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Case Report

Macula-Off Retinal Detachment with Refractory Macular Hole Previously Closed with Autologous Platelet-Rich Plasma: A Case Report

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Keywords
Full-thickness macular hole · Retinal detachment · Autologous platelet-rich plasma · Vitreoretinal surgery · Case report

Abstract
The purpose of this report was to present a case of a refractory full-thickness macular hole (FTMH) complicated with recurrent retinal detachment (RD) previously treated with an autologous platelet-rich plasma (aPRP) plug. A 65-year-old male patient presented to our department with a FTMH, RD, and a giant retinal break. Preoperative best corrected visual acuity (BCVA) was 1.40 logMAR (20/500). A 25-G pars plana vitrectomy (PPV) was performed, with peripheral retinal-breaks laser barrage, peeling of the internal limiting membrane, and silicon oil injection. One month later, spectral domain optical coherence tomography (SD-OCT) showed the persistence of the FTMH with a diameter of 712 μm. Therefore, the patient underwent silicon oil removal and aPRP injection with good anatomical outcome and improvement of BCVA to 0.6 log-MAR (20/80). Two months later a recurrence of macula-off RD was detected, but SD-OCT showed that the aPRP plug was still in place and kept the two margins of the macular hole together. The patient underwent a further PPV with silicon oil injection and subsequent silicon oil removal with no postoperative complications. Two months later, the retina remained attached, SD-OCT confirmed FTMH closure and BCVA was 0.52 logMAR (20/63). In conclusion, this case report aims to underline the remarkable efficacy of aPRP in promoting FTMH closure, which was maintained despite subsequent recurrence of macula-off RD.

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Introduction

The definition of a refractory full-thickness macular hole (FTMH) includes both a recurrent macular hole (MH) after previous surgical closure, and a persistent FTMH that remains unclosed after surgery [1]. The incidence of refractory FTMH is extremely variable, depending on several intraoperative and postoperative factors. Jackson et al. [2], for instance, reported an occurrence of refractory FTMH in 4.2% of patients after pars plana vitrectomy (PPV) with peeling of the internal limiting membrane (ILM) and gas tamponade. Several techniques have been proposed for the treatment of refractory FTMH, such as lens capsular flap, autologous ILM transplant, autologous retinal transplant, amniotic membrane plug, or autologous platelet-rich plasma (aPRP) [3–8].

In our paper, we report a case of refractory FTMH treated with aPRP injection which maintained its closure despite subsequent macula-off retinal detachment (RD). The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000530199).

Case Presentation

A 65-year-old man presented to our department complaining of important and rapid reduction of visual acuity (VA) in his left eye in the last days. He reported that the vision in his left eye had continued to decline over the past 6 months but had further deteriorated rapidly over the past week. Past medical history was negligible except for previous uneventful bilateral cataract surgery more than 5 years ago. He underwent a complete ophthalmological examination including determination of best corrected visual acuity (BCVA), slit-lamp microscopy, Goldmann tonometry, dilated fundus examination, and spectral domain optical coherence tomography (SD-OCT) (Spectralis HRA-OCT, Heidelberg Engineering). BCVA was 1.40 logMAR (20/500). The fundus examination revealed a FTMH with macula-off RD and a giant peripheral retinal break in the superior retinal quadrants. The SD-OCT confirmed the presence of a FTMH and macula-off RD (Fig. 1a).

Two days later, the patient underwent a 25-G PPV. The surgeon performed ILM peeling, laser photocoagulation to treat peripheral giant retinal break, and silicone oil injection, with successful retinal reattachment. However, after 1 month, SD-OCT examination showed the persistence of the FTMH with a diameter of 712 μm (Fig. 1b). BCVA was 1.0 logMAR (20/200).

Given the high risk of non-closure of the hole, as well as the overall clinical picture already complicated by the previous RD, the surgeon opted for silicon oil removal and injection of aPRP to promote hole closure. Surgery was performed 2 months after the previous one.

The autologous platelet-rich plasma was prepared for injection in cooperation with the Blood Bank of our hospital, according to an in-house validated protocol. A few hours before surgery, a trained nurse obtained a sample of 20 mL of whole blood of the patient by venipuncture. The sample was collected in sterile tubes (VI 1 PRP BiomedDevice, Italy) with acid citrate dextrose and the carried to the Blood Bank. There, the sample was manipulated in a class A area under laminar flow hood and was centrifuged for 12 min at 1,500 RPM. The plasma supernatant fraction was isolated and transferred into tubes with no anticoagulant (VI 2 PRP BiomedDevice, Italy). The supernatant was then centrifuged again at 1,800 RPM for 25 min. After the second centrifugation, the upper portion of the plasma in the tube has a low concentration of platelets, whereas in the lower portion of the

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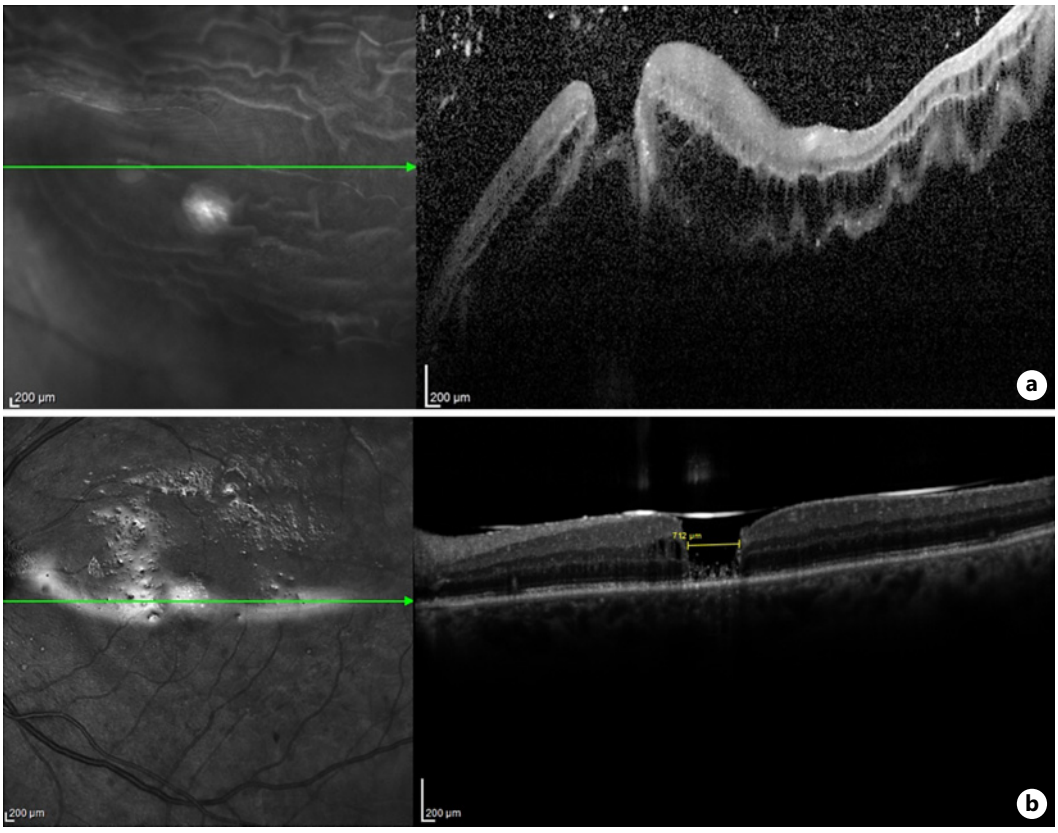

Fig. 1. a Baseline SD-OCT examination with FTMH and macular detachment. **b** 1 month postoperative SD-OCT showing FTMH and ILM peeling.

tube a platelet pellet is deposited. This pellet was then suspended in circa 1 mL of plasma so to obtain an estimated concentration of 1×10^6 platelets/1 mL ± 20%. The aPRP was then ready for use and was transported back to the operating room approximately 4 h after its collection.

The surgeon performed a 25G PPV approach with silicon oil removal, balanced saline solution-air exchange, injection of 0.1 mL of aPRP directly at foveal level and 20% sulfur hexafluoride (SF6) tamponade. The patient was asked to maintain a supine position for 4 h to promote aPRP adhesion to retinal tissue and subsequentially to maintain a supine position or downward gaze to promote MH closure.

Two weeks later, after gas tamponade reabsorption, BCVA reached 0.6 logMAR (20/80). SD-OCT examination showed FTMH closure and adequate positioning of aPRP plug (Fig. 2a).

At the 2 months postoperative follow-up visit, the patient again complained of recent VA reduction. A recurrent macula-off RD was detected, with a newly developed retinal break posteriorly to the previous laser barrage. BCVA was reduced to 1.70 logMAR (<20/800). Inquisitively, SD-OCT images showed that the aPRP plug was still in its original position despite the foveal detachment and that it kept the retinal tissue intact with no recurrence of the MH (Fig. 2b).

25-G PPV was again performed with subretinal fluid drainage, laser barrage of the retinal break, and silicone oil injection. Two weeks after surgery, BCVA was 0.7 logMAR (20/100), and fundus examination and SD-OCT showed successful attachment of the neuroretina with no recurrence of FTMH (Fig. 3a). Silicon oil was then removed after 2 months with no postoperative complications or recurrence of RD. At final follow-up visits, another 2 months

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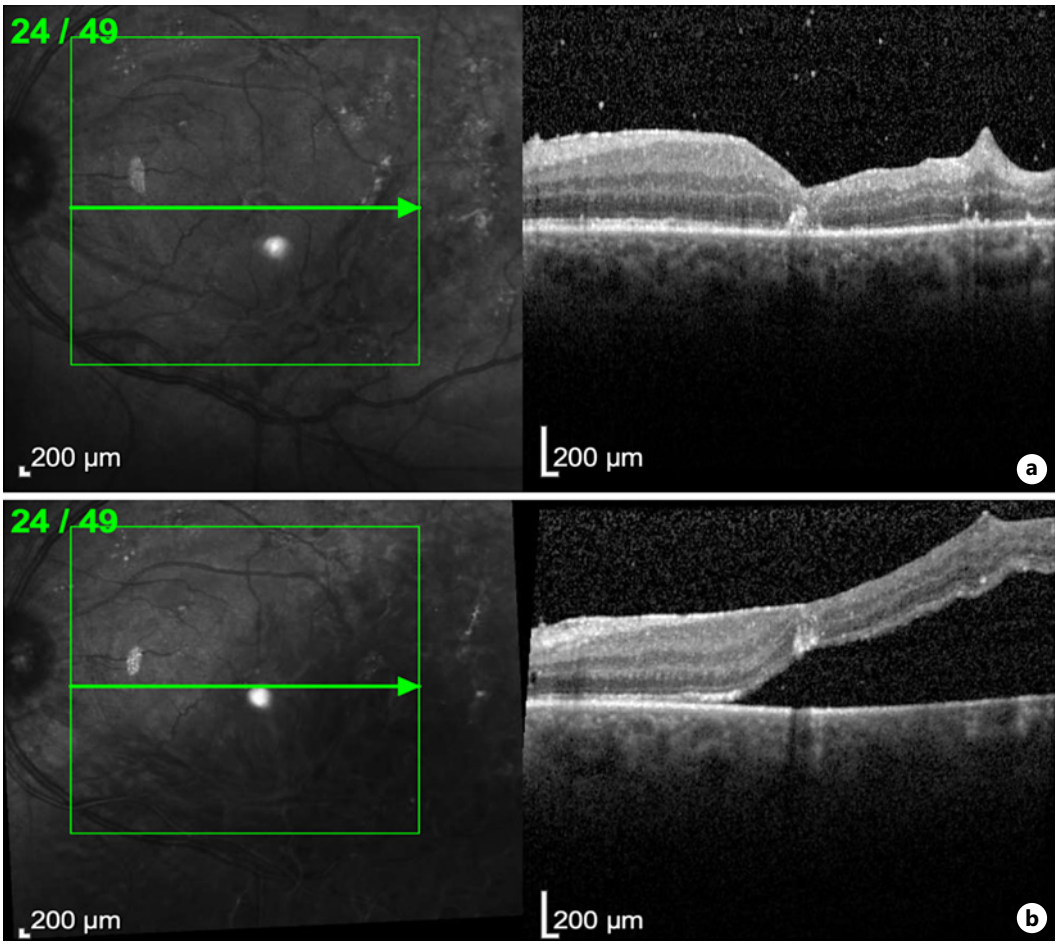

Fig. 2. a MH closure after aPRP injection. **b** Foveal detachment with aPRP plug in position.

later, there was no recurrence of RD. The SD-OCT images showed complete reabsorption of the aPRP plug with full-thickness integrity of the neuroretina, minimal intraretinal fluid, and partially visible external limiting membrane and ellipsoid zone. BCVA further improved up to 0.52 logMAR (20/63) (Fig. 3b).

Discussion

In 1995, Gaudric et al. [8] proposed for the first time the injection of aPRP as the second-line treatment for refractory FTMH. Several subsequent papers reported that platelet concentrate usage was associated with an increase in both idiopathic and refractory FTMH rate of resolution [9, 10].

In the case we report, considered the very large diameter of the refractory MH after the first surgery, the surgeon chose to use aPRP plugging because of its ease of use and reduced postoperative complications. The injection of aPRP into the MH is an easier approach for refractory MHs, especially if compared to other techniques such as lens capsular flap [4], autologous ILM transplant [7], autologous retinal transplant [6], or amniotic membrane plug [5], in terms of easier surgical technique, reduced surgical time, and reduced postoperative complications.

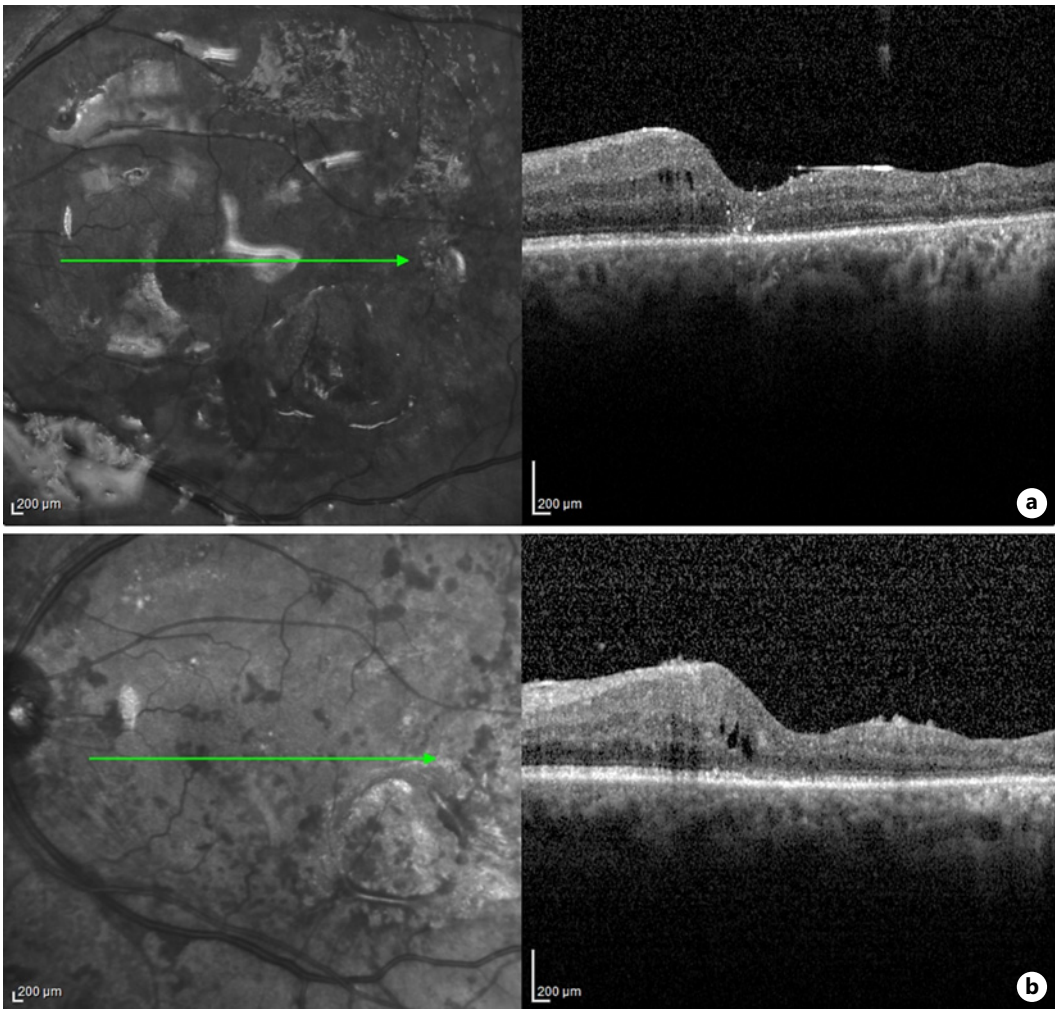

Fig. 3. a Silicone oil in vitreous chamber and foveal reattachment. **b** Final follow-up SD-OCT.

This procedure could potentially be applied to all refractory FTMH types, in which other strategies are contraindicated or just not feasible. For instance, in myopic eyes, obtaining an ILM-free flap could be challenging, moreover in such cases autologous retinal transplant could be contraindicated. Furthermore, patients with recurrent MH usually already underwent cataract surgery with posterior laser capsulotomy, so it could not be possible to use a lens capsular flap transplantation technique. Instead, aPRP injection can be safely performed on a wider number of eyes with different postsurgical conditions.

Early postoperative SD-OCT images of our case showed aPRP plug as a hyperreflective material within the fovea with MH closure. Surprisingly, the SD-OCT examination performed subsequently, when the second RD occurred, showed that the foveal plug had remained in its original position, maintaining the MH closed despite the presence of fluid underneath the neurosensory retina. This may not be surprising, as, according to Burmeister [11], the aPRP plug is capable of stimulating different mechanism of repair in the retinal tissue and thus promoting MH closure. After their injection, platelets produce various growth factors that stimulate Müller cells, such as platelet-derived growth factor, fibroblast growth factor, and others [11]. These factors induce tissue repair by stimulating glial cell proliferation, production of collagen and basement membrane, enhancing restoration of physiological foveal

architecture. It is also possible to speculate that aPRP-induced biomechanical changes at the retinal level and in particular the contraction of the MH may have contributed to the creation of the secondary retinal rupture located posteriorly to the laser treatment performed in the first surgery, propagating the tractional forces even more peripherally.

Conclusion

We believe this case is a fortuitous real-life example of the extent of the structural changes that aPRP plug can trigger in neuroretina after its injection. The biochemical and ultrastructural changes induced by the aPRP allowed the margins of the hole to remain closed despite the conspicuous mechanical stress brought about by the subretinal fluid as well as the intraretinal tractional forces themselves. This case also confirms that aPRP is an easy, low-risk, and versatile technique that can be successfully applied with both anatomical and functional improvement. Moreover, although a single case is not sufficient to draw broader conclusions and further studies are needed, it appears that aPRP is also a safe and "successful" technique even in cases of postoperative complications such as relapsed RD.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Any reference to the patient in this case report has been removed and the images are anonymous. Ethical approval is not required for this study in accordance with local and national guidelines.

Conflict of Interest Statement

All the authors have no conflict of interest to declare.

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Author Contributions

Guglielmo Parisi, Federico Ricardi, Giacomo Boscia, Andrea Ghilardi, Francesco Gelormini, Paola Marolo, Matteo Fallico, and Michele Reibaldi were equally involved in the design and implementation of the study and participated in the writing of the paper. Serigo D'Antico and Marika Salafia have been contributing in standardizing the aPRP preparation procedure and drafting the methods section. All authors approved the final version of this manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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