Surgical Management of Stage 4 ROP

13

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Abstract

Although the vast majority of eyes with type 1 ROP successfully regress following treatment, some eyes develop fibrosis. This fibrosis typically occurs along the ridge tissue and can contract, causing traction and resulting in retinal detachment. Over the last 40 years, the surgical approach to repair stage 4 ROP associated retinal detachments have been refined. With an understanding of the vectors of traction, surgery for stage 4 ROP retinal detachments has a high success rate, often with excellent visual outcomes, especially when performed early in the disease process.

Keywords

Retinopathy of prematurity · Pathogenesis of ROP
Cicatricial ROP · Stage 4A ROP · Stage 4B ROP
Lens-sparing vitrectomy

13.1 Epidemiology of Advanced ROP

The incidence of blindness from ROP around the world is variable, largely depending on the level of development that allows for the survival of premature babies. In countries where the infant mortality rate is low and screening programs are established, the rate of blindness from ROP is approximately 10% [1]. In countries with high infant mortality rates, the rate of ROP-related blindness is extremely low, since children are unlikely to survive to the age when ROP develops. In "middle-income" nations, however, ROP is a major cause of childhood blindness, with rates approaching 40% [2]. This is largely due to the absence of screening programs and, although premature infants survive, there is a high rate of progression to stage 5 ROP. In contrast, in the United States, the incidence of any stage of ROP is estimated to be between 1 in 511 and 1 in 820 live births [3, 4]. Among them, roughly 10% require laser photocoagulation, and 0.5% require surgical intervention, the vast majority for stage 4 disease.

13.2 Pathogenesis

The peripheral retinal ischemia in the premature infant drives the expression of high levels of Vascular Endothelial Growth Factor (VEGF). As a result, apoptosis of the hyaloid vessels is delayed, which is clinically visible as persistent tunica vasculosis lentis and rubeosis iridis [5]. In addition, VEGF drives neovascular vessels to proliferate into the vitreous along the vascularized border. Subsequent activation of TGFß1 contributes to excessive scar formation [6–8]. This fibrous proliferation typically follows the aberrant neovascularization, growing along the ridge tissue and extending into the overlying vitreous. The vitreous sheets act as scaffolds for the extension of the fibrotic tissue. Subsequent contraction of the fibrous tissue occurs along various vectors, most commonly toward the center of the eye, as well as posterior toward the optic nerve or anterior toward the lens. Without intervention, the traction will completely detach the neurosensory retina, ultimately leading to blindness.

13.3 Clinical Course

The progression of ROP is relatively predictable. Infants that develop disease, in industrialized nations, are almost all born at <31 weeks gestational age with a birthweight of <1250 g. The earliest manifestations are usually seen at approximately 32 weeks postmenstrual age (PMA), with the conversion to treatment warranted (type 1) disease reached at a mean of 37 weeks PMA [9, 10]. Retinal detachment after appropriate treatment occurs at a mean of 41 weeks PMA [11]. Once the retina begins to detach, it can progress quickly. Within

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W.-C. Wu, W.-C. Lam (eds.), *A Quick Guide to Pediatric Retina*, https://doi.org/10.1007/978-981-15-6552-6_13

weeks, the detachment can advance from an early Stage 4A to Stage 5, resulting in a far worse prognosis for visual recovery. Therefore, once surgery is determined necessary, earlier intervention is advisable to reduce the progression of the detachment.

A special consideration needs to be given to eyes treated with anti-VEGF therapy for type 1 ROP. Although multiple prospective studies have demonstrated short-term efficacy using these agents [12–14], late reactivation and progression to retinal detachment have been reported long after the traditional screening period. Some reports have identified retinal detachments up to several years following anti-VEGF injections [15–18]. There is increasing evidence that following anti-VEGF therapy, vascular development often remains incomplete, resulting in persistent avascular retina [19, 20]. One potential approach to mitigate the risk of reactivation is sequential therapy. That is, treatment with anti-VEGF to treat acute type 1 ROP, followed by laser to the persistent avascular retina at 50–60 weeks postmenstrual age. This approach has been investigated in one prospective study [21], with additional studies underway. With anti-VEGF therapy now highly prevalent worldwide as a primary therapy for type 1 ROP, strategies to reduce the risk of late detachments are actively being pursued.

13.4 Management

In order to maximize visual potential, the goal in ROP retinal detachment surgery is to normalize anatomy to permit visual development. Surgical success requires an understanding of the tractional vectors present in ROP. Interrupting the traction resulting from fibrous proliferation is the primary surgical goal in ROP detachments. Adequate release of traction can prevent progression, reduce dragging of the macula, and spare visual function. In general, surgical success and visual function is greatest when surgery is performed at the earliest stage of retinal detachment. For this reason, once the decision for surgery is made, it is recommended to proceed as quickly as possible. Successful reattachment has been reported in 74–91% of stage 4A detachments [22–25], 62–92% of stage 4B detachments [22, 24, 26–28], and 22–48% of stage 5 detachments [29–31]. Visual outcomes in successful repair of stage 4A detachment can be expected to be 20/80 or better [22, 32, 33], ambulatory vision following stage 4B repair [28], and form vision following stage 5 repair [34].

13.5 Lens-Sparing Vitrectomy

In general, outcomes are best in ROP surgery when the crystalline lens is retained. Therefore, as long as the anatomy permits adequate space, which is the case in most stage 4A and many stage 4B ROP detachments, a lens-sparing vitrectomy (LSV) is recommended. The surgery is initiated with a partial conjunctival peritomy, primarily to aid in suture closure of the sclerotomies at the conclusion of the case. Since infants have not developed a pars plana, the eye is entered at the pars plicata, approximately 0.5 mm posterior to the limbus (Fig. 13.1). Similar success rates have been reported using a two-port approach, using an infusing light pipe or pic, and three port-approach using a separate infusion line [22, 24]. Attention to the vector of trocar insertion is critical to avoid damage to the lens. The insertion of the trocar should be perpendicular to the iris plane, rather than pointed toward the center of the eye (Fig. 13.1). If using small gauge instruments (23G, 25G, or 27G), the cannula may be too long to allow access to the far periphery in order to segment the peripheral fibrosis. Therefore, it may be helpful to either insert the instruments directly through the sclerotomies or to partially withdraw the cannulas for peripheral maneuvers.

During the core vitrectomy, attention should be directed toward the vectors of traction. Specifically, an effort should be made to transect the transvitreal ridge to ridge tissue (the "drum head"), ridge to periphery, ridge to lens, and optic nerve head to the ridge (Figs. 13.2 and 13.3). Often, the release of traction will be evident with the relaxation of the

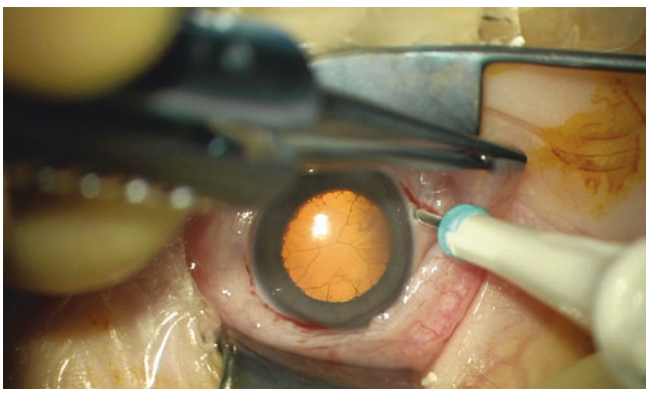

Fig. 13.1 Screen capture demonstrating the location and angle of the trocar insertion. Following a conjunctival peritomy, the trocar is inserted 0.5 mm posterior to the limbus with the angle parallel to the visual axis to avoid trauma to the crystalline lens. Note the persistence of the tunica vasculosis lentis, a common feature of ROP

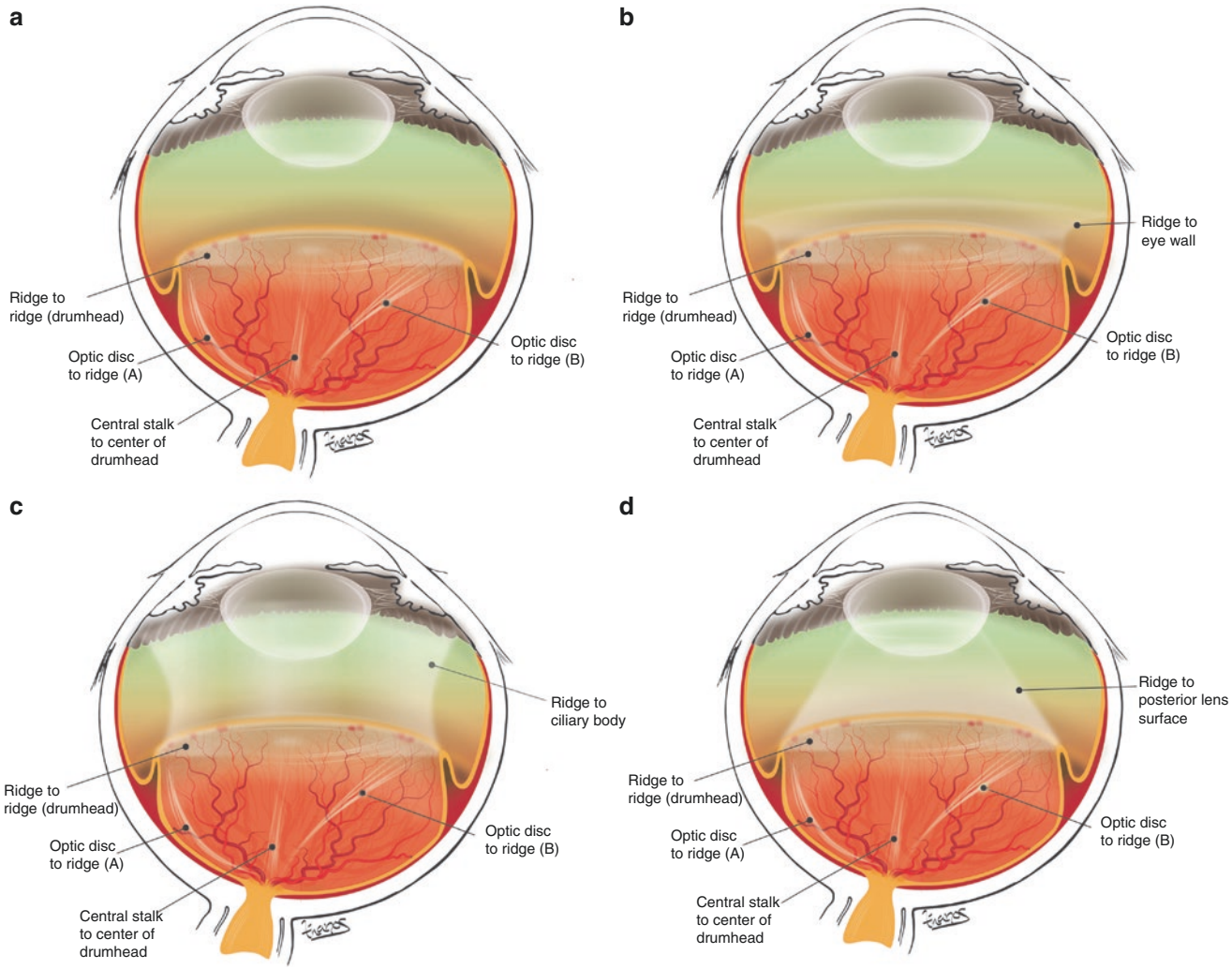

Fig. 13.2 Tractional vectors in ROP. The primary vectors include tissue extending from the optic disc to ridge, and ridge to ridge (**a**), ridge to eye wall (**b**), ridge to ciliary processes (**c**), and ridge to lens (**d**). Successful surgery requires that tractional forces from each of these vectors are adequately transected. Adapted from [35]

tented retina. The vitrector can be used as a pic by gently moving within the vectors of traction without cutting. This will allow the surgeon to see where the traction remains, since the underlying retina will react. These areas should then be addressed until the movement of the underlying retina no longer occurs. Once the dissection is complete, a partial fluid–air exchange is performed to prevent vitreous incarceration into the sclerotomies, and the sclerotomies are sutured. At the conclusion of the case, subretinal fluid is expected, and will reabsorb over the course of weeks to months (Fig. 13.4). During follow-up examinations, the key feature of success is the absence of progression.

In some cases, anterior ridge to ciliary body tissue may create a tight space that risks damage to the crystalline lens by a transvitreal approach. In such instances, an MVR blade can be used to cleave these anterior bands at the time of entry into the eye, an approach described as an *ab interno* incision [36]. The vectors of the initial incision must still be perpendicular to the iris to avoid the lens equator, but can then be turned parallel to the posterior lens capsule to transect the tissue. If the retina is pulled too anterior to safely access the fibrotic tissue bridging between the retina and the lens and ciliary body, then a lensectomy and anterior approach is recommended.

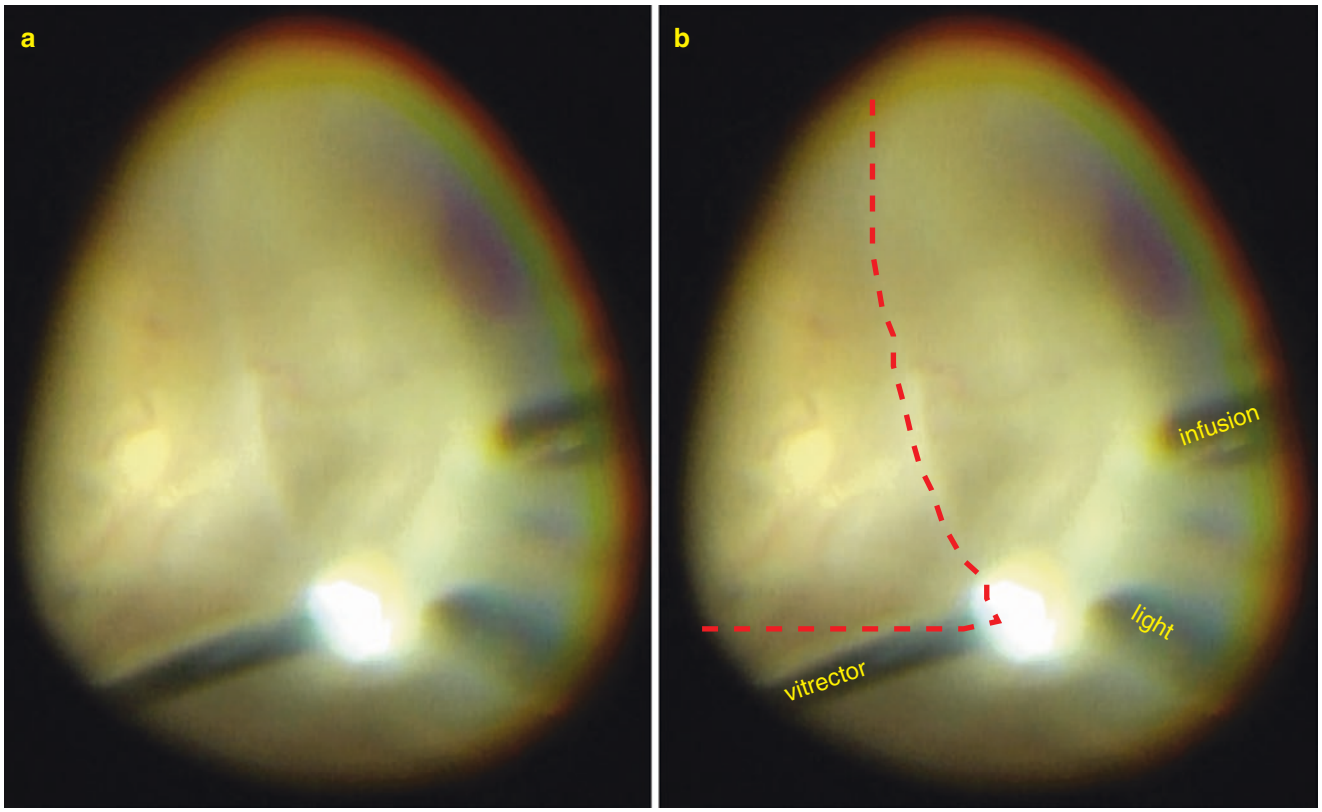

Fig. 13.3 Ridge to eye wall fibrosis. (**a**) Typical intraoperative appearance of ridge to eye wall fibrotic tissue undergoing segmentation using the vitrector. (**b**) Same image, outlining the fibrotic sheet, and the instruments within the eye

13.6 Limbal Approach for Lensectomy and Vitrectomy

Occasionally in Stage 4 ROP, due to anterior fibrosis or a limited view posterior to the lens, a lens-sparing surgery is not possible, necessitating an anterior (translimbal) approach to lensectomy and vitrectomy. In such cases, an inferotemporal or inferior infusion cannula is placed at the limbus, and limbal incisions are then made superonasally and superotemporally. The anterior lens capsule is incised using the trocar blade, and the crystalline lens nucleus and cortex are aspirated with the vitrector. Since the capsule can serve as a scaffold for subsequent fibrosis and traction, which can be very difficult to safely remove, it is recommended the capsule is entirely removed when a lensectomy is performed for ROP surgeries. The edges of the capsule can be easily visualized by externally illuminating through the cornea with the light pipe, and grasping the capsule edge using membrane forceps. Once the zonules are released, the capsule can be removed in a single sheet through the limbal incisions. Once the lens and capsule are removed, the anterior fibrosis can be safely accessed and dissected.

13.7 Minimal Intervention to Achieve Surgical Goals

The goal of Stage 4 ROP surgery is to relieve the vectors of traction. It must be emphasized that aggressive maneuvers during ROP surgery are extremely high risk and should be avoided. Creating an iatrogenic break carries a near certain consequence of massive fibrous proliferation with a devastating outcome. Although it may be tempting to shave close to the retinal surface while addressing fibrosis, such maneuvers are generally unnecessary to achieve surgical goals. In rare cases, a vitrectomy in a child without removing the posterior hyaloid can lead to posterior hyaloid contraction syndrome [37]. Nevertheless, to avoid the risk of iatrogenic breaks, routine removal of the adherent vitreous cortex is not recommended during ROP surgery.

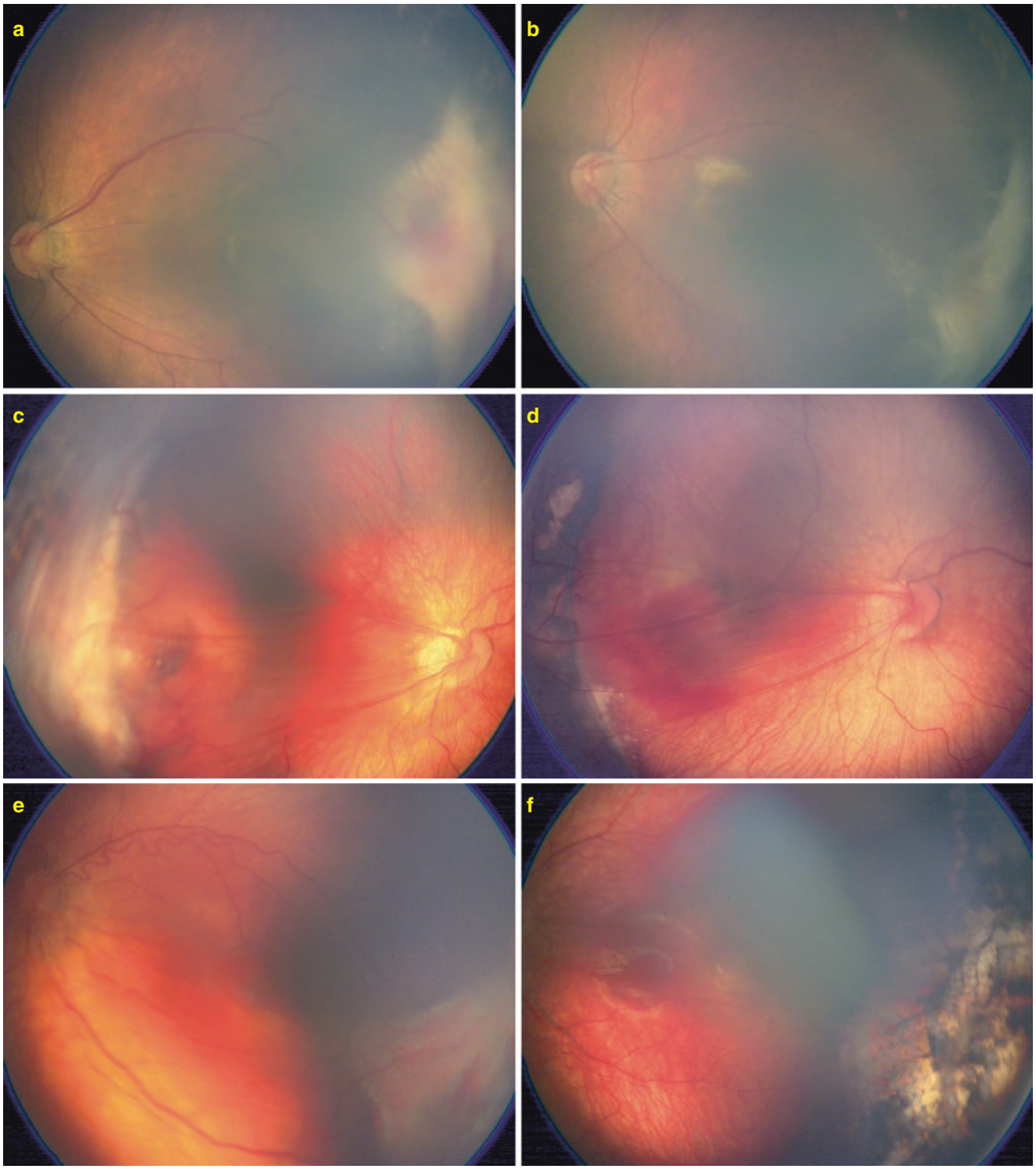

Fig. 13.4 Resolution of subretinal fluid following LSV for Stage 4 ROP at various time intervals. (**a**) Preoperative appearance of Stage 4A ROP. (**b**) Postoperative appearance of the same eye 2 weeks following LSV. The turbid subretinal fluid is improved, but not yet resolved. (**c**) Preoperative appearance of stage 4B ROP, with circumferential traction and subretinal fluid involving the fovea. (**d**) Postoperative appearance 5 weeks following LSV, showing near-complete resolution of subretinal fluid with residual subretinal hemorrhage and temporal dragging. (**e**) Preoperative appearance of Stage 4A ROP. (**f**) Postoperative appearance 10 weeks following LSV showing complete resolution of subretinal fluid

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