THE NATURAL HISTORY OF TRACTIONAL CYSTOID MACULAR EDEMA

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Background: To describe clinical outcomes in a series of patients with tractional cystoid macular edema, a variant of vitreomacular traction syndrome.

Methods: Twelve consecutive patients (15 eyes) with tractional cystoid macular edema of maximum diameter of ≤550 μm and presenting corrected-distance visual acuity of ≤0.3 (Snellen ≥20/40) were studied. Each patient underwent ophthalmic examination, including visual acuity testing in the logarithm of the minimal angle of resolution system, slit-lamp biomicroscopy, and optical coherence tomography. All patients were monitored at four-monthly intervals, unless a subjective change in symptoms prompted earlier follow-up.

Results: The mean corrected-distance visual acuity (±standard deviation) at presentation was 0.17 (Snellen 20/30) (±0.17). The mean (±standard deviation) maximum diameter of vitreofoveal adhesion was 267 (±139) μm. After a mean follow-up of 9.2 (±7.4) months, 8 eyes exhibited spontaneous and complete posterior vitreous detachment, with resolution of the tractional cystoid macular edema and restoration of normal foveal anatomy in 6 of these eyes and persistence of a single foveal cyst in 2 of these eyes. The final corrected-distance visual acuity (±standard deviation) in the 5 eyes that underwent spontaneous and complete posterior vitreous detachment improved from 0.20 (Snellen 20/32) (±0.13) to 0.16 (Snellen 6/8) (±0.12; P = 0.53).

Conclusion: Complete posterior vitreous detachment occurred spontaneously in 53% of eyes with tractional cystoid macular edema in this series.

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Vitreomacular traction (VMT) syndrome, first described by Jaffe1 in 1967, is considered a complication of partial posterior vitreous detachment (PVD). Once believed to be a rare and distinct clinical entity, VMT syndrome is now viewed as a spectrum of macular abnormalities,2 with the clinical characteristics and consequences depending on the size and configuration of the residual vitreomacular adhesion.3 Vitreomacular traction syndrome can therefore include foveal cysts (deemed a premacular hole condition),3–6 epiretinal membrane,3,7 lamellar and full-thickness macular holes,3,6 and tractional cystoid macular edema (TCME).3,8

Tractional cystoid macular edema is classified as a subtype of VMT syndrome, which results from subtle vitreous traction localized to the foveola and with an area of vitreofoveal adhesion of approximately ≤500 μm.3,8 Indeed, the natural history, prognosis, and treatment options in VMT syndrome depend on the size and configuration of the residual vitreomacular adhesion and the consequential macular anatomical changes,9 with anatomical evaluation of such adhesions only being possible since the advent of optical coherence tomography (OCT).10–15

There is a paucity of information regarding the clinical characteristics, natural history, and treatment options in TCME. In the largest series published to date, since the advent of OCT, Johnson8 reported on 11 eyes of 10 patients with TCME with an average duration of symptoms of 19.6 months (range, 3–52 months). Only 3 of 11 eyes (the ones with visual acuity of 0.4 or better on the logarithm of the minimal angle of resolution scale) (Snellen 20/50) were managed by observation alone, and of these, 1 eye developed a PVD and lamellar hole at 57 months of follow-up,
l eye exhibited no functional or morphologic change at 11 months of follow-up, and 1 eye exhibited increased foveal thickness and worsening of the TCME at 84 months of follow-up. The remaining eyes (8; 72%) underwent vitrectomy and induction of PVD (±peeling of epiretinal membrane, if any) with favorable outcome.3,8 Yamada and Kishi9 reported on 10 eyes with V-shaped vitreous detachment and residual vitreofoveolar adhesion, and an average duration of symptoms of 1.5 months (range, 0.7–7 months), and all eyes in this series underwent vitreoretinal surgery with functional and anatomical success.

The purpose of the present study is to describe a consecutive series of 15 eyes of 12 patients with TCME and good presenting visual acuity, where 8 of the 15 eyes exhibited spontaneous and complete PVD and a further 4 eyes exhibited progression (albeit incomplete) of PVD, within 9 months of presentation.

Methods

This study was a prospective, uncontrolled, observational case series of consecutive recently symptomatic patients presenting with VMT and associated cystoid macular edema caused by localized vitreofoveolar traction (TCME) of <550 μm in maximum diameter and corrected-distance visual acuity (CDVA) of 0.6 logarithm of the minimal angle of resolution or better (Snellen 20/80), at a retinal practice, between November 2008 and January 2010. Ethics committee approval was secured from the Local Regional Ethics Committee, and the tenets of the Declaration of Helsinki were adhered throughout. Patients with diabetes mellitus were excluded.

Tractional cystoid macular edema was defined as foveal thickening with multiple cystoid spaces associated with posterior hyaloid traction and no evidence on biomicroscopy or OCT of a defect in the outer foveola to suggest an evolving macular hole.3,6,8,16

Each patient underwent a complete ophthalmic examination, including logarithm of the minimal angle of resolution visual acuity testing, and slit-lamp biomicroscopy after pharmacologic pupillary dilation with one drop of single-dose, preservative-free guttae tropicamide 1% w/vol (Minims Tropicamide, Chauvin, Kingston-upon-Thames, United Kingdom), instilled 15 minutes before fundus examination. The vitreomacular relationship was further evaluated by OCT.

Slit-lamp biomicroscopy was performed by a single ophthalmologist (S.B.) with a 78-diopter indirect lens. Perifoveal vitreous detachment was diagnosed biomicroscopically when a faintly visible, typically taut, and often glistening membrane was noted in the perifoveal posterior pole, shallowly detached from the retinal surface, with a residual adhesion to the central macula.8

Optical coherence tomography was performed in each case through a dilated pupil by a single and certified ophthalmic technician using the Topcon 3D OCT-1000 (Topcon Corporation, Tokyo, Japan). The OCT scans were taken using the “3D” predefined scan pattern of the OCT software (Software Version 2.13). The scans were 6 × 6 mm in area, with a resolution of 512 × 128 pixels, oriented in a parallel grid pattern. Quantitative measurements of the maximum diameter of the vitreomacular adhesion were made from the OCT images.

All patients were monitored at regular intervals of four months, unless a subjective change in symptoms prompted earlier in the follow-up. The presence or absence of PVD at follow-up was assessed by slit-lamp biomicroscopy and OCT.

Statistical analysis was performed using the software program Numbers ’09 Version 2.0.5 (368) (Apple, Inc, Cupertino, CA). Paired t-tests were used to compare CDVA and maximum area of vitreofoveolar adhesion at presentation and at follow-up. Tests were 2-sided and P ≤ 0.05 was considered statistically significant.

Results

Fifteen eyes of 12 patients met the study inclusion criteria. This represented 15 of 46 cases (32.6%) of VMT (with an area of vitreofoveolar adhesion of any size) presented during this period. The mean patient age (±standard deviation) at presentation was 68.4 (± 8.5) years, ranging from 53 years to 85 years; female-to-male ratio was 7:5, and the ratio of right eye to left eye was 8:7. The clinical data of all eyes included in this study and the vitreomacular relationship for fellow eyes are given in Table 1. The mean (±standard deviation) CDVA for all eyes was 0.17 (±0.13), with a range of 0 to 0.60 (Snellen 20/20 to 20/80). The mean (±standard deviation) maximum diameter of vitreofoveolar adhesion, as measured by OCT, was 267 (±139) μm, with a range of 63 μm to 545 μm.

The mean (±standard deviation) follow-up was 9.2 (±7.4) months. Eight (53.3%) of the 15 eyes underwent spontaneous and complete PVD; of these, 6 eyes exhibited complete resolution of the TCME, whereas 2 of these eyes exhibited a single persistent foveal cyst (Figure 1). At the time of final follow-up, mean CDVA (±standard deviation) improved from 0.20 (±0.13) (Snellen 20/35) (range, 0.10 to 0.50) (Snellen 20/20 to 20/60) to 0.16 (±0.12) (Snellen
Table 1. Tractional Cystoid Macular Edema: Clinical Data

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Age at Onset (Years)/Sex/Eye</th>
<th>CDVA at Presentation</th>
<th>OCT Findings at Presentation</th>
<th>Maximum Diameter of Vitreofoveolar Adhesion at Presentation (μm)</th>
<th>Coexisting Ocular Pathology in Study Eye</th>
<th>Vitreomacular Relationship in Fellow Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53/M/OD</td>
<td>0.2</td>
<td>TCME</td>
<td>332 ERM</td>
<td>No PVD, normal macula</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>62/M/OD</td>
<td>0.5</td>
<td>TCME</td>
<td>250 LO, ERM</td>
<td>PVD, normal macula</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>75/F/OS</td>
<td>0.6</td>
<td>TCME</td>
<td>112 LO, geographic atrophy</td>
<td>PVD, normal macula</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>70/F/OD</td>
<td>0.1</td>
<td>TCME</td>
<td>353 LO, macular hyperpigmentation</td>
<td>TCME</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>64/F/OD</td>
<td>0.1</td>
<td>TCME</td>
<td>169 LO, ERM, large soft drusen</td>
<td>TCME</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>85/F/OS</td>
<td>0.2</td>
<td>TCME</td>
<td>282 ERM, macular hyperpigmentation</td>
<td>PVD, normal macula</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>71/M/OD</td>
<td>0.2</td>
<td>TCME</td>
<td>344 LO, macular hyperpigmentation</td>
<td>PVD, normal macula</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>66/F/OD</td>
<td>0.10</td>
<td>TCME</td>
<td>81 None</td>
<td>TCME</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>73/F/OD</td>
<td>0.0</td>
<td>TCME</td>
<td>545 LO</td>
<td>Macular hole, closed post-vitrectomy</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>57/F/OS</td>
<td>0.2</td>
<td>TCME</td>
<td>400 LO</td>
<td>No PVD, normal macula</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>71/M/OS</td>
<td>0.2</td>
<td>TCME</td>
<td>63 None</td>
<td>PVD, normal macula</td>
<td></td>
</tr>
</tbody>
</table>

(continued on next page)
20/30) (range, 0.00 to 0.30) (Snellen 20/20 to 20/40), in the 8 eyes that experienced complete PVD during this study period, but this change was not statistically significant (P = 0.5).

Four (26.7%) of the 15 eyes in this study underwent progression of PVD, but in these cases, the PVD remained incomplete and the anatomical and clinical characteristics of the TCME persisted (Figure 2).

In these 4 eyes with the progressive (but incomplete) PVD during the study period, the mean maximum diameter (±standard deviation) of vitreofoveolar adhesion decreased from 185 (±73) μm at baseline to 131 (±83) μm at the final follow-up, representing a decrease (±standard deviation) of 34% (±19%) in the mean maximum diameter of vitreofoveolar adhesion, and this reduction was statistically significant (P = 0.007). The CDVA (±standard deviation) in those eyes was unchanged over the study period (baseline, 0.20 [±0.30] [Snellen 20/30]; final follow-up, 0.20 [±0.20]; P = 0.6).

Finally, 3 (20%) of the 15 eyes in this study experienced no progression or regression of either the PVD or the TCME, respectively. In these 3 eyes that underwent no progression of PVD, the mean maximum diameter of vitreofoveolar adhesion remained unchanged over the study period (baseline and final follow-up, 426 [±125] μm), and the CDVA (±standard deviation) for these 3 eyes also remained unchanged over the study period (baseline and final follow-up, 0.03 [±0.06] [Snellen 20/25]). No eyes in the entire series developed a macular hole during the period of follow-up. OCT images of representative cases are given in Figures 1 to 4.

**Discussion**

Tractional cystoid macular edema is a described mild subtype of VMT syndrome. As in all subtypes of VMT syndrome, the prognosis and treatment options depend on the size and configuration of the residual vitreomacular adhesion and the consequential macular anatomical changes.

The extent of the residual vitreomacular adhesion also determines the classification of VMT subtype. Tractional cystoid macular edema is characterized by a maximum diameter of vitreofoveolar adhesion of no more than approximately 500 μm, whereas the diameter of the vitreomacular adhesion in a typical case of

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**Table 1. (Continued)**

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Duration of Follow-up (Months)*</th>
<th>CDVA at Final Follow-up</th>
<th>Progression of PVD at Follow-up</th>
<th>OCT Findings at Follow-up</th>
<th>Maximum Diameter of Vitreofoveolar Adhesion at Final Follow-up (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>6.3</td>
<td>0</td>
<td>No</td>
<td>No change in maximum</td>
<td>294</td>
</tr>
<tr>
<td>11</td>
<td>12</td>
<td>0.1</td>
<td>Yes, complete PVD</td>
<td>PVD, normal macula</td>
<td>N/A</td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>0</td>
<td>Yes, complete PVD</td>
<td>PVD, remaining single</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*Symptom duration at the time of follow-up/spontaneous resolution of symptoms.
OD, right eye; ERM, epiretinal membrane; N/A, not applicable; LO, lens opacity; OS, left eye.

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**Fig. 1.** Patient 7. A. Optical coherence tomography of the right eye showing perifoveal vitreous detachment with focal foveolar attachment causing tractional cystoid foveal thickening. B. Optical coherence tomography of the same eye at follow-up showing complete PVD with a residual foveal cyst.
VMT syndrome is typically >1,500 μm (or 1–2 disk diameters). We believe that the extent of the vitreofoveal adhesion in VMT syndrome is of prognostic value.

The key event in the resolution of VMT syndrome and its symptoms rests on the progression to complete PVD. This can be achieved either surgically or spontaneously, with the likelihood of spontaneous resolution probably being greatest in those cases where the maximum diameter of the vitreofoveal adhesion is approximately 500 μm (i.e., cases of TCME). Although favorable results after surgical intervention in TCME have been reported, there have been no cohort studies, since the advent of OCT, reporting on the natural history of this rare condition. In the current series of 12 patients (15 eyes), 8 eyes exhibited spontaneous and complete PVD, with the resolution or improvement of symptoms, within 7 months of presentation. Furthermore, of these 8 eyes, 6 exhibited complete resolution of the TCME and restoration of normal foveolar architecture. The authors believe that the reason why no statistically significant improvement in the CDVA was demonstrable in those eyes was the small number of eyes in the study and that a larger study with more eyes in each subgroup is warranted.

The largest series of VMT with TCME, to date, is a retrospective series of 53 eyes reported by Hikichi et al. The authors reported spontaneous PVD in only 6 (11%) of 53 eyes, a much smaller proportion to what our data would suggest. However, that series reported on patients presenting between 1983 and 1993, before the advent of OCT, and the vitreomacular relationship was studied biomicroscopically, while the macular condition was diagnosed by the findings of fluorescein angiography. This important difference in the methodology renders comparison of the results of that study to our findings difficult because our study included only eyes with maximum vitreofoveal adhesion of <550 μm, an exclusion criterion that would have been impossible to implement before the advent of OCT. The authors believe that the comparatively low...
Proportion of spontaneous PVD reported in the series by Hikichi et al17 might be attributable to the fact that eyes with maximum vitreofoveal adhesion of any size were probably included in that study.

Mechanical induction of PVD is the primary surgical objective of vitrectomy in cases of mild TCME. In this series, 12 (80%) of 15 eyes experienced spontaneous progression of PVD (which was complete in 8 eyes [53%] and incomplete in 4 eyes [27%]), while 3 eyes (20%) underwent no change in the extent or configuration of the vitreofoveal adhesion, during the study period. It should also be noted that the mean CDVA at presentation was 0.2 or better (Snellen 20/60 to 20/200) in 13 of the 15 cases of TCME in this study, and therefore, the risk–benefit analysis of surgical vitrectomy in these cases would not have favored an offer of surgical vitrectomy with its inherent risks. Of the 2 cases of TCME with presenting CDVA >0.2, 1 case had a presenting CDVA of 0.5 (Snellen 20/60), which improved to 0.3 (Snellen 20/40) after spontaneous and complete PVD. One case of TCME had a presenting CDVA of 0.6 (Snellen 20/80), but this eye had coexisting atrophic age-related macular degeneration. Corrected-distance visual acuity improved to 0.5 (Snellen 20/60) after progression (albeit incomplete) of PVD with consequential reduction in maximum diameter of the vitreofoveal adhesion.

In the largest series, since the advent of OCT, published to date, Johnson reported on 11 eyes of 10 patients with TCME. Eight eyes were treated by surgical vitrectomy, while 3 eyes were treated by observation alone. The mean CDVA of the 8 eyes that were treated by surgical vitrectomy ranged from 0.48 to 1 log minimal angle of resolution (Snellen 20/60 to 20/200), whereas the CDVA of the 3 eyes that were treated by observation alone ranged from 0.1 to 0.2 (Snellen 20/25 to 20/30), reflecting the reluctance, expressed by the authors, to offer surgical vitrectomy in cases with good presenting acuity. The postoperative CDVA of the 8 operated eyes ranged from 0.1 to 0.3 (Snellen 20/30 to 20/40). In another series, Yamada and Kishi9 reported on 10 eyes of 9 patients with VMT and a maximum area of vitreofoveal adhesion of ≤500 μm. They were all treated by surgical vitrectomy with visual improvement (preoperative CDVA range, 0.1 to 1 [Snellen 20/25 to 20/200]; postoperative CDVA range, 0.1 to 0.7 [Snellen 20/25 to 20/100]). The results of both series indicate that in TCME, visual acuity at presentation is and should be a determinant of whether to offer surgical vitrectomy, but it also reflects intersurgeon variability in thresholds for surgical intervention, and that surgical vitrectomy in properly selected cases leads to anatomical success and functional improvement.

Ours is the largest series to date reporting on the natural history of TCME, using OCT in combination with slit-lamp biomicroscopy to assess the relationship of the vitreofoveal adhesion, at presentation and follow-up. We report spontaneous PVD and resolution of TCME in 40% of eyes in this series, which is quite similar to that for impending (Stage 1) macular hole.18 This is not unexpected because both conditions are caused by the tractional forces associated with perifoveal vitreous detachment and resolve when complete PVD occurs.

Finally, no contemporary discussion of VMT is complete without comment on the promising and emerging data that suggests that PVD can be pharmacologically induced with intravitreous administration of vitreolytic agents and that such agents could be used as a preoperative facilitator of mechanical vitrectomy for VMT and its subtypes (epiretinal membrane, macular hole, and TCME) or possibly even preclude the need for surgical vitrectomy.19–24

In summary, although there have been reports of favorable results after mechanical induction of PVD in

![Fig. 4. Patient 4. A. Optical coherence tomography of the right eye showing perifoveal vitreous detachment with focal foveolar attachment causing tractional cystoid foveal thickening. B. Optical coherence tomography of the same eye at follow-up showing complete PVD and restoration of the foveal depression.](image-url)
cases of mild TCME, ophthalmologists should be aware that TCME can resolve spontaneously in a substantial proportion of cases within months of presentation. Therefore, it would seem prudent for the retinal specialist to observe cases with good presenting CDVA for at least 6 months (with appropriate counseling regarding the risk of macular hole formation if the vitreomacular traction progresses) before offering surgical intervention in the form of vitrectomy. This is especially true as we enter an era where pharmacologic induction of PVD may represent yet another alternative to mechanical vitrectomy in cases of TCME.

**Key words:** cystoid, edema, history, macular, natural, tractional.

**References**