Clinical Course of Vitreomacular Adhesion Managed by Initial Observation

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Purpose: The purpose of the study was to investigate the clinical course of patients with idiopathic vitreomacular adhesion (VMA).

Methods: A noncomparative case series of patients who had clinical symptoms and spectral-domain optical coherence tomography (SD-OCT) findings consistent with VMA. The VMA was graded based on the optical coherence tomography findings at initial and follow-up examinations. Grade 1 was incomplete cortical vitreous separation with attachment at the fovea, Grade 2 was the Grade 1 findings and any intraretinal cysts or clefts, and Grade 3 was the Grade 2 findings and the presence of subretinal fluid.

Results: One hundred and six eyes of 81 patients were identified as having VMA by spectral-domain optical coherence tomography at 3 retina clinics. The mean age was 73 years and the mean time of follow-up was 23 months. Forty-three eyes (41%) had Grade 1 VMA, 56 eyes (52%) had Grade 2 VMA, and 7 eyes (7%) had Grade 3 VMA. By the last follow-up, spontaneous release of VMA occurred in 34 eyes (32%), and pars plana vitrectomy was performed in 5 eyes (4.7%). Mean best-corrected visual acuity was 0.269 logarithm of the minimum angle of resolution or 20/37 at baseline (range, 20/20–20/200) and logarithm of the minimum angle of resolution 0.251 or 20/35 at the last examination (range, 20/20–20/400).

Conclusion: In this selected patient cohort with mild symptoms, the clinical course of patients with VMA managed by initial observation was generally favorable.

The clinical and spectral-domain optical coherence tomography (SD-OCT) features of vitreomacular traction (VMT) syndrome have been described previously. Typical symptoms include decreased vision, central metamorphopsia, photopsia, and micropsia. The emergence of SD-OCT has demonstrated that incomplete separation of the posterior vitreous with persistent attachment confined to the fovea is more common than is clinically symptomatic. The subset of eyes with adhesion limited to the fovea may be clinically distinct from eyes with broader zones of vitreomacular adhesion (VMA) and has been termed vitreofoveal adhesion or focal VMA. The SD-OCT allows documentation of the baseline and ongoing effects and extent of VMA, specifically those with central visual symptoms associated with VMA.

The purpose of this study was to investigate the clinical course of patients with VMA defined by SD-OCT imaging, and followed with noninterventional management. A classification of VMA based on the SD-OCT findings is proposed as part of this study.
Patients and Methods

The study design was a noncomparative case series of patients for whom observational management was recommended at the initial examination by vitreoretinal surgeons at three centers. Symptomatic patients with VMA localized to the fovea, noted on SD-OCT, were identified and included in this study by virtue of an intention not to treat them based on either good presenting visual acuity or minimal symptoms. Fellow eyes of the patients with macular hole and advanced macular diseases (neovascular age-related macular degeneration and diabetic macular edema) affecting vision were excluded from the current study.

Patient demographics and histories including age, gender, symptoms, best-corrected visual acuity (BCVA), and duration to last follow-up examination were recorded. The lens status and previous eye surgeries including intravitreal injections were also noted. The SD-OCT images at the initial and last visits were retrospectively placed into 3 categories that morphologically seemed to represent a spectrum of progressive traction (Figure 1). Grade 1 was incomplete cortical vitreous separation with attachment at the fovea, Grade 2 was Grade 1 and intraretinal cysts or clefts, and Grade 3 was Grade 2 with the presence of subretinal fluid. Statistical analysis using chi-square, analysis of variance, and paired t-tests was performed on the study data.

Results

One hundred and six eyes of 81 patients were included. The cohort included 33 men (41%) and 48 women (59%). The mean age of the patients was 72.7 years with a range of 41 years to 92 years at the initial visit. The mean BCVA was 0.269 logarithm of the minimum angle of resolution (20/37). The median time of follow-up was 18 months with a range of 1 month to 91 months. Previous interventions included intraocular surgery in 43 eyes (some patients had multiple previous procedures), including 37 eyes (35%) with cataract surgery with intraocular lens placement, 2 eyes (2%) with combined cataract and glaucoma surgery, 3 eyes (3%) with panretinal photocoagulation, and 4 eyes (4%) undergoing intravitreal injections. Sixty-seven patients (63%) were phakic at the time of initial visit, and 39 patients (37%) were pseudophakic.

Using the study classification criteria (Figure 1), 43 eyes (41%) had Grade 1 VMA, 56 eyes (52%) had Grade 2 VMA, and 7 eyes (7%) had Grade 3 VMA at the initial visit. The clinical course of SD-OCT findings is summarized in Tables 1 and 2. In Grade 1 eyes, the VMA released spontaneously on the OCT in 13 eyes (30%), was unchanged in 23 eyes, while the attachment progressed into a Grade 2 or 3 in 7 eyes. In Grade 2 eyes, VMA released spontaneously in 17 eyes (30%), remained unchanged in 31 eyes, and progressed to Grade 3 in 8 eyes, including 3 eyes that developed full-thickness macular hole, leading to surgery. Finally, within Grade 3 eyes, VMA released in...
4 eyes (57%), 1 eye improved to Grade 1, 1 eye remained unchanged, and 1 eye progressed to a full-thickness macular hole, prompting surgery. Thus, at the last examination, overall 34 eyes (32%) had spontaneously resolved VMA, 25 eyes (23%) had Grade 1 VMA, 38 eyes (36%) had Grade 2 VMA, 4 eyes (4%) had Grade 3 VMA, and 5 eyes (5%) underwent pars plana vitrectomy (PPV). The differences in spontaneous resolution rates for the various grades were not significant ($P = 0.35$). Similarly, the rates of worsening anatomy in all presenting VMA grades were equivalent ($P = 0.64$).

All but 5 of the 106 eyes were observed throughout the study. Those 5 patients (4.7%) underwent PPV (4 eyes for development of full-thickness macular holes, and one for progressive loss of vision from VMA). Four of the operated eyes were Grade 2 at initial visit, while one was Grade 3 at baseline. After vitrectomy, the mean visual acuity at last follow-up in the operated eyes was logarithm of the minimum angle of resolution 0.30 or 20/40 (20/30, 20/30, 20/40, and 20/100 in the 4 patients with macular hole, and 20/25 in the patient operated for worsening VMA). At the last examination, all four patients with macular hole had successful closure and the progressive patient with VMA had improved foveal anatomy (resolution of retinal cyst and subretinal fluid).

The BCVA among three VMA grades at presentation was significantly different ($P = 0.012$), with Grade 3 patients having the worst visual acuity at the initial visit. There were no significant differences between changes from the initial to the final mean BCVA in each of the 3 VMA grades (Table 1). At the last examination, the mean BCVA in the observation group (excluding the 5 operated patients) was 0.251 logarithm of the minimum angle of resolution (20/35), which was similar to the baseline visual acuity.

### Discussion

The main finding of this study is that the observational management of at least milder grades of VMA is a favorable initial option. The current study demonstrated stability of BCVA between the initial and last examinations, a high rate of spontaneous VMA release (32%), and a low rate of progression to a more severe anatomical configuration (16%). A grading scheme for VMA based on the SD-OCT features was also useful for clinical monitoring by better defining subgroups in the current study and may be useful for standardizing the observations and outcomes in future studies.

Debate about whether persistently attached vitreous always represents actual traction has led to the use of the terms, VMT or VMA. The Microplasmin for Intravitreal Injection-Traction Release Without Surgical Treatment (MIVI-TRUST) investigators used the term VMT when there were visual symptoms associated with VMA. The patients in that study represented relatively small zones of VMA, limited to the fovea as documented by the OCT. In the pre-OCT era, only patients with relatively advanced VMA, as observed by slit-lamp biomicroscopy, were clinically recognizable. These were categorized according to the

### Table 1. Visual Acuity at Presentation and at the Last Follow-up for Each Grade of VMA in the Study of Patients Managed by Initial Observation

<table>
<thead>
<tr>
<th>Presenting VMA Grade</th>
<th>No. Eyes</th>
<th>Mean LogMAR (SD) at Presentation</th>
<th>Mean LogMAR (SD) at the Last Examination</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>43</td>
<td>0.21 (0.18)</td>
<td>0.21 (0.19)</td>
<td>0.88</td>
</tr>
<tr>
<td>Grade 2</td>
<td>56</td>
<td>0.30 (0.20)</td>
<td>0.32 (0.28)</td>
<td>0.54</td>
</tr>
<tr>
<td>Grade 3</td>
<td>7</td>
<td>0.43 (0.31)</td>
<td>0.34 (0.30)</td>
<td>0.34</td>
</tr>
</tbody>
</table>

*Paired t test.

LogMAR, logarithm of the minimum angle of resolution; SD, standard deviation; VMA, vitreomacular adhesion.

### Table 2. Final Status of VMA in the Study of Patients Managed by Initial Observation

<table>
<thead>
<tr>
<th>Presenting VMA Grade</th>
<th>No. Eyes</th>
<th>Improved (%)*</th>
<th>Stable (%)†</th>
<th>Worse (%)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>43</td>
<td>13/43 (30)</td>
<td>23/43 (53)</td>
<td>7/43 (16)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>56</td>
<td>17/56 (30)</td>
<td>31/56 (55)</td>
<td>8/56 (14)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>7</td>
<td>4/7 (57)</td>
<td>1/7 (14)</td>
<td>2/7 (28)</td>
</tr>
</tbody>
</table>

*Improved: release of VMA.
†Stable: VMA is still present, and no change.
‡Worse: progression from Grade 1 to Grade 2 or Grade 3, OR, progression from Grade 2 to Grade 3 or a macular hole or surgery, OR, progression from Grade 3 to a macular hole or surgery.
VMA, vitreomacular adhesion.
extent of the persistent vitreous attachment only as observed by slit-lamp biomicroscopy.\textsuperscript{14} This subset was deduced to be more likely to progress and surgical intervention was proposed.\textsuperscript{15–17} Initially, the rationale for surgery was to avert macular hole formation,\textsuperscript{18} but subsequent clinical experience demonstrated that releasing apparent traction allowed partial normalization of anatomy and function in more clinically severe cases. In a retrospective case series of 36 patients undergoing PPV for VMA, Davis et al\textsuperscript{19} demonstrated favorable visual outcomes (50% improved visual acuity by \(\geq 2\) lines). In a pre-OCT era study, in 53 symptomatic VMA eyes (diagnosed clinically) with a median follow-up of 5 years, most (64%) had a decrease in visual acuity over time. Better visual acuity and resolution of cystoid edema on fluorescein angiography were noted in 11% of the patients in the study who underwent a complete posterior vitreous detachment.\textsuperscript{14} These findings seemed to justify surgical intervention in more severe VMA cases.

The OCT allows for more precise means for categorization and longitudinally monitoring of such patients. Chan et al\textsuperscript{20} classified a subset of VMA on OCT as Stage 0 macular holes and postulated it as a group at risk for developing macular holes in the fellow eyes. Additionally, Gaudric et al\textsuperscript{16} documented the progression of VMA to full-thickness macular holes using OCT in fellow eyes of some patients with macular hole.\textsuperscript{16} A 2012 OCT study of eyes with tractional cystoid macular edema secondary to VMT reported a complete and spontaneous posterior vitreous detachment in 53% of eyes.\textsuperscript{21}

However, the clinical course of patients with VMA is not well established, especially when the degree of visual loss is mild. The SD-OCT has identified many more patients with earlier, minimal, or mild visual loss symptoms,\textsuperscript{4,9} making indications for the management of milder cases even less clear. Many such patients remain stable without surgical intervention, but the natural history is not well established.\textsuperscript{1} The 32% rate of spontaneous VMA resolution in the current study might be even higher with longer follow-up. The relatively favorable anatomical course was commensurated with the stable mean BCVA for patients in the current study (0.269 logarithm of the minimum angle of resolution initially and 0.251 logarithm of the minimum angle of resolution at the last follow-up examination).

Surgical treatment consisting of PPV with a release of the vitreofoveal attachment, and possibly with consideration of internal limiting membrane peeling, has been the contemporary interventional option for VMA.\textsuperscript{15,17} Chan et al\textsuperscript{22} described the induction of a posterior vitreous detachment by injecting an expansile gas as a treatment for impending macular holes in the early 1990s,\textsuperscript{22} but few clinicians adopted that technique since that time. Recently, Rodrigues et al\textsuperscript{23} reported 40% rate of the VMA release at 1 month after a single injection of expansile perfluoropropane (\(C_{3}F_{8}\)), confirmed by SD-OCT. With very little adverse effects reported in the study, and the relatively low cost of the gas bubble, this pneumatic vitreolysis could be an alternative to the more invasive surgical option of PPV.\textsuperscript{23,24} Approved in 2012 by the Food and Drug Administration, a pharmacologic intervention with the intravitreal injection of microplasmin for the release of symptomatic VMA has been introduced for patients with visual loss to 20/25 or worse. In patients with VMT, 10% of patients injected with saline had a release of vitreofoveal adhesion at 28 days compared with 26.5% of patients injected with microplasmin.\textsuperscript{13} It is possible that vitreoretinal surgeons may use this pharmacologic option in the more severe VMA cases rather than less symptomatic milder cases, in an attempt to avoid the need for future PPV. Conversely, they may also use it to treat patients with milder symptoms and less extensive VMA so as to halt progression and avoid PPV. The ability of microplasmin to induce posterior vitreous detachments and its use in managing small macular holes with VMA has been demonstrated through the MIVI trials.\textsuperscript{13} However, its value in eyes with good vision and minimal symptoms is less clearly defined. The 32% spontaneous VMA release rate in the current study compared favorably with the rate in the MIVI-TRUST study, raising questions as to the value of ocriplasmin in milder cases.

The limitations of the current study include its retrospective nature, relatively few patients, and potential bias in that the individual attending physician made the decision to assign patients to observational management. Patients with both VMA and early macular holes were not included in the current study. Patients with VMA with more severe visual symptoms were likely managed with PPV and, therefore, were not included in the study. In contrast, patients with better visual acuity and minimal symptoms were selected by the study investigators for observational management. Thus, the study cohort may have represented a milder or at least different group of patients with VMA compared with MIVI-TRUST.

In conclusion, the present study demonstrates that the clinical course of patients with relatively mild symptomatic VMA is often favorable during follow-up. Hence, patients with VMA diagnosed by SD-OCT but with minimal or nonprogressive symptoms can be initially considered for noninterventional management.

**Key words:** vitreomacular traction, vitreofoveal adhesion, microplasmin, macular hole.
References


