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Case Report

Autologous Retinal Transplant Repeat Surgery after Initial Graft Failure: A Case Report

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Autologous retinal transplant · Refractory macular hole · Graft dislocation

Abstract
Autologous retinal transplant (ART) has become an increasingly explored surgical option for managing large chronic holes refractory to standard surgical treatments. However, management strategies for patients who already failed a previous ART are less well-understood. Here, we report on a case of a successful repeat retinal transplant for a refractory macular hole after a previously dislocated ART graft. Subretinal injection of balanced salt solution was used to partially elevate the macular hole and secure the edge of the harvested retinal graft under the edge of the macular hole in the second operation. Postoperatively, the patient developed intraretinal fluid within the retinal graft with an appearance similar to cystoid macular edema, which was controlled with topical steroids. In addition, two separate choroidal neovascular membranes along the subretinal injection sites were seen and treated with vascular endothelial growth factor downregulation. This case illustrates successful repeat ART surgery, but further optimization of ART surgical techniques is necessary to minimize ART's complication rate.

Introduction

Autologous retinal transplant (ART) has become increasing explored surgical option for managing chronic large macular holes (MHs) refractory to standard treatments [1, 2]. A recent large retrospective multi-center study found patients with large MHs could achieve good anatomic results with ART in 89% of refractory MHs, and improvement in visual acuity in 43% of the eyes by three lines or more [3]. Intraoperative complications of ART can

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include graft slippage, undersized graft, subfoveal RPE hemorrhages, and intraoperative hemorrhages [3, 4]. Postoperative complications of ART can include retinal detachment, vitreous hemorrhage, endophthalmitis, proliferative vitreoretinopathy, graft dislocation, and perfluorocarbon (PFO) in the sub-ART space [3–5]

ART is typically reserved for refractory MHs that have previously failed the more standard surgery with vitrectomy, peeling of the internal limiting membrane (ILM), and gas tamponade, when repeating the standard procedure is expected to be of limited benefit [2]. If the ART procedure also fails, further options are limited.

The herein wish to report a case of repeat ART surgery after failed ART, due to first graft dislocation. To our knowledge, such a situation has only been reported once previously [4].

Case Report

Here, we report a case of a patient who had repeat ART surgery after failed ART, due to first graft dislocation. The patient has consented in writing to the publication of his case. This case is also part of a case series approved by the Institutional Review Board of University Hospitals Cleveland Medical Center. 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/10.1159/000534142).

A 78-year-old Caucasian male presented with a chronic MH in the right eye measuring 655 μm in the narrowest diameter, as shown in Figure 1. His past ocular history was notable for the repair of a macula-involving retinal detachment with pneumatic retinopexy several years prior that developed after cataract surgery. His best-corrected visual acuity was 20/200 in the right eye. He initially underwent a 25-gauge pars plana vitrectomy with ILM peel, placement of ILM flat over the MH, and C3F8 gas tamponade with positioning for several days, which was unsuccessful in closing the MH. Due to the size of the MH and previously failed surgery, decision was made to proceed with an ART. An oversized ART graft was harvested superior to the optic nerve and placed over the MH with PFO tamponade. Repeat vitrectomy with PFO removal and C3F8 gas tamponade was performed 2 weeks later. As shown in Figure 2a, initial follow-up found a well-centered graft with the closure of the MH, with subjective improvement in vision. Patient's vision the time, viewing through the gas, was at 20/400. However, by postoperative week three, soon after the resorption of gas, the patient returned with decreased vision back to baseline. On exam, the MH was noted to be reopened, and the ART graft completely dislodged, as shown in Figure 2b and c.

Given the patient's subjective visual improvement with the previous graft in place, the decision was made to attempt repair of the MH with repeat ART, as shown in the accompanied surgical online supplementary Video. 25-gauge pars plana vitrectomy with a chandelier accessory light source was utilized. An area superonasal to the optic nerve, adjacent to the first graft site, was selected as the second graft harvest site. An area of approximately 150% of the MH, estimated intraoperatively, was harvested as the graft. A 38-gauge cannula was then inserted through the retina at several sites adjacent to the MH, and used to inject buffered saline solution into the subretinal space and slightly elevate the MH. After the retinal graft placement, the edges of the graft were then manipulated under the edge of the MH, in order to better secure the second graft. PFO was again used to tamponade the graft, with repeat vitrectomy, PFO removal, and C3F8 gas placement 2 weeks later.

At postoperative month one, the hole was closed on exam and optical coherence tomography (OCT) imaging. Some slippage of the graft at the nasal edge was noted on OCT imaging at postoperative month two but has remained non-progressive and outside the central fovea for approximately 1 year, as shown in Figure 3b. His best-corrected visual acuity in the right eye improved to 20/100 at postoperative month one and 20/60 at postoperative

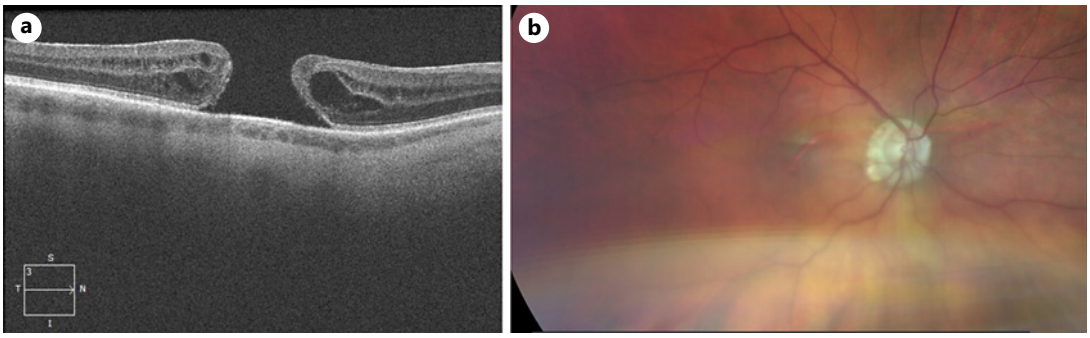

Fig. 1. Optical coherence tomography (OCT) of the macular hole (**a**) and color fundus photo of the fundus prior to both ART procedures (**b**).

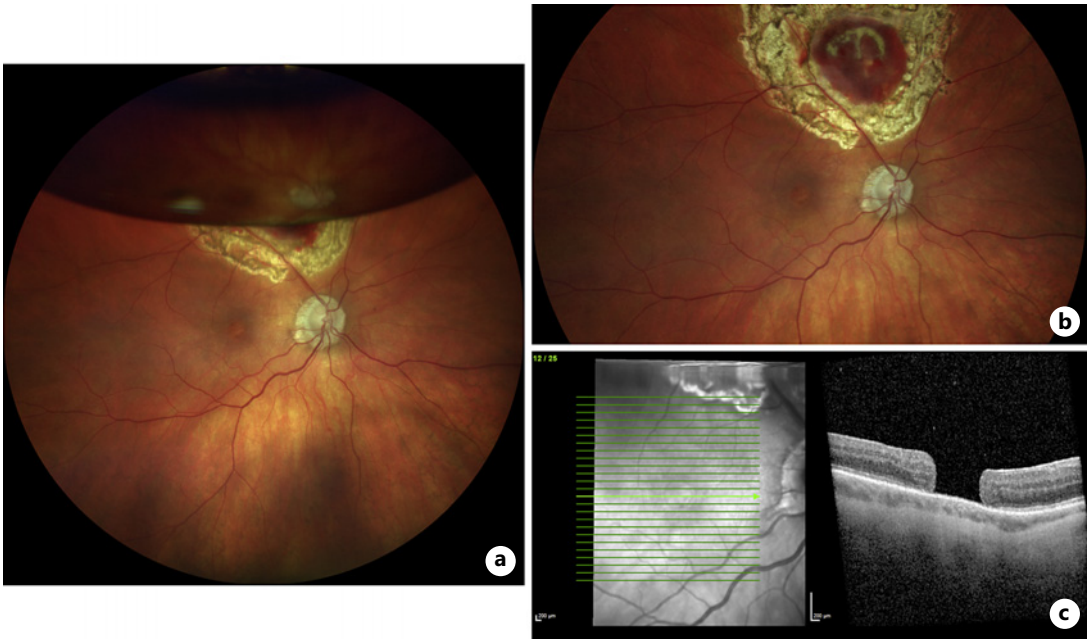

Fig. 2. Color fundus photo after first ART surgery with graft initially within the macular hole with superior gas (**a**). Color fundus photo at postoperative week three showing graft now dislodged from the macular hole (**b**). OCT showing dislodged graft (**c**).

month two. Inner retinal edema in the graft with an appearance similar to cystoid macular edema was observed at postoperative month 6, which was treated with topical steroids with gradual improvement. At postoperative month three, two separate choroidal neovascular membranes (CNVM) were seen at the sites of previous interoperative subretinal balanced salt solution (BSS) injection, presumably from Bruch's membrane compromise, as shown in Figure 3a. The patient was subsequently treated with monthly injections of aflibercept with slow involution of the CNVM changes, and his vision remained stable between 20/60 and 20/70 at postoperative month 18. OCT imaging over the past 18 months has shown continued graft integration into the original MH, as shown in Figure 3d and e. Subjectively, patient noted stability in his vision postoperatively after his repeat ART.

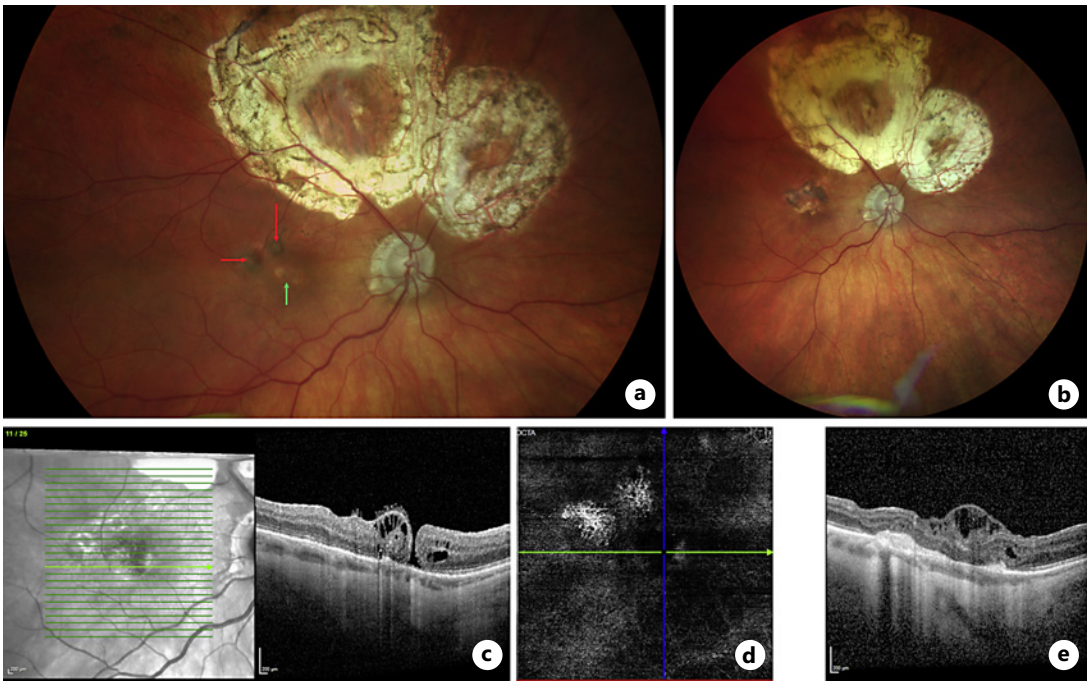

Fig. 3. Color fundus photo at postoperative month four showing the graft within macular hole (green arrow) and adjacent two areas of CNVM (red arrows) (**a**). OCT at postoperative month four showing graft integration to the host tissue with slight graft "slippage" nasally (**b**). OCT angiography of the avascular layers at postoperative month three showing two areas of choroidal neovascular membranes near the macular hole (**c**). Color fundus photo at postoperative month 18 (**d**). OCT showing graft integration and "CME-like" inner retinal edema (**e**). CME, cystoid macular edema.

Discussion

In this case report, we described a case of repeat ART in an eye with refractory MH following graft dislocation from the initial ART. Successful graft placement was possible with bimanual manipulation of the graft and elevation of MH edges with subretinal BSS injection, allowing for placement of the graft edges under the host retina. The second graft has remained in place with stable central vision. Late-developing CNVMs at the sites of the subretinal cannula insertion initially noted at postoperative month 18 have remained stable with continued anti-vascular endothelial growth factor treatments.

Conventional treatment strategies for MHs are well-described, typically including vitrectomy, peeling of the ILM, gas tamponade, and frequently a period of postoperative face-down positioning [6, 7]. The prognosis of this strategy is generally very good, with an anatomic MH closure rate approaching 100% [5]. Most patients also gain at least two lines of visual acuity in various studies [8].

Treatment for refractory MHs, however, is more challenging. Described treatment options include repeat vitrectomy with larger ILM peel, autologous ILM transplant, silicone oil tamponade, autologous platelet concentrate transplantation, and amniotic membrane transplantation, among others [9–13]. Visual results are unpredictable but generally improve if the closure of the MH is successful [10, 13].

Most recently, ART has been considered as a promising option for chronic refractory MHs [3, 5]. ART for refractory MHs has been associated with good anatomical closure rates as well

as improved visual acuity [3, 5]. Given that ART is indicated for treatment for refractory MHs already, a repeat ART is indicated as the "last resort" for patients who have failed other surgical treatments discussed above.

The proposed rationale for ART involves the transplanted neurosensory retina serving as a scaffold for MH closure, allowing for better structural integration and revascularization of the graft by promoting centripetal migration of tissue from the MH edges [14]. ART may also promote adaptive synaptogenesis, which possibly allows the rebuilding of functional connections between photoreceptors and bipolar or horizontal cells [15].

Our case offers insights regarding the surgical techniques of ART and the potential for a repeat procedure after the initial failure of the graft to integrate. From our experience in this case, it appears as though placement of the graft edges under those of the MH allows for improved long-term stability of the graft. In addition, the initial failure of an ART does not preclude placement of a second graft, although this does require a second harvest site with the associated risks. Finally, the known complication of CNVM developing at the site of subretinal injection of BSS, presumably from Bruch's membrane disruption, is demonstrated in the case. Thus far, the CNVM has been successfully treated with anti-vascular endothelial growth factor downregulation.

Other rare complications of ART include partial dislodgement of graft, sub-ART PFO, delayed proliferative vitreoretinopathy, retinal detachment, high intraocular pressure, and endophthalmitis [3, 4]. Larger series or studies would be useful to better elucidate these risks and optimize technical details, such as the ideal graft size and the benefit of using PFO for tamponade versus other agents. In addition, other ART-related issues such as the incidence and the optimal treatment of "CME-like" edema in the inner layers of the graft, functional testing of the graft, and potential late revascularization of the graft are yet to be fully understood. Lastly, our experience showed that if subretinal injections of BSS are placed, careful surveillance for future CNVM development is prudent for early detection and treatment of this potential complication.

Conclusion

Repeat ART surgery following initial ART failure can be considered to improve vision. Securing the edges of the graft under elevated edges of the MH seems to be important to reduce the risk of graft dislocation. Late complications, including graft "slippage" and late CNVM at the site of subretinal injection of BSS are possible and continued postoperative monitoring is indicated.

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Statement of Ethics

This case report is part of the case series approved by University Hospitals Cleveland Medical Center Institutional Review Board (STUDY20230203).

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

Authors have no conflicting interests that need to be disclosed.

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Author Contributions

Conceptualization and supervision: W.S.; writing – original draft preparation: T.C. and J.C.; writing – review and editing: W.S. and A.M.; project administration: T.C.; all authors have read and agreed to the published version of the manuscript.

Data Availability Statement

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

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