatment. The average time between the treatment for CM and the RD was 44.2 months (SD 58.3, range 0.5-156).

In 15 eyes (79%) a posterior vitreous detachment (PVD) was present, and absent in 4 eyes (21%). With respect of the macula status, 13 eyes (68%) were macula off and 6 (32%) were macula on. Thirteen eyes (68%) had a single retinal tear. Among them, retinal tear was located in the area of the tumour in one case (Fig. 1). Two retinal tears were seen in 5 eyes (26%) and 1 eye (5%) had 10 retinal tears. At the time of the first operation, PVR was documented in 7 eyes, (37%);all had PVR grade C posterior (PVR CP).

Choroidal melanoma treatment:

The majority of patients underwent Ruthenium-106 (Ru-106) plaque (17 eyes, 90%) treatment, 1 eye had proton beam radiotherapy and 1 eye was enucleated. The patient who underwent enucleation had a large pigmented lesion with an indistinct border, measuring 17 mm in diameter. This lesion was discovered during vitrectomy performed to repair the RRD. The tumor was not initially observed prior to the operation, but three weeks later, enucleation was carried out. Subsequent biopsy results confirmed the presence of a choroidal melanoma composed of spindle B-type cells.

Within the group of patients that had plaque radiotherapy, 16 eyes (94%) had 20 mm Ru-106 and 1 eye (6%) 15 mm Ru-106 plaque. The radiation doses delivered to the tumour apex was 100 Gy in 12 eyes (67%), 80 Gy in 4 eyes and 120 Gy in 1 eye. During the plaque insertion, 10 eyes did not require muscle disinsertion and 7 eyes required muscle disinsertion, of which the medial rectus was the most commonly disinserted muscle (3 eyes), followed by inferior oblique (2 eyes) and superior oblique and superior rectus (1 eye each). One eye had a globe

perforation during the plaque insertion. Two patients had histological analysis; aforementioned enucleated eye showed spindle B cell choroidal melanoma and 1 vitrectomy biopsy resulted in a hypocellular biopsy that did not contribute to diagnosis.

Retinal detachment treatment:

A total of 16 eyes (84%) underwent pars plana vitrectomy (PPV) of which 1 eye had combined phacoemulsification and vitrectomy. One patient underwent scleral buckle in which a segmental silicone tire was used, another patient had barrier laser and one did not undergo surgery following discussion between surgeon and patient due to potential risk of seeding.

Primary silicone oil (SO) was used in 9 eyes (56%) and gas in 7 (44%) (C3F8 four eyes, SF6 3 eyes). In terms of the anesthesia for the RRD surgery, data was available for 13 (72%) patients. Majority of them received sub-tenon block accounting for 9 patients. Peribulbar block was used in 1 patient and 3 patient had sedation plus sub-tenon block. Of the latter 3 patients,1 patient need to be converted to general anesthesia as inadequate anaesthesia was achieved despite a repeat of the sub-tenon block and increase in sedation. Remaining 2 patients in the latter group needed additional sub-tenon block and increase sedation due to intense pain during the operation.

Outcomes:

Ten out of 17 eyes that underwent surgery in our study had complete retinal reattachment with one surgery, giving an overall primary success rate of 59%. Of the 7 patients who had primary failure, 5 had gas as primary tamponade and 2 had silicone oil.. The main cause of failure was proliferative vitreoretinopathy (PVR), accounting for 86% (6 eyes) and in 1 patient a new break was the cause of redetachment.

Seventeen additional operations were performed in patients with primary failure as well as in patients with attached retina after one operation. The type of surgeries are summarised in the table 1.

Of the total of 6 removal of oil procedures, 2 (33%) re-detached and 4 (67%) remain attached. Overall, at final follow up, three eyes (16%) had a detached retina (2 detached under oil).

Sixteen eyes, accounting for 84% of the total were attached at final follow-up. Among them, 8 eyes were attached under silicone oil. One eye developed neovascular glaucoma needing enucleation.

Visual outcomes and follow up:

At the moment of the diagnosis of the RRD, the initial mean BCVA was 0.71 logMAR (Snellen 20/100) (SD 0.9) and the final mean BCVA had deteriorated significantly to 1.5 logMAR (Snellen 20/630) (SD 1.0, p=0.01). At presentation, 5 patients had a BCVA of 20/200 or worse, with a mean of 2.2 logMAR (SD 0.83) (Snellen 20/4000). Conversely, 14 patients exhibited a BCVA better than 20/200, with a mean of 0.2 logMAR (SD 0.2) (Snellen 20/32). The group of patients with a vision of 1.00 logMAR (Snellen 20/200) or worse did not demonstrate a significant difference in their BCVA at the end of the follow-up period, as indicated by a mean final BCVA of 1.8 logMAR (Snellen 20/2000) (SD 0.7) (p=0.3). However, the group with an initial vision better than 1.00 logMAR (Snellen 20/200) exhibited a statistically significant deterioration at the end of the follow-up period, with a BCVA of 1.4 logMAR (Snellen 20/500) (SD 1.1, p=0.0006). Six eyes (32%) achieved a BCVA better than 20/200 (mean 20/32, SD 0.4). Thirteen (68%) eyes had a BCVA 20/200 or worse at the end of follow-up (mean 20/4000, SD 0.6). Differences between patients with CM located in the posterior pole and those with CM located in the mid-periphery were analyzed. The results indicated no significant difference in terms of the final BCVA (p=0.25). In our series, 7 patients developed radiation retinopathy

during the period of follow-up. Among them 4 developed a combined RRD+TRD (as a consequence of radiation retinopathy).

When comparing combined RRD+TRD to RRD alone, no statistically significant difference was found in terms of the final best-corrected visual acuity (BCVA) (p=0.2). Similarly, there was no significant difference observed in the total number of operations between the two groups either (p=0.6).

The mean duration of follow up was 66 months (SD 60, range 5-240).One patient presented with liver and lung metastasis at diagnosis of CM and before the RRD. Following retinal detachment surgery there was no evidence of recurrence, local seeding or metastasis during the course of follow-up period.

DISCUSSION:

Choroidal melanoma is the most commonly diagnosed primary intraocular tumour in adults,[9] but remains a rare tumour with a reported incidence of uveal melanoma between 1.3 to 8.6 cases per million in Europe[10]. RRD in choroidal melanoma is even more rare - the incidence has not previously been reported in the literature. In rare conditions observational studies can play an important role because of the lack of prospective or randomized clinical trials. Our study reviews an extended period of time in a large tertiary centre. The vitreoretinal service at Moorfields deal with on average 1800 new RRDs per year (*audit department Moorfields eye hospital 2019*) and the ocular oncology department treats 239 to 301 new uveal melanomas in a calendar year (*CQUIN Meetings 2020-2*). We identified 21 cases in a period of 20 years - approximately 1 case per year. Rhegmatogenous retinal detachment (RRD) and tractional retinal detachment (TRD) have been reported as a complication of different treatment modalities for choroidal melanoma, including RRD after trans-scleral resection,[4] TRD and

combined RRD and TRD after brachytherapy,[5] and RRD after transpupillary thermotherapy.[5,6] To date case reports and one small series of spontaneous RRD in patients with CM have been published.[12-16] In a retrospective study, RRD surgery outcomes of 10 patients with posterior uveal melanoma were reported, 7 underwent scleral buckle, 2 PPV and 1 pneumatic retinopexy.[16] In our study surgical management differs with a majority of patients undergoing PPV (94% of patients who underwent surgery) and just 1 case treated with scleral buckling. This decision was made based on the complexity of the RRD in our series.

Another important finding observed in our study is the low primary success rate (59%), less than the series of Haimovici et al, who reported a primary success rate of 90%.[16] However, they report no PVR at presentation compared to 37% of cases in our report, which inevitably increases the overall complexity of the detachment repair. The main cause of failure in our series was PVR, accounting for 86% of the redetachments. As a result, our cohort had 17 reoperations and including the primary surgeries, the total number of procedures was 34. Nevertheless, with repeat procedures, we achieved a final rate of retinal attachment of 84%. All these features are comparable in severity and outcomes of patients who present late with retinal detachment, with a primary success rate of 69%. PVR was the main culprit leading to failure in 83% in this subgroup of patients who present late with their primary RRD.[17] They too had a high number of reoperations that eventually led to retinal attachment in 87% of patients at the end of follow-up.[17]

Visual outcomes were generally disappointing, with a statistically significant deterioration and final mean BCVA of 20/630 In addition, 68% of eyes had a BCVA 20/200 or worse at the end of follow-up (mean 20/4000). It is likely that this relates to a combination of factors, including radiation treatment for CM, PVR and retinal redetachment requiring multiple surgeries. In

report number 16 of the Collaborative Ocular Melanoma Study (COMS), 49% of eyes had a loss of six or more lines of visual acuity from the pre-treatment level and 45% of patients had visual acuity of 20/200 or worse at 3 years after Iodine plaque brachytherapy.[18] In an animal model, Lewis et al showed that reattachment stops or slows many of the cellular changes initiated by detachment. However, reattachment after complex detachment results in more severe disruption of the retina and initiates more potentially irreversible changes.[19] In addition, previous clinical studies showed that eyes that developed PVR resulting in disappointing visual outcomes.[20-23] Among these, Wickham et al reported that if PVR is absent at the time of failure, visual acuity is relatively well preserved after reattachment. [20] However, if PVR developed, visual outcomes were significantly worse compared with those without PVR, and successive redetachment appeared to have a much greater impact on visual function.[20]

With respect to the safety of retinal detachment surgery concomitant with CM, in our series vitrectomy appeared to be safe in terms of local and systemic dissemination. Different series have previously reported vitrectomy as a safe procedure in eyes with previously treated choroidal melanoma with a good safety profile.[24-26] However, local seeding and extraocular extension after vitrectomy have been reported in patients with previous stable treated CM.[27,28] Foster and colleagues reported intraocular tumour dissemination in one eye 54 months after vitrectomy due to recurrent vitreous haemorrhage.[27] In another case, Shabto and colleagues reported a case of extraocular extension of a regressed CM 1 year after PPV and scleral buckle for RRD, The eye was enucleated, and pathology confirmed enlargement of the melanoma with extension of the tumor into the ciliary body, displacing the iris anteriorly and forming a nodule overlying the sclera.[28]

There are few reports in the literature on the safety of vitrectomy in patients with untreated CM. Laqua et al, reported 3 patients who underwent pars plana vitrectomy for vitreous

haemorrhage secondary to CM, in all cases the tumour was unsuspected.[29] - A 35-year-old patient 7 months after vitrectomy and 2 weeks after 2 consecutive lavage procedures for recurrent vitreous haemorrhage, developed a diffuse spreading of tumour cells covering all intraocular surfaces, including iris, drainage angle and posterior corneal surface, and most of the inner retinal surface confirmed histologically. It is important to highlight that this patient never received any treatment for CM because the diagnosis was subsequently confirmed after enucleation and histopathology.[29] Similarly, Bechrakis et al described 34 patients who underwent intraocular biopsy, 23 of which had three-port pars plana vitrectomy due to unclassifiable choroidal tumour. [30] Thirteen cases had a confirmed CM. One patient developed a multifocal intraocular tumour spread 5 months after biopsy. This patient was treated by ruthenium brachytherapy a few days after biopsy, followed 4 months later by phacoemulsification. Fifty-two months after enucleation, there was no evidence of further local tumour recurrence or metastases. In our series, the RRD repairwas done before CM treatment in 4 patients; 3 by vitrectomy and 1 scleral buckle, with no evidence of local or systemic seeding. Nevertheless, this is a small number of patients with RRD repaired by vitrectomy and the safety in patients with untreated CM remains uncertain. Moreover, in a clinicopathologic study, Boniuk and Zimmerman[31] showed twenty-two out of 57 eyes with extraocular extension of the tumour through sites of scleral perforation in eyes with unsuspected choroidal melanoma subjected to retinal detachment repaired by transscleral diathermy in most of the cases, 4 with scleral resection and 3 with scleral buckle. [31] Therefore, we advocate that for optimal safety the RRD repair should be delayed until the CM is treated and that cryotherapy is applied to the sclerotomy sites at vitrectomy surgery.

In regard to the anaesthesia, we recommend a careful selection of patients for local anaesthesia due to the scarring of previous radiation treatment, which contributes to a difficult technique for sub-tenon block and less anaesthesia uptake.

This is the largest series of patients with RRD in the context of CM with the longest follow-up reported. RRD in patients with CM is uncommon, complex and is best managed by a multidisciplinary team of vitreoretinal surgeons and ocular oncologists. Cases may require multiple procedures to achieve successful anatomical outcomes, however, visual outcomes are poor due to a combination of factors related both to the melanoma treatment and the retinal detachment. Vitrectomy as a surgical intervention for RRD appears to be safe in terms tumour dissemination in patients with previous treated CM.

Conflicts of interest

The authors report no conflicts of interest

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Author Contribution Statement

RA, MS and DGC conceived and designed the research. AM, MB and MK collected the data. RA and DGC analysed the data. RA, MS and DGC analysed and interpreted the literature. RA, AM, MB, MK, MS and DGC drafted the manuscript and made critical revision of the manuscript.

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Figure 1. Representative case: A pre-operative image of rhegmatogenous RD with an untreated choroidal melanoma. A retinal horseshoe tear (arrow) is observed.

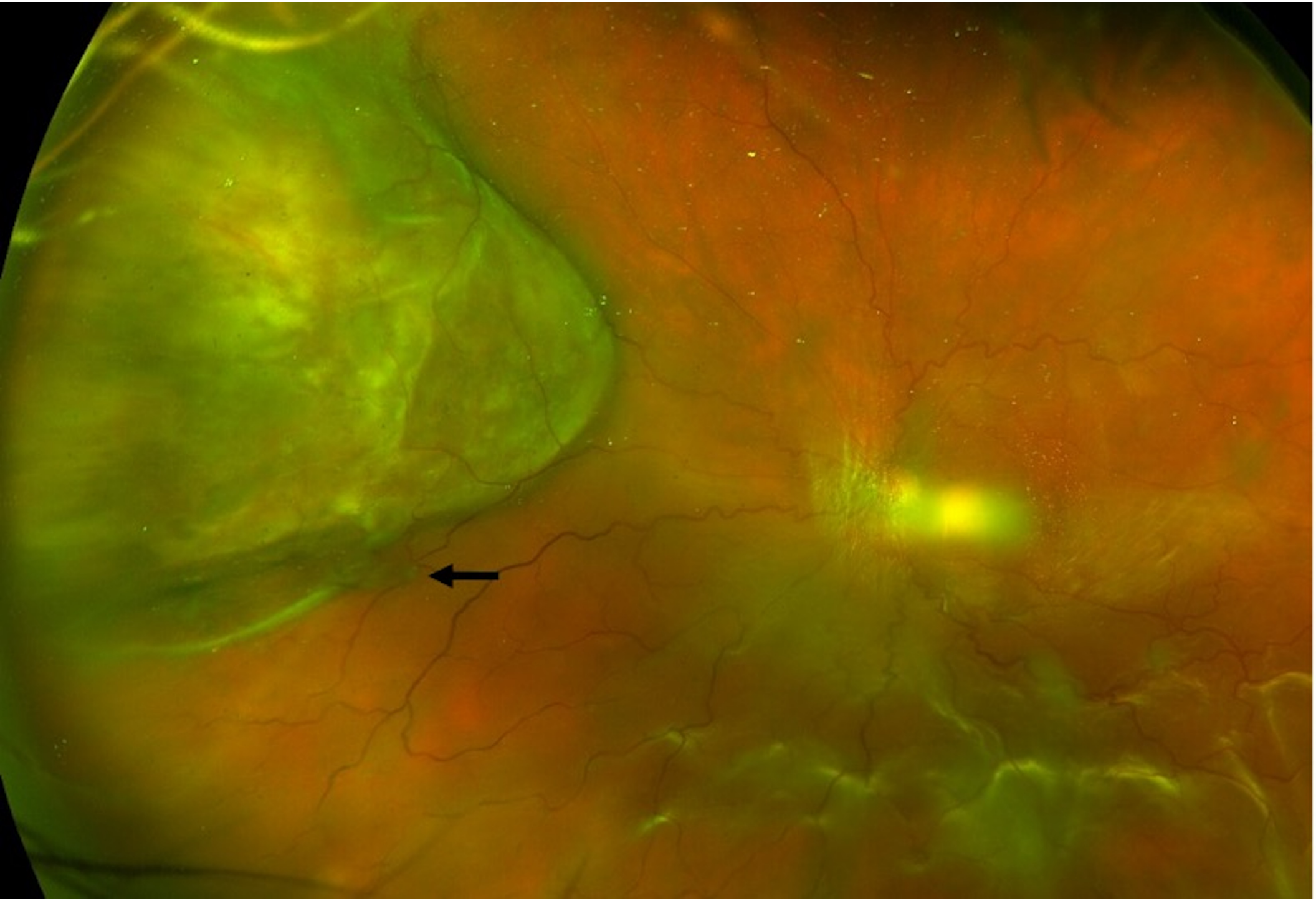

Table 1, summary of additional surgeries performed

Retinectomy + silicone oil	5
PVR peel + endolaser + silicone oil	4
Phaco + Removal of silicone oil	4
ACIOL + Removal of silicone oil	1
Removal of silicone oil	1
Pars plana lensectomy	1
IOL removal + endolaser + peel PVR + silicone oil re-insertion	1