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Macular Translocation with 360-Degree Retinotomy for Management of Retinal Pigment Epithelial Tear: Long-term Results

Antonio Polito, MD, Matteo Cereda, MD, Federica Romanelli, MD, Grazia Pertile, MD

Department of Ophthalmology, Ospedale S. Cuore - Don Calabria, Negrar, Verona, Italy

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Correspondence and requests to:

Antonio Polito, MD

Department of Ophthalmology,

Ospedale S. Cuore - Don Calabria

Via Don Sempreboni 5 ,

37024 Negrar, Italy.

Phone: 0039-045-6013857

Fax: 0039-045-6013026

e-mail: apolito23@yahoo.it

Abstract

Background: to determine long-term functional and morphological changes after full macular translocation (FMT) with 360° retinotomy in patients with retinal pigment epithelium (RPE) tears, in light of the increasing number of reports of this complication following vascular endothelial growth factor (VEGF)-modulating therapy. **Methods:** We retrospectively reviewed a consecutive series of six patients with RPE tears secondary to neovascular age-related macular degeneration (AMD) who underwent FMT with 360° retinotomy between March 2005 and June 2006. Preoperative and postoperative visual acuity, fundus fluorescein angiography (FA) and optical coherence tomography (OCT) were reviewed. RPE tears occurred spontaneously in 3 cases and after intravitreal triamcinolone in 3 cases. Preoperative and postoperative best-corrected visual acuity was converted to logarithm of the minimal angle of resolution visual acuity for analysis. **Results:** Mean postoperative follow-up was 39 months (range 36-50 months). At 12, 24 and 36 months mean visual acuity increased by 6.00 ± 5.3 , 5.57 ± 5.54 and 6.67 ± 4.76 lines, respectively. This improvement was maintained at final examination. FA and OCT revealed pigment epithelium atrophy extending to the new fovea in one case only, which also had longer symptom duration. **Conclusions:** Long-term follow-up of FMT showed significant improvement in the majority of patients. FMT may be an option for cases of RPE tears of recent onset. Further investigations are necessary to determine FMT's role in tears developing during the course of anti-VEGF therapy.

Introduction

Tears of the retinal pigment epithelium (RPE) in the setting of neovascular age-related macular degeneration (AMD) have been described spontaneously¹ or after various treatments, such as laser², photodynamic therapy³, intravitreal triamcinolone⁴ and, more recently, intravitreal vascular endothelial factor (VEGF)-modulating therapy, including pegaptanib⁵, bevacizumab⁶⁻¹² and ranibizumab¹³⁻¹⁵. The most common lesion subtype associated with RPE tears is a fibrovascular pigment epithelium detachment (PED) or serous PED associated with choroidal neovascularization (CNV). Since most PED characteristics for spontaneous RPE tears, such as signs of underlying CNV (i.e., heme, exudate, notching, hot spot or irregular fluorescence) are similar to those of RPE tears following treatments, anti-VEGF therapy may accelerate the natural history of these lesions.

Patients often experience a sudden and severe loss of vision if the tear involves the fovea, with visual prognosis generally poor due to the scarring of fibrovascular tissue¹. Even when the fovea is not involved, and despite relatively intact visual acuity initially, long term functional prognosis is often 20/200 or less¹⁶. Moreover, these lesions are often bilateral, raising the issue of treating patients with one eye already affected and with high risk characteristics in the fellow-eye^{17,18}. Once the tear has occurred, no effective treatment exists, since current anti-VEGF therapies can not reconstitute a disrupted interface between photoreceptors and RPE.

The growing use of anti-VEGF therapy for neovascular AMD and the likelihood of an increase in RPE tears in a sub-population of eyes with high risk characteristics, together with a lack of treatment modalities, makes alternative treatments an important objective. Restoration of a healthy subretinal environment in eyes with RPE tears by relocating the fovea over apparently healthy RPE has the theoretical potential of improving visual function. This can be achieved by surgically removing the CNV and either rotating the macula to a new location with a 360° retinotomy or translocating an RPE-choroidal graft under the macula. Preliminary results of RPE-

choroid graft translocation and single case reports on macular translocation with 360° retinotomy for RPE tears found vision restoration that was sustained for up to two years^{15, 19-21}.

This study presents the data of the first series of patients with an RPE tear with full macular translocation (FMT) with 360° retinotomy treated at our hospital and follow-up examinations of at least three years.

Materials and methods

Institutional review board approval was obtained for this study. The medical records of six eyes of six consecutive patients who had undergone FMT with 360° retinotomy for an RPE tear between March 2005 and June 2006 were retrospectively reviewed. One vitreoretinal surgeon (PG) performed all surgeries. All patients had a history of neovascular AMD and RPE tear in the study eye and advanced AMD with very limited visual acuity (BCVA < 20/400) in the fellow eye. Three patients had spontaneous RPE tear associated with fibrovascular PED and, in the other three, a tear had developed one month after intravitreal triamcinolone (IVT) (table 1).

FMT with 360° retinectomy was performed as initially described by Eckardt and colleagues and later by Pertile and Claes^{22, 23}. Briefly, compensatory muscle surgery was performed to obtain a counter-rotation of the globe. Crystalline lens extraction with intraocular lens implantation into the capsular bag was performed on all patients by phacoemulsification through a corneoscleral incision. Complete pars plana vitrectomy was performed with posterior vitreous detachment and meticulous vitreous base shaving. Through a small posterior retinotomy, balanced salt solution was injected into the subretinal space with a 41-gauge subretinal cannula. Detachment of the entire retina was accomplished after three or four injections followed by repeated fluid-air exchanges. A 360° retinectomy was performed as peripherally as possible with two specially-designed curved scissors (DORC International). The subfoveal lesion was removed.

The neurosensory retina was then rotated off the area of RPE and choriocapillaris loss; this was followed by an infusion of perfluorocarbon liquid. Both the small strip of retina remaining attached to the ora serrata and the excess of retina covering the pars plana in the superior nasal quadrant were removed with the vitreous cutter. Laser photocoagulation was applied to the retinectomy margins, followed by perfluorocarbon-to-silicone oil exchange. Silicone oil was removed in a second operation at 5.5 (2.1) (mean (SD)) months after surgery. Complete ophthalmic and visual acuity examinations with Snellen charts were performed periodically. Color fundus photography, fluorescein and ICG angiography and optical coherence tomography (OCT) were performed on all patients preoperatively, at 12, 24 and 36 months. During follow-up visits, OCTs were performed at all visits while angiographies were done only if recurrent CNV was suspected. The Snellen best-corrected distance visual acuity measurements were converted to the logarithm of the minimal angle of resolution (logMAR) units for analysis.

Results

The mean follow-up time was 39.2 months with a range of 36 to 50 months. All six patients presented the distinctive appearance of an RPE tear on biomicroscopy and fluorescein angiography in the treated eye (Figures A,B) and a disciform scar in the fellow eye. In all but one eye, the tears involved the fovea; the fovea was located above the folded RPE, clearly visible on OCT (Figure C). In patient 2 a large area denuded of RPE was located just inferonasal to the macular region, where a fibrovascular pigment epithelium detachment was present. In patients 3 and 5, a large subretinal hemorrhage covering more than 50% of the area of the entire lesion was also present. The subretinal hemorrhage obscured the area of folded RPE, but allowed clear visualization of the bare choroid and the corresponding window defect adjacent to the fovea on fluorescein angiography. All patients had visual disturbances within 3 months of surgery, except for patient 2, who complained of decreased vision after 1 year. Patient 2 had also been

previously treated with IVT, photodynamic therapy and IVT at 6-month intervals between treatments at another clinic.

Best corrected visual acuity at baseline ranged from 20/2000 to 20/80 (mean 20/200). Baseline characteristics of the patients and the RPE tears in the six study eyes are summarized in Table 1. At 3, 6 and 12 months after surgery, best-corrected visual acuity had improved to a mean of 20/125, 20/80 and 20/63, with a mean increase of 6 lines of logMAR visual acuity at one year. At 24 and 36 months, mean visual acuity had improved to 5.57 ± 5.54 and 6.67 ± 4.76 lines over baseline, respectively. The improvement was maintained at the final visit (Table 2). All patients had at least 3 lines of improvement in visual acuity.

Fundus examination showed a dry macula and a pigment epithelial defect inferior to the fovea extending beyond the inferior temporal arcade at 1 month in all treated eyes. Fluorescein angiography at 1 year revealed a transmission defect inferior to the macula corresponding to the area of RPE defect caused by the RPE tear and surgical removal of choroidal neovascularization (Figures D,E). The extent of retinal rotation was sufficient to relocate the center of the fovea away from the atrophic zone in all but one eye (patient 2), which presented RPE atrophy extending toward the new fovea. This finding was also confirmed by OCT at one year (Figure F). OCT revealed a restoration of retinal morphology and foveal contour in all but one eye (patient 2), which showed a significant reduction in neurosensory retinal thickness with absence of outer retinal layers. After three years, a slight progression of RPE atrophy not extending to the new fovea could be observed (Figures G,H) and preservation of foveal photoreceptor integrity could be confirmed by OCT in all eyes, with the exception of patient 2 (Figure I).

Patient 1 presented a mild postoperative inferior retinal detachment, successfully reattached with one additional surgery with silicon oil tamponade 6 days after FMT. Patient 4 complained of diplopia two months after surgery, which spontaneously resolved at 3 months. Patient 6 developed a moderate choroidal hemorrhage during the cleaning of the vitreous base; the operation was suspended without performing the retinal separation and continued 17 days

later, after the hemorrhage had been reabsorbed. Recurrent CNV occurred in patient 4 fifteen months after surgery, with vessels growing along the superonasal margin of the postoperative atrophic zone, approximately 1 disc diameter from the foveal center. In this patient CNV was successfully treated by photocoagulation of the feeder vessel and intravitreal injection of bevacizumab.

Discussion

RPE tears are frequently associated with severe visual loss due to their poor natural history and progressive subretinal scarring¹⁶. Moreover, patients affected by this lesion in one eye have a high risk of a similar event occurring in the fellow eye^{17, 18}. While effective in improving vision in a large number of patients with neovascular AMD, anti-VEGF therapy does not improve vision in patients with RPE tears due to the irreversible loss of the integrity of the photoreceptor - RPE complex. In addition, this therapy appears to precipitate the occurrence of RPE tears in predisposed eyes⁷. Although it has been noted that RPE tears are an infrequent complication of anti-VEGF therapy, an increasing number of reports have described such events after intravitreal injection of triamcinolone, pegaptanib, bevacizumab and ranibizumab⁷⁻²⁹. Unfortunately, no therapy has been shown beneficial once an RPE tear has occurred. At present, restoration of the subretinal anatomy with potential improvement of photoreceptor function can only be achieved by surgery. In fact, only through the surgical removal of the neovascular lesion can the fovea overlying the diseased macula be relocated into contact with an area of healthy-appearing RPE, either by macular translocation or RPE transplantation. This approach has the theoretical advantage of re-establishing the interaction between the RPE and photoreceptors which is fundamental to sight. In this study, we investigated the long term results in a consecutive series

of six patients who underwent FMT for RPE tears in the study eye and suffered from severe visual loss due to advanced AMD in the fellow-eye. The extremely encouraging results of 5 to 16 logMAR lines of vision improvement at 1 year (mean 6 lines) were maintained at three years, when mean visual acuity was 20/50. Although in 2 eyes (patient 3 and 5) visual improvement may have also been influenced by removal of a large submacular hemorrhage, preoperative imaging clearly showed foveal involvement in the RPE tear implying a similar risk for further visual loss without FMT. Moreover, it is unlikely that the degree of visual improvement achieved in these patients could have been obtained by submacular hemorrhage displacement alone.

The outcomes of this series compare favourably with previous studies on FMT²³⁻²⁵. This is probably due to timely surgical intervention with respect to the onset of RPE tear and vision loss - no more than 3 months in five of the six eyes, which may account for minimal retinal damage to the neurosensory retina and the increased possibility of photoreceptor rescue and recovery of visual function. The only patient with visual symptoms of approximately one year duration (patient 2) was alone in having unchanged vision throughout the first two years and lower final visual acuity. A large atrophic RPE area extending toward the prospective fovea was also present in this patient. A recent paper on long term follow up of FMT has shown how progressive atrophy of the RPE presumably related to a more advanced stage of disease prior to surgery may significantly limit the beneficial effect of the treatment. Therefore early treatment seems a key factor in possible visual recovery. In addition, a good final anatomic result was achieved in all eyes, with few intraoperative and postoperative complications and with no incidence of proliferative vitreoretinopathy. Complications were successfully resolved in all cases. Because of a limited inferior retinal detachment, patient 1 required an additional operation shortly after the first; patient 6 developed a choroidal haemorrhage during vitrectomy and FMT was completed a few weeks later, when the haemorrhage had been completely reabsorbed; patient 4 underwent laser photocoagulation followed by intravitreal bevacizumab for recurrent CNV 15 months after FMT. These outcomes support the observation that a refined surgical technique aimed at minimizing intraoperative and postoperative complications as well as the correct

management of such events when they do occur are additional crucial factors for the achievement of improved visual acuity.

At present only three cases of RPE tears treated with FMT have been reported in the literature. In 2001 Meyer and Toth, in a report focusing on the pathomechanisms of RPE tears described a patient with RPE tear whose vision improved from 20/70 to 20/60 following FMT surgery, which was maintained at 15 months¹⁹. In 2004 Gelisken et al reported a case of RPE tear, with a 2-month history of decreased vision, treated with FMT; vision improved from 20/200 to 20/50 at 22 months with no PVR or recurrence of CNV²⁰. In 2007 Gibran et al described a case of RPE tear following 2 bevacizumab injections, with vision decreasing from 20/40 to 20/320, no improvement was noted following a third bevacizumab injection and the eye was then treated with FMT surgery - final vision acuity was 20/80 at 7 months²¹. These three cases all showed visual improvement consistent with our findings. More recently, Maaijwee et al presented preliminary data on six patients with an RPE tear treated with RPE-choroid graft translocation¹⁵. At final examination, between 6 months and 2 years post-operative, mean visual acuity improved from 20/160 to 20/80. The authors preferred this technique to FMT because it was faster and less complex. It also offered potentially fewer postoperative complications without the need for counter-rotation of the globe. However, with submacular insertion of an RPE-choroid patch graft, long-term gain in visual acuity has been achieved in a limited number of cases only and, when it does occur, improvement is minimal in the majority of patients, whereas many patients suffer significant vision loss. Our preliminary experience with this surgery in cases of RPE tears confirm such modest outcomes. Nevertheless, given the small number of patients and differences in surgical technique and surgeon experience, direct comparisons between these two treatments can not be made.

In conclusion, our findings show that FTM may represent an important therapeutic option to improve vision in patients with RPE tears of recent onset and a known natural history of visual deterioration. This study has several limitations, including its retrospective nature, the absence of a control group and the small number of patients. In particular, although we attempted to include

consecutive patients during a definite time period, otherwise eligible patients may not have been selected because of lack of preoperative imaging. However, the long follow-up period enhances the clinical relevance of our encouraging results. Although this is a complex surgical procedure with potentially serious complications, the lack of response to anti-VEGF therapy, the absence of alternative treatments, the advanced disease of the fellow eye implying a similar risk for the affected eye, the continuous refinement of the surgical technique and the potential to achieve 20/80 or better visual acuity with early intervention, suggest that this treatment modality may have a role for the management of RPE tears in neovascular AMD.

Table 1. Clinical characteristics of the six patients with a retinal pigment epithelium (RPE) tear treated with a full macular translocation with 360° retinotomy

Patient No.	1	2	3	4	5	6
Sex	F	F	F	F	M	F
Age	83	76	64	85	76	68
Prior treatments	No	2 IVT, 1 PDT	No	IVT	IVT	No
Baseline BCVA	20/2000	20/400	20/125	20/200	20/100	20/80
Size of RPE tear (disc areas)	5,5	12	15	8	12	7
Subretinal Hemorrhage	no	no	>50%	<50%	>50%	<50%
Duration of symptoms	3 months	1 year	2 months	3 months	3 months	2 months
Fellow Eye BCVA	20/2000	Hand motion	20/2000	20/2000	20/2000	20/2000

IVT, intravitreal triamcinolone; PDT, photodynamic therapy; BCVA, best corrected visual acuity.

Table 2. Best corrected visual acuity (Snellen and LogMAR) change after surgery

Patient No.	Baseline	1 month	3 months	6 months	12 months	24 months	36 months
1	20/2000	20/1250	20/100	20/40	20/50	20/50	20/50
2	2.0 20/400	1.7 20/400	0.7 20/400	0.3 20/400	0.4 20/400	0.4 20/400	0.4 20/125
3	1.3 20/125	1.3 20/63	1.3 20/50	1.3 20/50	1.3 20/32	1.3 20/40	0.8 20/40
4	0.8 20/200	0.5 20/400	0.4 20/200	0.4 20/200	0.2 20/80	0.3 20/80	0.3 20/80
5	1.0 20/100	1.3 20/125	1.0 20/125	1.0 20/40	0.6 20/32	0.6 20/40	0.6 20/32
6	0.7 20/80	0.8 20/200	0.8 20/50	0.3 20/50	0.2 20/25	0.3 20/25	0.2 20/25
Mean ± SD	0.6 20/200	1.0 20/200	0.4 20/125	0.4 20/80	0.1 20/63	0.1 20/63	0.1 20/50
	1.07 ± 0.520	1.10 ± 0.424	0.77 ± 0.350	0.60 ± 0.438	0.47 ± 0.446	0.48 ± 0.47	0.36 ± 0.27

The Corresponding Author declares that there are not competing interests

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FIGURE LEGENDS

Figure. A, Preoperative colour photograph showing a retinal pigment epithelium (RPE) tear in a patient with neovascular age-related macular degeneration (patient 6, table 2). A large crescentic area of bare choroid is present temporal to the fovea with adjacent area of relative hyperpigmentation nasally, corresponding to retracted RPE. **B**, Preoperative fluorescein angiogram (FA) showing sharply demarcated transmission defect temporal to the fovea, consistent with the bed of the RPE tear and subfoveal choroidal neovascularization (CNV) within the area of retracted RPE. **C**, Preoperative OCT revealing irregularly elevated and folded hyper-reflective RPE layer and break point temporal to the fovea (arrow). **D**, Fundus autofluorescence (FAF) at 12 months after surgery, with a visual acuity of 20/25. The FAF defect inferior to the macula corresponds to the area of RPE defect caused by the tear and surgical removal of CNV. This area appears as a hyperfluorescent window defect on FA (**E**). **F**, OCT at 12 months showing a normal foveal anatomy over a healthy appearing RPE layer. **G** and **H**, FAF and FA at 36 months after surgery, visual acuity maintained at 20/25. Note the slightly increased RPE defect, but still not involving the new fovea. **I**, Spectral Domain OCT showing preservation of macular architecture, with clear visualization of the intraretinal microstructure of the new fovea and in particular the photoreceptor inner and outer segment junction (arrow).

