Cutting-edge Vitreoretinal Surgery

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15 Principles in the Management of Proliferative Vitreoretinopathy

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15.1 Introduction

Proliferative vitreoretinopathy (PVR) formerly known by terms like "massive vitreous traction" or "massive periretinal proliferation" is the most common cause of failed repair of rhegmatogenous retinal detachment (RD). Surgical management of RD and PVR are pneumatic retinopexy, scleral buckling, and pars plana vitrectomy (PPV) alone or in combination. Newer techniques and instrumentation for vitrectomy have resulted in greatly improved outcomes of surgery. However, despite these advances, more than one-fourth of initially successful cases do land in re-detachment due to recurrent or persistent vitreoretinal traction [1]. As a result, PVR remains a challenge for the vitreoretinal surgeon and necessitates continuing efforts for development of other forms of therapy to inhibit the pathologic cascade causing traction. It is a well-known fact that retinal pigment epithelial (RPE) cells play a key role in triggering development of PVR [2]. The participation of soluble mediators and the extracellular matrix components is critical in cellular events like proliferation and tissue contraction, which result in PVR formation. Recent efforts have been directed toward the biochemical inhibition of cellular proliferation and membrane contraction in PVR. The need of the hour is a multimodal, combinatorial approach, involving inhibition of reactive oxygen species, blocking the direct and indirect pathway of platelet-derived growth factor receptor-α (PDGFRα) activation to halt the process of PVR. Furthermore, in the future, attention should be given to optimizing the correct dosing and administration of drugs, since some of the past failures may be due to the manner and time of administration rather than due to lack of true efficacy of the drugs tested [3].

15.2 Risk Factors and Pathogenesis

Certain factors are associated with increased probability of PVR formation. These can be grouped as pre, intra, and post-operative. Preoperatively trauma, uveitis, giant tears, multiple breaks, large break, detachment involving more than two quadrants, vitreous hemorrhage with RD, aphakia, and multiple surgical interventions in the past contribute to the increased risk of PVR formation (Fig. 15.1). Presence of choroidal detachment with retinal detachment, pre- or postoperatively is a significant precursor to PVR formation [4–7]. In a recent study by Kunyong et al., association of cigarette smoking and macular involvement were identified as significant risk factors predictive of PVR formation

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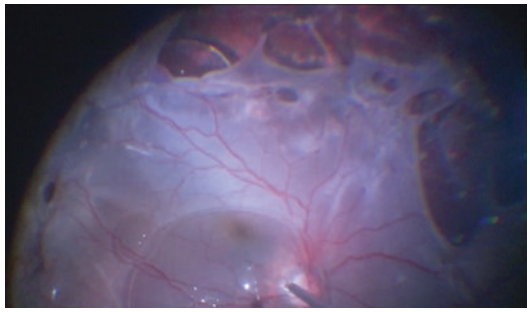

Fig. 15.1 Intraoperative photograph showing retinal detachment with advanced proliferative vitreoretinopathy. There is inferior retinal shortening along with multiple breaks noted inferiorly

after uncomplicated primary retinal detachment repair [8].

In giant retinal tears, the incidence of PVR varies from 16 to 41%, while in penetrating ocular traumas the mean incidence is 25%, range being from 10% to 45% [5]. In eyes with Rhegmatogenous retinal detachment (RRD) with grade B PVR, the incidence of severe PVR after surgery was reported to be 25.8% when using cryotherapy and 2.2% when using argon laser photocoagulation [6]. Intraoperatively, intraocular hemorrhage during or after surgery, use of air or sulfur hexafluoride, excessive cryotherapy, diathermy or photocoagulation, repeated surgical procedures, and loss of vitreous during subretinal fluid (SRF) drainage also lead to the increased incidence of PVR [7].

15.3 Pathogenesis of PVR

The pathological process of PVR is not completely understood but is thought to be analogous to the defective wound healing process leading to a keloid formation in the skin [9]. The retinal pigment epithelial cells play a key role by dedifferentiating and migrating through a retinal break and undergoing proliferation on the retinal surface. Retinal glial cells and macrophages may also play an important role, perhaps by providing the scaffold for membrane formation or by releasing trophic factors [3, 9].

Basically, PVR results from the growth and contraction of cellular membranes within the hyaloids, retina, and retinal surface owing to intraocular inflammation. These membranes exert traction, causing opening up of otherwise successfully treated retinal breaks, creating new retinal breaks, or promoting proliferation at the posterior vitreous base and anterior cortical vitreous resulting in re-detachment. This in turn causes antero-peripheral traction on the retina with a displacement of the peripheral retina toward the pars plana. Membrane contraction on the inner retina causes distortion and folding, resulting in star folds at the inferior quadrant [10].

Clinical and pathological changes occurring in eyes after posterior segment trauma and grade C PVR, was studied in a recent publication by Ying Zin et al. They documented PVR changes with intraoperative photographs during vitrectomy at serial intervals and observed that retinal fold formation occurred at around 30 days after injury. Within this time frame, they observed, that the retina was soft, easily flattened, thereafter, the retina was observed to become edematous, opaque and swollen, lost its elasticity subsequently to become stiff and undergo shortening [11].

15.4 Surgery in PVR

15.4.1 Scleral Buckling in PVR

Treatment of proliferative retinopathy, being essentially surgical, poses a challenging situation to the vitreoretinal surgeon. Although, vitrectomy with all its modern advances is the procedure of choice, some surgeons are still in favor of 360° scleral buckling for PVR. Scleral buckling acts as an adjunct in relieving the vitreoretinal traction, supporting the vitreous base and minimizing the chance of leakage from small postoperative retinal missed or de novo break. Inferiorly, the vitreous base continues to contract, as it is virtually impossible to remove the vitreous base completely. In eyes with focal or relatively inactive PVR, reattachment may be achieved by scleral buckling alone, with drainage of subretinal fluid and laser photocoagulation.

The width of the scleral buckle is decided based upon the contraction of the vitreous base and size of peripheral breaks if any. It may vary from a broad 7.0-mm, style 277 or 276 encircling tire and 40 band through a solid encircling 5.0-mm wide scleral band down to a 2.5-mm wide style 240 encircling band. The current trend is toward narrower bands. If larger, more posterior tears are present, an extra meridional explant can be placed under the tear, however, in most cases after complete relief of traction, internal tamponade and retinopexy may deem it unnecessary. The scleral sutures should be passed at two-third scleral thickness, at least 1 mm anterior and posterior to the encircling buckle, one or two in each quadrant. The sutures are tied and the buckle tightened at the end after completing vitrectomy.

15.4.2 Combined SB+ PPV Versus PPV Alone for PVR

The rate of successful reattachment of retina declines with increasing complexity of detachment. The anatomical success rate, i.e., retina remaining attached at the end 12 months after surgery for RRD with PVR is reported to be between 60 and 80%. In a study by Frank H et al., a comparison of the anatomical success of combined pars plana vitrectomy–scleral buckle (PPV–SB) and pars plana vitrectomy (PPV) for RRD with grade C PVR was done [12]. They achieved single surgery anatomical success rate of 70.1%, which was comparable to most studies. Even then, the utility of scleral buckle in addition to vitrectomy for PVR remains debatable. Storey et al. compared single surgery anatomical success rate in patients with retinal detachments at high-risk PVR, defined by the presence of preoperative PVR, vitreous hemorrhage, retinal tears >1 clock hour, or retinal detachment in two or more quadrants [13]. Single surgery attachment rate was 75.0% in the PPV and scleral buckle group versus 48.3% in the PPV alone group at 3 months follow-up. EVRS Retinal Detachment Study, on the other hand, postulated that combined vitrectomy and supplemental scleral buckling in Grades B and C1 PVR cases were associated with a higher failure rate of 8.9% versus 3.0%. Owing to the discrepancies in the above findings, determining the optimal management in PVR poses a challenge. Also, various confounding variables like the anatomical and pathological variables in patients with PVR add to the pre-existing dilemma [14].

With the advent of MIVS, most simple and moderate complexity RRD are best managed with PPV alone. Nonetheless, some surgeons may be inclined to add scleral buckle for more complicated retinal detachments. For noncomplex RRD, the addition of SB does not improve the anatomic success and is associated with slightly lower VA than with PPV alone. Current trend may be favoring the use of minimal and efficacious supplemental SB, as it inevitably causes a myopic shift and potentially extraocular movement dysfunction [15].

15.4.3 Vitrectomy in PVR

The vitreoretinal surgery for PVR is aimed at providing permanent support to the retina from any ongoing traction and to close any open retinal breaks. These can be successfully achieved by an encircling scleral buckle, meticulous relief of all retinal traction with vitrectomy, and temporary or long-term tamponade of the retina with long-acting agents. These steps must be achieved without causing prolonged ocular inflammation or further cellular access to the retinal surface or else recurrence is frequent. A comprehensive vitrectomy is essential in the management of PVR. Some surgeons rely on a meticulous vitrectomy and silicone oil (SO) tamponade without scleral buckling and report comparable results with a combined procedure. In any event, almost all eyes with retinal detachment and PVR also require a vitrectomy to remove all vitreous gel, cellular and inflammatory material, blood, and fibroblastic membranes. It is necessary to relieve all traction by division and peeling or delamination of fixed membranes and to remove as much as possible of the vitreous base.

15.5 Surgical Sequence and Techniques for Established PVR

15.5.1 Anesthesia

As with most vitreoretinal surgeries, either general or local peribulbar anesthesia is acceptable. The anesthetist must be informed if long-acting gas is to be used, so as to avoid nitrous oxide in general anesthesia cases. Most cases of PVR can be operated with local anesthesia. The block can be supplemented during the operation, if required, with further injection and by the attending anesthesiologist with intravenous sedation and analgesia.

15.5.2 Placement of Transconjunctival Cannulas

The three 23G, 25G entry ports are placed in the inferotemporal, superotemporal, and superonasal quadrants with an angled entry to diminish the risk of postoperative leakage of air or fluid. The first port is placed near the horizontal meridian in the inferotemporal quadrant, facilitating rotation of the eye downward during surgery while removing inferior vitreous base. The remaining two ports are for the fiberoptic and vitrector or other instruments such as endodiathermy, endolaser, vitreous scissors, vitreous forceps, and extrusion needle. A separate port has to be made if chandelier is to be used. The entry cannulas should be placed above the midline almost opposite each other, to facilitate peripheral visualization by superior and inferior globe rotation. Care must be taken to check that the position of indwelling ports inside the vitreous cavity and avoid subretinal or suprachoroidal infusion during vitrectomy.

15.5.3 Management of Lens in PVR

In cases of posterior PVR, the crystalline lens could be retained, however, presence of anterior PVR warrants its removal to facilitate adequate dissection of the anterior vitreous and prevent formation of cyclitic membrane. A planned cataract extraction with an intraocular lens (IOL) placed in the bag should be considered prior to starting vitrectomy. A posterior chamber IOL, if present, should be retained. Anterior chamber IOLs and iris plane lenses may have to be removed. Implant removal can occasionally result in an intraoperative hemorrhage or corneal and iris damage and compromise the surgical result. Clear lens always becomes cataractous with SO, for which phacoemulsification with or without IOL implantation at the time of SO removal can be done or when it hampers the view of the posterior segment. If the surgeon prefers pars plana lensectomy, there can be two situations, firstly when the capsule is removed completely, corneal decompensation can occur in the long term for which an inferior iridotomy can reduce risk. On the other hand, if capsule is left intact, then it almost always becomes opaque in the presence of SO. Subsequently, at the time of IOL implantation in the sulcus, YAG laser capsulotomy or formal capsulotomy can be done.

15.5.4 Core Vitrectomy and Removal of Vitreous Base

Complete removal of the central vitreous after induction of a posterior vitreous detachment is a critical step, although most patients with established PVR have a pre-existing PVD. Next step is the meticulous removal of the peripheral vitreous, with special care taken to completely remove inferior vitreous, as gravity causes pigment debris and inflammatory material to settle inferiorly.

Adherent vitreous membranes and the base can be visualized better by injecting intravitreal triamcinolone. With the advent of MIVS, the modern high-speed vitrectomy cutters having a port close to the tip facilitate shaving of the attached vitreous off the surface, without causing inadvertent retinal breaks. Scleral depression by an assistant can also help while removing the inferior vitreous base. In case of mobile detached retinas, filling of the vitreous cavity by heavy perfluorocarbon liquid can help to stabilize the

retina while attempting removal of the peripheral vitreous. PFCL has a dual action, displacing subretinal fluid anteriorly by ironing the retina and breaking down invisible microscopic retinal bridges of scar tissue.

15.5.5 Epiretinal Membrane Removal and Use of Perfluorocarbon Liquid

After complete vitrectomy, any fixed folds or retinal contraction due to epiretinal membranes should be tackled. Peeling of the membranes is begun from the surface of the retina starting from the posterior pole and going outward. A blunt vitreous spatula or pick may help find a plane or elevate the membrane, if it is not pre-existing which can be peeled by vitreous forceps. Care must be taken to avoid creating iatrogenic retinal breaks. Fixed folds with the contracted membrane overlying tend to fold the retina in the crevices. Membrane spanning across the macula needs to be peeled (Figs. 15.2 and 15.3). An injection of vital dye such as methylene blue can be used to stain the internal limiting membrane and allow its peeling, especially if retinal surface at the posterior pole is stiff or shiny. The degree of adherence of epiretinal membranes to the retinal surface is variable, so that few may be peeled easily in a single sheet, while others have to be freed up in a piecemeal fashion or delaminated. In areas where retina is attached, peeling of surface retinal membranes and internal limiting membrane is easier. Next comes the drainage of the subretinal fluid, which can be done through an open retinal break or by creating a small retinotomy away from scar tissue. This process can be facilitated by the injection of the heavy liquid fluorocarbon.

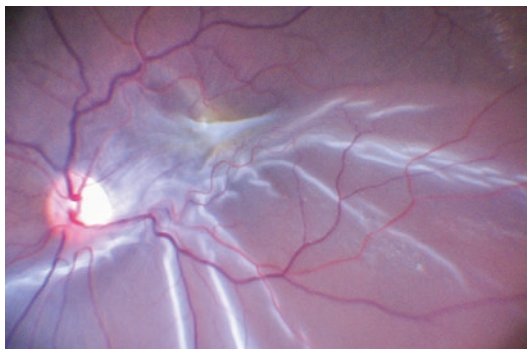

Fig. 15.2 Intraoperative photograph showing detached retina along with a star fold at macula and wrinkles on the retinal surface due to contraction of epiretinal membrane

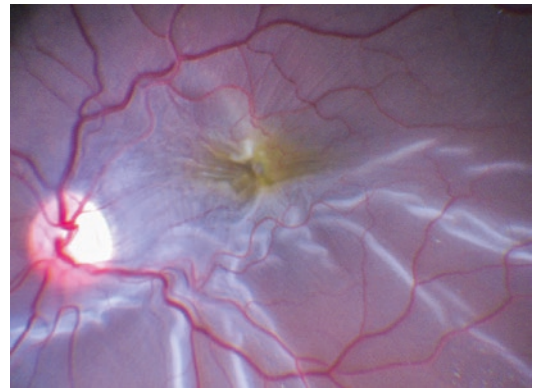

Fig. 15.3 Post-membrane peeling photograph of the eye in Fig. 15.2 showing the release of star-fold at macula

However, there is always a risk that the heavy fluid can pass through a retinal break to lie in the subretinal space which will make its removal difficult, apart from having unknown toxic effects. This risk escalates where tractional membranes are still elevating the retinal break. It is preferable to fill heavy liquid just short of any such retinal break until it is dissected, mobilized, and flattened.

15.5.6 Anterior PVR

By definition, anterior PVR occurs anterior to the posterior insertion of the vitreous base. Anterior PVR (A-PVR) is said to occur when proliferation extends over the ciliary body causing elevation of peripheral retina and anterior loop traction. It can also lead to hypotony, and the development of phthisis bulbi if left untreated, hence carries a poorer prognosis [16]. This makes complete dissection of the anterior loop traction extremely important. Ultrahigh speed cutters should be used to mobilize as much as peripheral retina as possible. Tatsuhiko et al. in their study concluded that

25G vitrectomy can be effective for A-PVR, although eyes with A-PVR in the study required more complex surgical procedures and longer surgical times. Wide-angle viewing system, bimanual surgery by using chandelier, and scleral depression are a value addition whose importance cannot be emphasized enough. Posterior pole can be kept stable during dissection of the anterior membranes by perfluorocarbon liquid. Although wide-angle viewing system facilitates complete anterior dissection, lens can be sacrificed, in case extensive anterior traction is noted preoperatively.

15.5.7 Testing Adequacy of Relief of Traction

Residual traction at the end of vitreous dissection prevents the retina from opposing to the pigment epithelial surface. This forms the major reason for poor anatomic results in PVR. The operating surgeon can test the adequacy of retinal mobilization by doing a complete fluid–air exchange. It can be performed by an extrusion needle aspirating all vitreous fluid, the injected heavy fluid and any residual subretinal fluid by positive suction. Residual subretinal fluid can also be aspirated by a silicone soft tubing extension on the needle. Incomplete relief of traction is evident when retina fails to flatten despite subretinal fluid drainage following fluid–air exchange, or subretinal passage of air over taut membranes. The cause being shortening of the retina by surface or intraretinal gliosis which will not permit adequate mobilization of the retina. At this stage, additional dissection around a retinal tear may help but more often than not, the surgeon will have to take a decision to perform a peripheral relaxing retinotomy or a circumferential or radial retinotomy and retinectomy in cases of badly fibrosed retina.

15.5.8 Relaxing Retinotomy and Retinectomy

The need for a relaxing retinotomy rarely arises in posterior PVR because the membranes can be removed surgically. The tractional vector forces contributing to anterior PVR are three, namely anteroposterior, circumferential, and perpendicular [17]. Relaxing retinotomy is the only savior when epiretinal membrane dissection and scleral buckling fail to relieve the preretinal traction and retinal foreshortening. Indeed, the retina can only be reattached by retinotomy in these very complicated cases [18].

In a study by Lim et al. [19], 30 cases having RRD and grade C PVR were subjected to combined large radial retinotomy and a circumferential retinectomy. The authors believed that although circumferential retinectomy can achieve a flat retina owing to release anteroposterior retinal shortening, more often to obtain adequate relief of circumferential intrinsic retinal shortening, large retinectomies are usually essential. As a result, patient is left to face potential complications such as large visual field defects, ocular hypotony causing phthisis bulbi, recurrent retinal detachment. To overcome this, the authors proposed making a large radial retinotomy with micro scissors, plus a radial retinotomy at 6-o'clock. The edges of radial retinotomy will be redistributed superiorly upon flattening. This salvages the retina from the PVR microenvironment inferiorly. In addition, the resultant loss of a superior visual field is usually better tolerated than an inferior one. The authors reported a 90% reattachment rate and a modest visual recovery with the above procedure.

In a study by the author [20], on 51 patients with RD complicated by grade D PVR who underwent retinectomy of 180° or more, 76.8% achieved improvement or stabilization of visual acuity with 35% achieved ambulatory vision. This finding stresses the importance of trial of surgical intervention in advanced PVR, more so in one-eyed patient. Literature suggests that in patients with PVR in one eye, 50–74.3% of fellow eyes can have a rhegmatogenous event resulting in profound visual loss, and often the eye that was initially thought to be worse, becomes the better-seeing eye with appropriate management. This study reported a 45.4% of one-eyed patients achieving ambulatory vision, supporting the work of some authors who suggested surgery of

PVR being cost effective as determined by the quality adjusted life year.

Even though retinotomy and retinectomies are done to salvage the eye in certain advanced PVR cases, its complications should be kept in mind. Contraction of the posterior free edge of the retina after a large circumferential retinotomy under SO tamponade can extend up to the disc and the macula, thereby compromising the visual outcome. To prevent this, a radial retinotomy sometimes helps. Hypotony is more prevalent in eyes that underwent retinectomy versus that did not, and silicone oil had a lower incidence of hypotony as compared to gas in the Silicone study. In a study by the author [20], size of retinectomy had no bearing on postoperative hypotony. Morse et al. found that hypotony was seen in 43% of attached retinas in a case series. In a study by Alturki et al., 40% hypotony was observed in patients in which 360° retinectomy was performed [21]. Diffuse anterior contraction is a significant predictor of postoperative hypotony. In a study by Federman et al., 78% of eyes having hypotony preoperatively became normotonic after surgery and it was attributed to removal of anterior PVR membranes which were covering ciliary epithelium of the pars plicata and resulting in ciliary body detachment [22]. To conclude, retinectomy aims to relieve all existing traction and should be minimum required to achieve retinal reattachment without causing significant hypotony [18].

15.5.9 Removal of Subretinal Membranes

In eyes with excessive inflammation, extensive PVR, subretinal bands may develop and contract to cause tenting of the retina [23]. Subretinal bands that prevent retinal reattachment should be removed prior to fluid–air exchange by creating a small retinotomy with scissors over the taut membrane, grasping the membrane through the retinotomy with 25G vitreous forceps, and pulling it through the retinotomy into the vitreous compartment [24, 25].

15.5.10 Technique of Stretching the Retina

In a study by Homayoun Tabandeh et al. [26], they described a surgical technique in seven patients with severe PVR in which they used two Tano diamond-dusted membrane scrapers to gently stretch the retina–PVR complex and facilitate partial relaxation of the pre-retinal membranes. The rationale behind this technique as described by the authors lies in the fact that the edges of the membranes are mostly indistinct and lifting the edge for peeling is limited by severe infolding of the retina. Using two membrane scrapers for bimanual gentle stretching of the PVR–retina complex results in partial relaxation of the contracted PVR membrane and loosening of its adhesion to the retina. They achieved complete reattachment in all patients at the end of follow-up period. The authors also suggested that this technique may be used in selected cases of diabetic tractional detachments with fibrovascular proliferation with caution, as the ischemic retina is often atrophic, thin, and predisposed to tearing, may also result in intraoperative bleeding and breaks.

15.5.11 Fluid–Air Exchange

After removal of all membranes and relaxing the retina, fluid–air exchange results in a flat retina. A 25G or 23G extrusion cannula is used to aspirate subretinal fluid, heavy fluid, vitreous fluid, and residual opacities such as blood maintaining continuous air infusion to maintain IOP. Subretinal fluid drainage may be completed via an open retinal break, or a small posterior retinotomy can be made after a diathermy mark on a spot chosen nasal to the disc, away from any fixed fold but over detached retina and avoiding retinal vessels. A suction cannula, 23G/25G, or a soft flexible silicone tip can then be used to make a small opening in the weakened spot, while keeping in mind the need to continuously aspirate the egressing subretinal fluid. Care should be taken to avoid spreading the mobilized pigment cells onto the retinal surface. Alternatively, it can also be passed under the pre-existing retinal break.

15.5.12 Retinopexy

Retinopexy is achieved most commonly by endolaser photocoagulation, although some surgeons prefer laser photocoagulation by indirect ophthalmoscope with scleral depression if required for 360°. All retinal breaks, along with retinotomies are surrounded by 2–3 rows of visible laser burns (Fig. 15.4). 360° laser burns are applied from the vitreous base extending posteriorly toward the equator. In case an extensive retinotomy or retinectomy has been carried out, endolaser is extended up to the arcades. The duration of laser should be longer than used for in office setting, but excessive increase in the power should be avoided for choroidal hemorrhage and rupture of Bruch's membrane can occur. Cryotherapy is generally avoided as it triggers more inflammation breakdown of the blood–vitreous barrier, cellular proliferation, and recurrence of PVR. In case there is persisting subretinal fluid or hazy view of the peripheral retina, cryotherapy may still be necessary.

15.5.13 Intraocular Tamponade

It was the Silicone Study Group, back in 1992 which established the superiority of longer acting tamponade agents, silicone oil, and perfluoro propane (C3F8), over sulfur hexafluoride (SF6) in PVR Grade C or worse. Long-term tamponade with silicone oil has many well-recognized advantages over long-acting gases like quicker visual rehabilitation and does not restrict air travel.

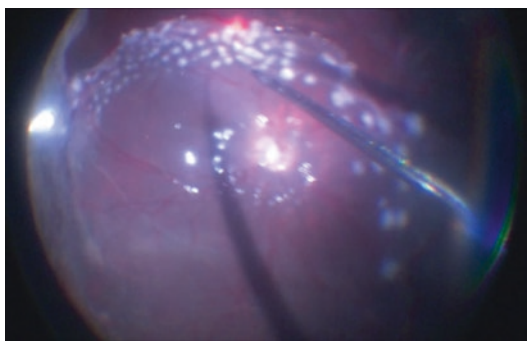

Fig. 15.4 Intraoperative photograph showing the margins of the retinectomy being treated extensively with 3–4 rows of endolaser photocoagulation

15.5.13.1 Silicone Oil

Silicone oil injection can be carried out after complete fluid air exchange, or if PFCL was injected, a direct PFCL–silicone oil exchange can also be done. Alternatively, some may prefer to do an intermediate step of PFCL–fluid exchange followed by fluid–air exchange. This step may be of particular importance to bring any fluid that may be trapped anteriorly under the heavy liquid to the posterior pole after air injection. The modern vitrectomy machines have a specially designed rigid syringe provided with SO injection driven by a pressurized air pump. The SO infusion is begun while air infusion is still connected to the eye, where air can pass out of the air infuser port, with continued infusion pressure is lowered to 10–15 mmHg as silicone enters the vitreous compartment from the superior site, thus maintaining IOP. As the oil reaches the sclerotomy port, air infusion stops, and IOP may rise exponentially. This is prevented by removing the air infusion cannula can allowing SO injection continued until the residual air is expelled. Alternatively, in case of valved cannulas, a vent can be placed to expel the air while injecting silicone oil. A complete fill of the vitreous cavity with SO, having IOP between 10 and 15 mmHg. 1000–1300 cSt silicone oil because is the choice of most surgeons owing to its relative ease of removal. Silicone oil with a higher viscosity is theoretically less prone to pass subretinal through breaks, however, incomplete relief of traction would be the primary reason for such an occurrence (Fig. 15.5).

15.5.13.2 Heavy Silicone Oil

Standard SO has the property of buoyancy resulting in inadequate tamponade to the inferior retina in upright position, which is the major cause of accumulation of inflammatory substrate for PVR occurrence. To tackle this problem, fluorinated SO or heavy SO can be used which effectively tamponades the inferior retina. It can be used in combination with conventional SO, but more

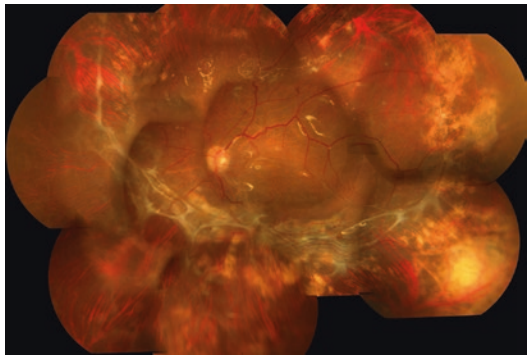

Fig. 15.5 Postoperative photograph showing a well-attached retina, after Pars Plana Vitrectomy for Proliferative vitreoretinopathy, with an inferior relaxing retinectomy andsilicone oil tamponade

often it is used as a substitute particularly after inferior relaxing retinotomy. Complications of these agents were frequent rise of IOP, inflammation, and earlier emulsification, with unknown long-term toxic effects warranting early removal. Multiple studies report excellent anatomical outcomes with the use of heavy silicone oils. Rizzo et al. [27] found out single surgery success rate of 84.6% and final anatomical attachment of 100%, improvement in visual acuity in 32 patients with inferior PVR heavy silicone oil. Other studies, however, failed to show any direct benefit of heavy silicone oils over standard silicone oil. In the Heavy Silicone Oil Study by Joussen et al. [28], visual acuity and anatomical success rates in patients with inferior PVR treated with standard silicone oil versus heavy silicone oil were compared and they found no statistically significant difference in visual acuity or reattachment rate.

15.5.13.3 PFCL as Medium-Term Tamponade

Sigler et al. [29] in their study on 44 eyes with recurrent inferior RD with grade C PVR, perfluoro octane was injected for 2–3 weeks, followed by its subsequent removal in a planned staged procedure. They found this technique to be effective management of recurrent inferior retinal detachments, achieving successful reattachment in 86%. However, it is associated with potential complications of transient inflammation and intraocular pressure elevation are potential complications associated with this technique.

15.6 Removal of Silicone Oil

Higher rate of retinal re-detachment after removal of silicone oil (ROSO) caused by PVR has been reported in the literature. Although, there is no consensus on an ideal time of silicone oil removal, most surgeons prefer removal after 3 months, as delayed removal has no benefits in terms of functional outcome. Retina should be screened at the time of SO removal for presence of missed breaks, ERM, tractional membranes which can be removed during surgery, in addition to laser. A retrospective study on 608 patients by Rizzo et al. [30], described adjunctive use of stains, which is mixture of trypan blue and brilliant blue G dyes re-detachment compared with standard care, which enabled achieving a higher probability of complete removal of ERM and PVR processes, perhaps including subclinical but active pathology.

In a study by Nagpal et al. [31], the presence of encirclage, laser retinopexy and presence of emulsified silicone oil were factors found to have a lower rate of re-detachment post SOR. However, the duration of tamponade had no bearing on the rate of re-detachment. In another study by the author [32], small hyper-reflective spherical bodies observed in sub-silicone oil-foveal depression (SSO-FD) space were studied using spectral domain optical coherence tomography (SD-OCT) in eyes undergoing silicone oil removal. The results were indicative of significantly improved visual outcomes after SOR, hyper-reflective bodies representing emulsified silicone oil globules.

Cataract occurs in 100% cases with silicone oil within 1 year, a combined phacoemulsification with implantation of an intraocular lens, and removal of the SO can be done in a single sitting. Occurrence of delayed glaucoma can occur with or without emulsified SO, and is an indication for removal, so is band keratopathy in young.

Newer generation vitrectomy machines are equipped with controlled active suction through a 23G or 25G, while maintaining IOP by continu-

ous infusion. Heavy fluorinated silicone is more difficult to remove, automated equipment makes it relatively easy. Most surgeons prefer to have intraocular air at the end of surgery, while BSS in the remainder.

In a recently presented paper (publication underway) by the author, microperimetry was used to evaluate functional changes on the macula pre and post SOR. The results are indicative of improved retinal sensitivity in all patients even when best-corrected visual acuity remained the same, thus highlighting the importance of microperimetry in assessing functional status of the macula predicting visual prognosis post SOR.

15.7 Postoperative Care

Initial face down positioning in the first 24 h is deemed critical for the RPE to pump out residual SRF and retinopexy to develop initial adhesions. Strict face down positioning is advocated by some to be done for 7–10 days, more so for inferior breaks. In case of heavy SO tamponade, the patient needs to be supine for 24–48 h before being mobilized. Postoperative regime consists of corticosteroids, mydriatic/cycloplegic drops for 3–4 weeks, in addition, require antihypertensive drops and acetazolamide tablets for postoperative ocular hypertension. High IOP despite maximum tolerated medical therapy implies an overfill, and a small amount may need to be aspirated back from the vitreous cavity.

15.8 Complications of Surgery for PVR [33]

The surgery for PVR is not without complications. The patient of PVR posted for surgery should have realistic expectations, should understand that even after multiple procedures, visual gain may be moderate and that complications can occur during and after the surgery.

15.8.1 Intraoperative Complications

Intraoperative complications are creation of retinal breaks while membrane dissection, incidence of which depends on the degree of adherence of preretinal membrane to retina. It is acceptable to err on the side of creating a retinal break while peeling membranes to mobilize the retina. Hemorrhage while membrane dissection can be tackled by raising the infusion pressure, or the use of endodiathermy. Serous choroidal detachment can occur due to incorrect subretinal or suprachoroidal placement of the cannula, whereas hemorrhagic detachment can occur due to rupture of a choroidal vessel or prolonged hypotony. The former can be dealt with the placement of the infusion cannula at a different port, whereas the latter requires drainage during the same surgery or a later date.

15.8.2 Postoperative Complications

Early postoperative complications are a rise in IOP, inflammation which can most commonly be managed medically. IOP rise more than 25 mm Hg, not controlled by ocular hypotensive drops or oral acetazolamide can result from overfill of gas/SO, which may need to be removed partially. Endophthalmitis is very rare but is a possibility. The most frequent late complication of PVR is the recurrence of surface membranes or macular pucker. Under effective superior SO tamponade, there exists a vitreous pocket containing inflammatory substrate in between the silicone oil meniscus and inferior retina called “perisilicone oil proliferation.” Progressive retinal shortening may be accompanied by the late development of large inferior retinal breaks and passage of the SO under the retina. Heavy SO formulations show promise of decreasing perisilicone proliferation. If the macula is not compromised, the membranes can be left alone or re-surgery can be considered. Prolonged intraocular silicone oil is associated with emulsification, cataract formation, glaucoma, corneal decompensation, more in aphakics. Late cystoid macular edema with or without preretinal membranes can be readily analyzed with

spectral domain optical coherence tomography and treated with topical steroid and nonsteroidal drops, intravitreal triamcinolone injection, and peeling of the internal limiting membrane over the macula in selected can be tried.

15.9 Adjuncts to Surgery for PVR

15.9.1 Anti-VEGF Agents

Various adjunctive agents like 5-fluorouracil, heparin, daunomycin, corticosteroids, colchicine, and retinoids have been tried unsuccessfully to prevent the formation of PVR. As vascular endothelial growth factor (VEGF) is known to play a crucial role in proliferative diseases of the eye, the probability of anti-VEGF being effective for the treatment and prevention to have been investigated extensively. In a study by Ricker et al. [34] concluded the level of VEGF to be threefold higher in eyes with PVR-related RDs than RDs without PVR. Armstrong et al. [35] reported VEGF concentration in PVR-related membranes to be equivalent to proliferative diabetic retinopathy-related membranes. However, anti-VEGF drugs in PVR-related RDs have been of limited value. A meta-analysis on the effect of Bevacizumab on PVR by Xin-Yu Zhao et al. [36], found that bevacizumab neither enhanced the BCVA 6 months 6 nor reduced the rate of retinal re-detachment, disproving the role of bevacizumab in vitrectomy for PVR-related RD. As PVR is like healing process, the multifactorial pathways like cytokines have a role in its pathogenesis and should be targeted for its prevention. Also, it is believed by Hsu et al. [37] that once the inflammatory cascade begins, the application of anti-VEGF drugs is insufficient to stop the progression of the disease.

15.9.2 Steroids—Intra- and Post-operative

The rationale for including steroids in the prevention of PVR is obvious for their anti-inflammatory properties and by inhibition of cell proliferation by reducing histamine and prostaglandin levels. Agents, like prednisone, dexamethasone, and triamcinolone acetonide (TA), are routinely used during RRD surgery to reduce the risk of PVR. Intraoperative TA is used for delineating adherent posterior hyaloids and epiretinal membrane during vitrectomy, postoperatively it can suppress the intraocular inflammation reaction [38]. The meta-analysis by Hui Shi et al. documented that the use of steroids is an adjunct to RRD surgery to reduce incidence of PVR, more so grade B PVR [39].

Slow-release dexamethasone implant, Ozudex was evaluated in a recent study by Philip J. Banerjee for vitrectomy in PVR, did not show any difference in anatomical success rate compared to controls, but it suggested a greater reduction in CMO [40].

15.10 Pharmacotherapy

Preclinical research continues to throw light on the pathogenesis of PVR formation at a molecular level, aiding in the development of prophylactic and therapeutic agents. Drugs under investigation target one or more (combination therapy) of the involved pathologies, including anti-inflammatory agents, antiproliferative agents, antineoplastic agents, antigrowth factor agents, and antioxidant agents.

Low molecular weight heparin (LMWH, Fragmin) has also been used by adding it to the infusion fluid. It acts by binding to fibronectin which is the most potent stimulator for RPE cell migration, and prevents hypocellular gel contraction [41].

Antiproliferative agents aid by inhibiting the cell cycle and cellular proliferation, which follows the breakdown of blood–retinal barrier [42]. These include compounds like 5-fluorouracil (5-FU), daunorubicin, taxol, colchicine. But the optimal therapeutic dosage that does not cause ocular toxicity is yet to be determined.

Clinical research suggests the Anti-VEGF agents might have a role in the prevention of postoperative PVR. Vascular endothelial cell growth factor (VEGF) A has been reported to be

able to activate the platelet-derived growth factor (PDGF) receptor α, a receptor tyrosine kinase that is key to the pathogenesis of PVR [43]. Intrasilicone oil injection of Bevacizumab has been tried [44].

TGF-β is another key player in the pathogenesis of this disease. It plays a role in extracellular matrix production, membrane contraction, and inflammation. Tranlisat, an inhibitor of TGF-β used as an antiallergy drug, showed promising results in terms of reducing the severity of PVR following intravitreal injection in a rabbit model in preclinical phase without apparent toxicity to the eye [45].

15.11 Future Scope

Future studies might further elucidate the real of Anti-VEGF in the prevention and management of PVR DNA–RNA chimeric ribozymes targeting proliferating cell nuclear antigen (*PCNA*), a cell cycle-controlling gene that inhibits cell division, have been tested [42].

Preclinical studies continue to throw light on different molecular pathologies, which leads to PVR development, thereby helping identify new targets for potential prophylactic or therapeutic agents in future.

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