

Case Report

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# Vitreotomy with Silicone Oil Tamponade and Single-Dose Intravitreal Methotrexate for Recurrent Retinal Detachment with Proliferative Vitreoretinopathy

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## Keywords

Retinal detachment · Proliferative vitreoretinopathy · Vitreoretinal surgery · Silicone oil · Intravitreal methotrexate

## Abstract

Our case emphasizes the approach of a single-dose of intraoperative methotrexate (MTX) – applied directly into silicone oil – to arrest the anomalous progression of proliferative vitreoretinopathy (PVR). A 78-year-old male presented with severe vision loss secondary to a pseudophakic macula-off rhegmatogenous retinal detachment oculus sinister (OS). He was initially treated with primary pars plana vitrectomy and intraocular gas; however, the patient developed recurrent macula-off retinal detachment complicated by proliferative vitreoretinopathy OS. Subsequent management involved vitrectomy with membrane removal, silicone oil tamponade, and adjuvant intravitreal MTX. The patient had an uneventful postoperative recovery with a dramatic vision improvement after silicone oil removal OS. Here, we highlight the use of silicone oil tamponade with single-dose adjuvant MTX for the management of complex retinal detachment associated with proliferative vitreoretinopathy.

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## Introduction

Recurrent rhegmatogenous retinal detachments (RDs) are most commonly caused by proliferative vitreoretinopathy (PVR), with an incidence of approximately 5–10% for all RD cases [1]. Overall, 75% of RD surgical failures are precipitated by recurrent PVR, resulting in the need for multiple surgical interventions [1–3]. PVR is typified by the emergence of proliferative epiretinal fibrocellular membranes, with or without the presence of subretinal membranes [1, 2]. Contraction of these preretinal membranes causes subsequent complex tractional RD [1, 2].

A complete understanding of PVR pathophysiology remains elusive, but it is believed that retinal pigment epithelial (RPE) cells are involved via an anomalous injury-repairing mechanism blood-retinal barrier compromise [1–4]. Epithelial to mesenchymal transition (EMT) of migrated RPE cells into contractile myofibroblasts produce the offending extracellular matrix of the periretinal fibrocellular membranes [1, 2]. Concomitant activation and migration of astrocytes, glial cells, and immune cells are observed and augments the intricacy of the fibrocellular membranes [1–4]. Significant risk factors for PVR formation after uncomplicated primary RD repair include cigarette smoking, macula-involvement, large-gauge vitrectomy, and preexisting ocular inflammation or uveitis [1, 4].

Current surgical treatments for PVR include pars plana vitrectomy (PPV), scleral buckling, long-acting tamponade (e.g., silicone oil), and membrane removal [1, 5]. Adjuvant therapies aimed at reducing inflammation include corticosteroids, 5-fluorouracil, and methotrexate; the latter have all conveyed inconsistent efficacy results [1, 3, 6]. Methotrexate (MTX), a folate (vitamin B9) analog, and competitive dihydrofolate reductase inhibitor [2, 7, 8], prevents the regeneration of an essential cofactor (tetrahydrofolate) in the eukaryotic thymidine and purine ring synthesis pathways, resulting in halted DNA and RNA synthesis and subsequent cellular death, particularly for rapidly proliferating cells [9]. Intraocular preparations of MTX are typically concentrated to less than 400 µg/0.10 mL (usually in silicone oil) and have a therapeutic half-life of 3–5 days [2, 7, 10, 11]. At this dosage, MTX inhibits cellular proliferation and suppresses immune cell-mediated cytokine production, which addresses the observed RPE EMT and immune cell proliferation observed in PVR [2, 7, 8, 10, 11]. Current studies are assessing multiple-dose paradigms; however, our case is unique in the use of a single intraoperative intravitreal MTX application.

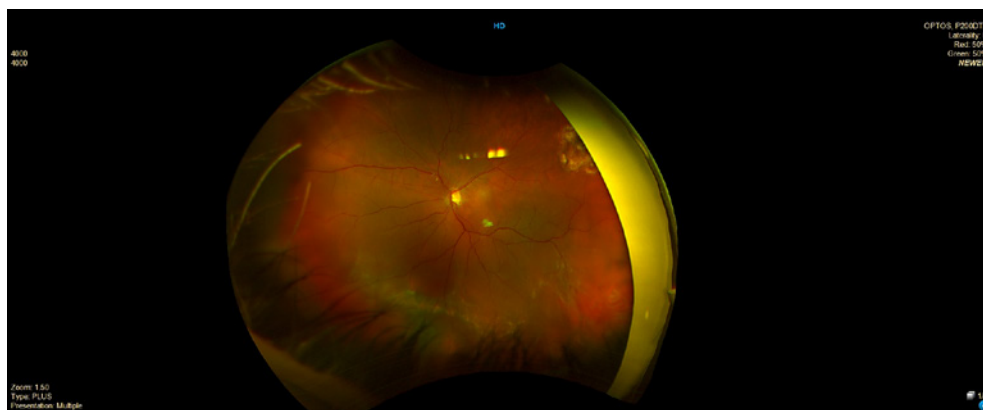
Here, we present a case of a recurrent pseudophakic macula-off RD complicated by PVR. Initial treatment included PPV and intraocular gas; however, recurrent RD with PVR was subsequently successfully managed with vitrectomy, membrane removal, and silicone oil tamponade with adjuvant single-dose intravitreal MTX. This case highlights the therapeutic utility of single-dose intravitreal MTX and silicone oil tamponade for complex RDs associated with PVR.

## Case Report

A 78-year-old white male presented with a 2-day history of severe vision loss OS (20/400). Examination revealed posterior vitreous detachment, rhegmatogenous RD (extending 1:00 clockwise to 7:00) with macular involvement (Fig. 1). There were multiple peripheral retinal tears in the superotemporal and inferotemporal retinal quadrants. No retinal vascular occlusion, macular hemorrhage, disc edema, or disc pallor were present. Past medical history was relevant for type 2 diabetes mellitus, hypertension, and previous coronary artery bypass grafting. Initial surgical intervention included primary 25-gauge PPV and endolaser with 14% C3F8 intraocular gas tamponade.



**Fig. 1.** Preoperative widefield fundus image.

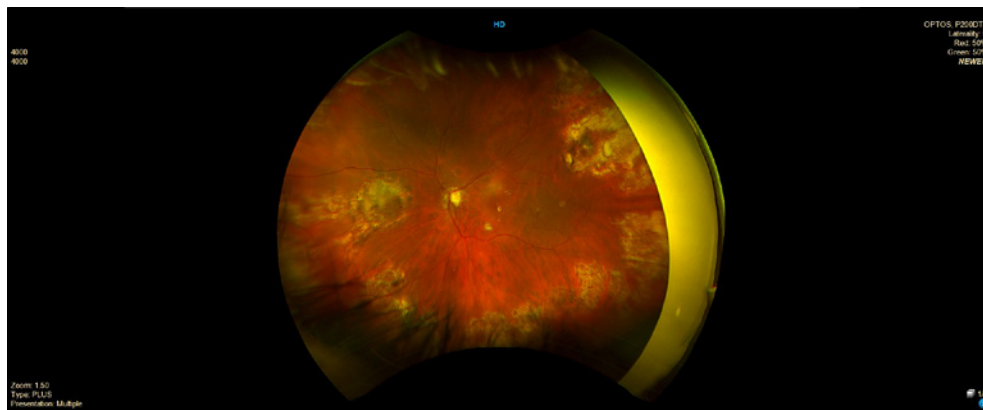


**Fig. 2.** Redetachment widefield fundus image.

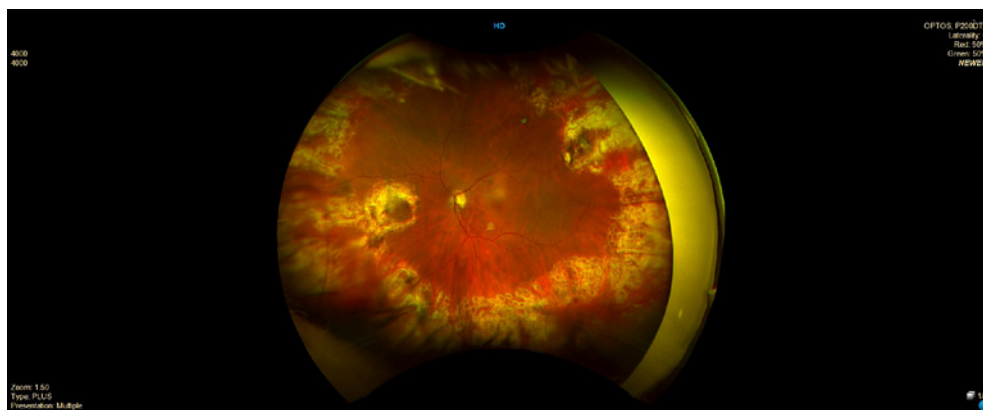
Four months after primary repair, the patient presented with a complex macula-off retinal detachment (Fig. 2) with grade C PVR (predominantly involving the inferior retinal periphery). Subsequent surgical management included 25-gauge PPV with membrane removal, endolaser, and silicone oil (1,000 centistoke) tamponade. Intraoperatively after silicone oil placement, a single dose of 0.10 mL (400 µg) MTX was administered into the silicone oil. At 4 months follow-up, there were no signs of recurrent detachment or PVR (Fig. 3). The patient later underwent 25-gauge PPV with silicone oil removal. At final follow-up, 5 months after silicone oil removal, the patient had no recurrent PVR (Fig. 4), and a final postoperative visual acuity of 20/40 OS.

## Discussion

The most common cause of primary retinal detachment failure is PVR, and over 75% of RD surgical failures are precipitated by new-onset or recurrent PVR [1–3]. Unfortunately, PVR continues to present considerable challenges for vitreoretinal surgeons and often necessitates multiple surgical interventions. The prevalence of PVR in the context of RD repair – which has been known for nearly half a century – remains at a similar 5–10% of RD cases [1]. This subset of complex RDs may be managed surgically via PPV, scleral buckle, membrane removal, and long-acting tamponade.



**Fig. 3.** Silicone oil tamponade widefield fundus image.



**Fig. 4.** Oil removed (final) widefield fundus image.

Recently, there has been a resurgence in the use of adjuvant therapies like MTX, corticosteroids, and 5-fluorouracil for the management of PVR-associated complex RD [1, 3, 6]. MTX is an antineoplastic agent that inhibits dihydrofolate recycling for DNA synthesis in proliferative cells, such as those observed in the pathophysiology of PVR. Another mechanism of MTX in the treatment of PVR is the inhibition of the cytokine IL-6, which is implicated in the fibrogenesis observed in PVR and is a suggested therapeutic target [12, 13]. Worth noting, a case-control study evaluating the vitreous cytokine levels in PVR did not identify corticosteroid pathways as therapeutic targets, which supports the inconsistent efficacy results of corticosteroid treatment for PVR [12].

Initial case series utilizing adjuvant MTX for PVR produced promising results [2, 7, 10, 11]; moreover, the current ongoing GUARD (gain understanding against retinal detachment) trial employs a multiple-dose postoperative MTX regimen [14]. While results are pending, limitations of multiple MTX doses in the postoperative period are patient discomfort, need for more frequent visits, and addressing renumeration for procedures performed in the postoperative global period.

Our case emphasizes the approach of a single-dose of intraoperative MTX – applied directly into silicone oil – to arrest the anomalous progression of PVR. Whereas undiluted MTX is toxic to the neurosensory retina, and diluted concentrations up to 400 µg/0.10 mL have been demonstrated to be tolerable without toxicity and effective at inhibiting the RPE EMT immune

cell proliferation observed in PVR [2, 7–9]. This single-use MTX paradigm mitigates the need for multiple postoperative procedures and minimizes patient discomfort. While we recognize the need for larger comparative studies, our case supports single-dose MTX in silicone oil as a possible valuable pharmacological adjuvant in the armamentarium of PVR management.

## Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

## Conflict of Interest Statement

The following authors have no financial disclosures: Adrian Babel, Eric K. Chin, and David R.P. Almeida.

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## Author Contributions

Adrian Babel: conceptualization, methodology, data curation, visualization, validation, investigation, writing – original, reviewing, and editing. Eric K. Chin: methodology, validation, writing – reviewing and editing. David R.P. Almeida: conceptualization, methodology, data curation, visualization, supervision, validation, investigations, writing – reviewing and editing. Adrian Babel, Eric K. Chin, and David R.P. Almeida attest that they meet the current ICMJE criteria for authorship.

## Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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