Recurrence of Retinal Pigment Epithelial Changes After Macular Translocation With 360° Peripheral Retinectomy for Geographic Atrophy

Mark T. Cahill, MCh, FRCSI(Ophth); Prithvi Mruthyunjaya, MD; Catherine Bowes Rickman, PhD; Cynthia A. Toth, MD

Objective: To assess the prevalence of recurrence of macular geographic atrophy (GA) of the retinal pigment epithelium (RPE) after macular translocation with 360° retinectomy (MT360) in one institution.

Methods: A retrospective review of all cases of GA that were treated with MT360 in 1 institution. Demographic and clinical data including the duration of preoperative visual loss, preoperative and postoperative visual acuity, and the prevalence of postoperative foveal RPE atrophy were recorded for these patients, and these data were compared with similar data from patients who underwent MT360 for neovascular age-related macular degeneration (AMD) as part of the prospective Duke Macular Translocation Study, Duke University Eye Center, Durham, NC.

Results: Four eyes in 4 patients with GA secondary to AMD underwent MT360 and were compared with 63 eyes in 63 patients who underwent MT360 for neovascular AMD as part of the Duke Macular Translocation Study. The mean duration of preoperative visual loss was higher in the GA group (11.3 months) than in the neovascular AMD group (1.7 months) (P = .08). The prevalence of postoperative foveal RPE atrophy was significantly higher in the GA group (n = 3; 75.0%) than in the neovascular AMD group (n = 5; 8.3%) (P < .01); in the GA group, this corresponded to recurrence of the GA lesions. In contrast, the postoperative RPE atrophy seen in the neovascular AMD group was due to postoperative mechanical forces such as laser therapy or RPE tearing. There was no significant difference in the mean preoperative or postoperative visual acuity in either group.

Conclusions: Subfoveal RPE atrophy can reoccur following MT360 in eyes with nonneovascular AMD and GA; RPE atrophy similar to this has not been found in a large consecutive series of patients with neovascular AMD after MT360. Further research is needed to assess if the potential for visual recovery in eyes with end-stage nonneovascular AMD is outweighed by the possibility of postoperative recurrence of GA.

Arch Ophthalmol. 2005;123:935-938

MACULAR TRANSLOCATION with 360° peripheral retinectomy (MT360), originally designed for neovascular age-related macular degeneration (AMD),1 rotates the retina away from a subretinal lesion onto healthy retinal pigment epithelium (RPE), restoring visual function.1,2 Recently, MT360 has been performed in the second-affected eyes of patients with bilateral geographic atrophy (GA) secondary to AMD with good initial visual outcomes.3,4 However, it has been shown that GA can recur after MT360 as evidenced by a study of 7 eyes of which GA recurred in 1 eye 6 months after MT360.5 We performed a retrospective study to compare the prevalence of atrophic RPE changes after MT360 in 2 groups of eyes; one group had an initial diagnosis of GA secondary to nonneovascular AMD while the other group had an initial diagnosis of subfoveal choroidal neovascularization (CNV) secondary to neovascular AMD.

METHODS

Eyes with GA secondary to AMD that underwent MT360 were identified by reviewing surgical reports of MT360 in a quality assurance database from 1998 to 2003 in Duke University Eye Center, Durham, NC. Any eye that had no CNV removed at the time of surgery was noted and the preoperative fluorescein angiograms in this subgroup of eyes were subsequently reviewed to confirm the presence of GA secondary to AMD. Medical records were examined for clinical factors including patient sex, patient age at the time of the procedure, duration of follow-up, time to recurrence of GA if applicable, preoperative visual acuity, best postoperative visual acuity, and visual acuity at last follow up. The comparison group was composed of a consecutive series of eyes in the institutional review board–approved, prospective, Duke Macular Trans-
location Study, clinical details of which have been previously reported.\(^5,6\) Preoperative and postoperative fluorescein angiograms of this series of eyes were reviewed to identify any postoperative RPE atrophy. Clinical and demographic data from the 2 groups of eyes were compared using the \(t\) test for categorical variables and the \(t\) test for continuous variables.

### RESULTS

Reviewers identified 4 eyes with GA secondary to AMD in 4 patients who underwent MT360 with simultaneous cataract surgery in 1 patient (patient 3, Table 1). Three eyes in 3 patients were identified from the quality assurance database and 1 eye in patient 1 (Table 1) was identified from the Duke Macular Translocation Study. The initial clinical course of 1 patient (patient 1) was previously reported with recurrence of GA seen after the publication of the article (Figure 1).\(^4\) Sixty-three eyes in 63 patients in the Duke Macular Translocation Study had subfoveal neovascularization, fibrosis, or blood without GA. Four eyes in the Duke Macular Translocation Study had RPE atrophy secondary to postoperative thermal laser or photodynamic therapy with injectable verteporfin (Visudyne; QLT Inc, Vancouver, British Columbia) for recurrent CNV. One patient had a postoperative RPE tear that involved the subfoveal RPE. There was no evidence of GA after MT360 in any eye that had a preoperative diagnosis of neovascular AMD. The demographic and clinical data of both patient groups are summarized in Table 1 and Table 2.

### Table 1. Demographic and Clinical Data on Patients With Recurrence of RPE Changes After MT360 for Geographic Atrophy

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y</th>
<th>Duration of Visual Loss, mo</th>
<th>Duration of Follow-up, mo</th>
<th>Time to Recurrence, mo</th>
<th>Visual Acuity, logMAR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preoperative</td>
<td>Best</td>
<td>At Last Follow-up</td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td>-------------</td>
<td>------</td>
<td>------------------</td>
<td></td>
</tr>
<tr>
<td>1/M/68</td>
<td>2</td>
<td>NA</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>2/F/85</td>
<td>3</td>
<td>7</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>3/F/73</td>
<td>9</td>
<td>10</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>4/F/80</td>
<td>22</td>
<td>12</td>
<td>0.7</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: logMAR, logarithm of the minimum angle of resolution; MT360, macular translocation with 360° retinectomy; NA, not applicable; RPE, retinal pigment epithelium.

*The patient did not have a recurrence documented in the 7 months of follow-up.

### Table 2. Comparison of Demographic and Clinical Data of 2 Groups of Patients*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients With Geographic Atrophy (n=4)</th>
<th>Patients With Neovascular AMD (n=63)†</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>79.3 (6.0)</td>
<td>76.6 (5.7)</td>
<td>.38</td>
</tr>
<tr>
<td>Female, No. (%)</td>
<td>3 (75.0)</td>
<td>35 (55.5)</td>
<td>.63</td>
</tr>
<tr>
<td>Duration of visual loss, mean (SD), mo</td>
<td>11.3 (9.7)</td>
<td>2.9 (2.5)</td>
<td>.08</td>
</tr>
<tr>
<td>Preoperative logMAR VA, mean (SD)</td>
<td>0.7 (0.4)</td>
<td>0.8 (0.3)</td>
<td>.62</td>
</tr>
<tr>
<td>Duration of follow-up, mean (SD), mo</td>
<td>19.3 (2.5)</td>
<td>12.03 NA</td>
<td>NA</td>
</tr>
<tr>
<td>Postoperative foveal RPE atrophy, No. (%) of patients</td>
<td>3 (75.0)</td>
<td>5 (8.3)                           &lt;.01</td>
<td></td>
</tr>
<tr>
<td>Last follow-up logMAR VA, mean (SD)</td>
<td>0.7 (0.2)</td>
<td>0.7 (0.4)</td>
<td>.99</td>
</tr>
</tbody>
</table>

*The 2 groups being compared are those who had recurrence of RPE changes after MT360 for geographic atrophy with those who underwent MT360 for neovascular AMD.
†Data were available for 60 patients (adapted from Mruthyunjaya et al\(^6\)).
‡Data were available for only 12 months.

Abbreviations: AMD, age-related macular degeneration; logMAR, logarithm of the minimum angle of resolution; MT360, macular translocation with 360° retinectomy; NA, not applicable; RPE, retinal pigment epithelial; VA, visual acuity.

Comparison of demographic and clinical data of patients who had recurrence of RPE changes after MT360 for GA with the group of patients who underwent MT360 for neovascular AMD is summarized in Table 2. There was no significant difference in the mean age of patients in either group. However, there was a higher proportion of female patients in the GA group when compared with the neovascular AMD group. The mean duration of visual loss prior to surgery was higher in the GA group than in the neovas-
cular AMD group. There was no significant difference in the mean preoperative visual acuity in either group. Patients with GA were followed up for a mean of 19.3 months with 3 patients having follow-up between 7 and 12 months. Only 12-month follow-up data were available for patients with neovascular AMD. Postoperative foveal RPE atrophy was seen in a significantly higher proportion of patients in the GA group. This postoperative foveal change corresponded to recurrence of the pattern of GA similar to that seen before surgery in the GA group (Figures 1, 2, and 3); the causes of postoperative RPE atrophy in the neovascular AMD group were outlined previously. Mean postoperative visual acuity was the same in both groups at the last follow-up visit.

COMMENT

In this study we have reported 3 cases in which patients who underwent MT360 for the treatment of GA developed new RPE changes under the translocated macula. This was in striking contrast to the absence of new GA under the fovea in a series of 63 eyes with more than 1 year follow-up after MT360 for neovascular AMD. One previous study has reported clinical outcomes after MT360 for GA in 7 eyes. In that series, GA recurred in 1 eye, although recurrence of RPE changes under the translocated macula were not seen in the other 6 eyes. This patient with the noted GA recurrence had a 14-month follow-up, whereas 4 of the remaining 6 eyes had less than 12 months’ follow-up. In a subsequent presentation, Claus Eckardt, MD, reported a total of 4 eyes with recurrent GA of 14 eyes translocated for GA (oral communication to the American Academy of Ophthalmology Retina Preacademy meeting, November 2002). The pattern of the GA seen in the 3 cases documented in this article was similar to the recurrence reported by Eckardt and Eckardt and was characterized by mild RPE atrophy in the neovascular AMD group. The exact timeframe for development of recurrent RPE atrophy cannot be accurately determined by these retrospective studies. Thus, to date, including the current series and the updated series presented by Eckardt,
7 (39%) of 18 eyes had recurrence of GA under the new fovea after MT360 for GA.

As in the previously reported cases, recurrence of GA was not associated with a decrease in visual acuity in most eyes. However, the long-standing GA in one of the cases reported in this article is likely to have resulted in some sensory retinal damage or cell death and may, therefore, account for the poor postoperative visual acuity in this eye. Interestingly, GA has been treated with limited macular translocation in both eyes of 1 patient with postoperative improvement in visual acuity in both eyes and no recurrence of the preoperative lesions after follow-up periods of 13 and 22 months.7

It is unclear why GA recurs after MT360 in eyes with previous GA. Geographic atrophy is the end stage of a chronic process affecting both retinal photoreceptors and RPE cells that are interdependent and communicate through diffusible trophic factors and direct cell-to-cell contact.6,9 Histological studies of nonneovascular AMD have shown that RPE cells degenerate first followed by sequential degeneration of overlying rod and then cone photoreceptors.10,11 If GA is a panretinal condition, repositioning of the more densely packed and, therefore, more metabolically demanding macular photoreceptors over peripheral RPE cells may be sufficient to precipitate RPE cell loss, particularly if those RPE cells are already unhealthy or stressed. However, it is also possible that the primary defect in GA arises in the photoreceptors leading secondarily to RPE death. If this is the case then translocation of the defective sensory macula could result in accelerated damage to the RPE if it is placed over. Alternatively, apoptosis has been implicated as the cause of cell death in AMD as evidenced by Fas receptor expression in RPE and photoreceptors, with the strongest Fas labeling seen in photoreceptors at the edge of atrophic areas or overlying fibrovascular scars.12 The translocated photoreceptors expressing Fas receptor may be able to induce apoptosis in underlying RPE cells at the new macular site.

Eyes with GA that underwent MT360 in this study had already suffered a chronic degenerative process, as evidenced by the longer duration of symptoms prior to surgery documented in patients with GA when compared with patients with neovascular AMD. This relatively shorter period in eyes with subfoveal neovascular AMD may be insufficient for the neovascular degenerative process to trigger either the apoptotic pathway or another, as yet undetermined, metabolic pathway. Alternatively, eyes with neovascular AMD may have sustained less irreversible photoreceptor damage than eyes with GA because of this temporal difference, thus allowing postoperative recovery. Surgical trauma associated with the retinal detachment that is an inherent part of MT360 is unlikely to be a cause of the GA recurrence seen in the cases reported herein and previously it is not seen in cases treated with the same techniques for neovascular AMD. Furthermore, MT360 for GA does not include removal of subretinal CNV which is potentially the most traumatic part of the MT360 procedure. Interestingly, significant postoperative foveal RPE atrophy occurred in only a small proportion of 63 consecutive eyes that had MT360 for neovascular AMD and in all cases this was due to postoperative mechanical forces such as laser therapy or an RPE tear.8 In addition, Mruthyunjaya et al8 reported that all of the recurrent neovascularization (21% of eyes) arose from the original site where CNV had been removed and not de novo under the new fovea.

Geographic atrophy poses a significant problem as 3.5% of all people older than 75 years have this form of AMD and it accounts for approximately 80% of all cases of the disease.13 Geographic atrophy is bilateral in up to 56% of cases14 and 50% of eyes with early GA and good vision have reduced contrast sensitivity and reading rates secondary to parafoveal scotomas.8 Furthermore, profound visual loss secondary to severe GA occurs in up to 42% of affected eyes.15 Besides macular translocation, no treatment has been demonstrated to prevent visual loss in patients with GA. Further research is needed to assess if the potential for visual recovery in eyes with end stage nonneovascular AMD is outweighed by the possibility of postoperative recurrence of the atrophic lesions.

Submitted for Publication: July 9, 2004; final revision received September 10, 2004; accepted October 18, 2004.

Correspondence: Cynthia A. Toth, MD, Duke University Eye Center, Erwin Road, PO Box 3802, Durham, NC 27710 (toth0004@mc.duke.edu).

Funding/Support: This study was supported in part by funds from the Ronald G. Michaels, Riderwood, Md, Heed Ophthalmologic Foundation, Cleveland, Ohio; and AOS/ Knapp Fund Fellowship, Cleveland (Dr Mruthyun jaya); grant R01 EY11286 from the National Eye Institute, Bethesda, Md (Dr Bowes Rickman) and a Career Development Award from Research to Prevent Blindness, New York, NY (Dr Bowes Rickman); and funds from the D. Euan and Angelica H. Baird, New York, NY, and the Andrew Family Foundation, Boston, Mass (Dr Toth).

REFERENCES