Diagnosing and Treating Vitreomacular Adhesion

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Abstract

Perifoveal vitreous detachment with residual vitreofoveal adhesion is considered as the first stage of posterior vitreous detachment. A key point is the transition from an innocuous vitreomacular adhesion (VMA) to a pathological vitreomacular traction (VMT). By using optical coherence tomography (OCT), VMA is defined as adhesion of the posterior hyaloid cortex involving the centre of the foveal region with or without a hyper-reflective signal on the inner surface of the retina. VMT is diagnosed when the inner macular surface slopes steeply, or sharp angulation and localised deformation of the retinal profile is detected at the VMA site. Otherwise, VMA is simply considered to be persistent adherence of the cortical vitreous. The tractional effects of perifoveal vitreous detachment cause a variety of macular pathologies determined by the size and the strength of the residual vitreoretinal adhesion. Vitreomacular adhesion plays a major role in the development of diseases such as vitreomacular traction syndrome (VMTS), macular hole, epiretinal membrane, tractional macular oedema and myopic macular retinoschisis. In addition, clinical evidence supports the theory that the course of diabetic retinopathy and age-related macular degeneration may be strongly influenced by an incomplete posterior vitreous separation. The current standard of care of vitreomacular interface pathologies is vitrectomy and membrane peeling – a procedure that is thought to relieve epiretinal traction – followed by regeneration of the retinal architecture and recovery of visual function. Over the last few years, with the introduction of 25-gauge (0.50mm) and 23-gauge (0.72mm) instruments, there has been another major shift toward transconjunctival microincisional vitrectomy surgery (MIVS). Pharmacological induction of posterior vitreous detachment (PVD) can become a further step toward a real 'minimally invasive vitreous surgery' for VMTS.

Keywords

Chromovitrectomy, optical coherence tomography, posterior vitreous detachment, small-gauge vitrectomy, vitreomacular adhesion, vitreomacular traction.

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In the ageing eye, vitreous body liquefaction (syneresis) and collapse (synchisis) occur together, with changes at the interface that weaken vitreoretinal adhesion and promote vitreoretinal separation in the majority of individuals. When vitreous gel liquefaction and weakening of vitreoretinal adhesion occur concurrently, the posterior vitreous cortex separates away from the internal limiting membrane (ILM) without interface pathologies, thus resulting in an innocuous posterior vitreous detachment (PVD).[1]

The completion of PVD is preceded by earlier stages that are typically chronic, occult and asymptomatic. Perifoveal vitreous detachment with residual vitreofoveal adhesion is considered as the first stage of PVD (see *Figure 1*).[2]

Vitreous gel liquefaction in excess of the degree of vitreoretinal dehiscence defines anomalous PVD.[3] An incomplete posterior vitreous separation can leave residual sites of vitreoretinal adhesions. In addition, when PVD occurs, there is typically complete separation of all vitreous cortex layers from the ILM, although splitting of the posterior vitreous cortex (vitreoschisis) occurs in a large subset of eyes, leaving remnants of cortical vitreous attached to the ILM in areas of firm vitreoretinal adhesion (see *Figure 2*).[4]

A key point is the transition from an innocuous vitreomacular adhesion (VMA) to a pathological vitreomacular traction (VMT).

The tractional effects of perifoveal vitreous detachment cause a variety of macular pathologies determined by the size and the strength of the residual vitreoretinal adhesion.[2,5–11]

VMA plays a major role in the development of diseases such as vitreomacular traction syndrome (VMTS), macular hole, epiretinal membrane, tractional macular oedema and myopic macular retinoschisis. In addition, clinical evidences support the theory that the course of diabetic retinopathy and age-related macular degeneration may be strongly influenced by an incomplete posterior vitreous separation.[2,11]

A landmark scanning electron microscopic study of autopsy eyes with spontaneous PVD found remnants of vitreous cortex in the foveal area. Most remnants had the configuration of a 500 or 1,500µm diameter plaque of vitreous adherent to the foveola.[12]

These observations and similar observations during intra-operative induction of PVD strongly suggest that the central 500µm foveolar

Figure 1: Spectral-domain Optical Coherence Tomography of Early Stage of Posterior Vitreous Detachment with Perifoveal Vitreous Detachment with Residual Vitreofoveal and Papillary Adhesions

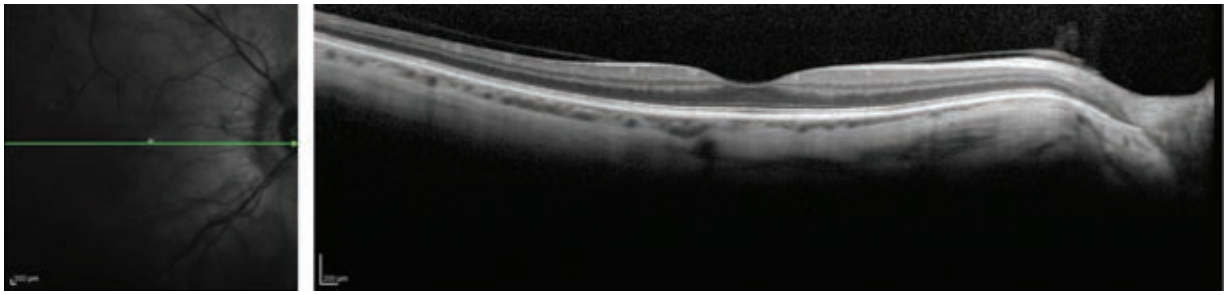
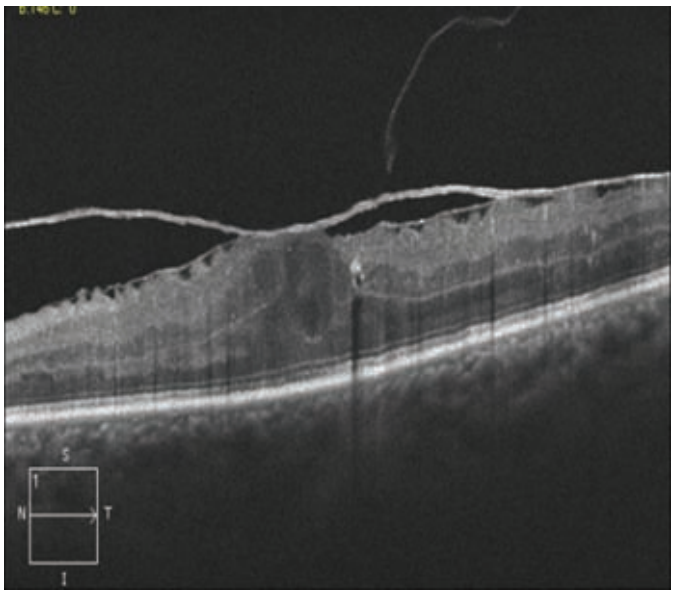


Figure 2: Spectral-domain Optical Coherence Tomography of Tractional Macular Oedema Linked to Incomplete Posterior Vitreous Detachment, Vitreoschisis and Related Vitreomacular Traction



area and the margin of the 1,500µm fovea are sites of firm vitreoretinal adhesion.[13]

Vitreous traction forces resulting from perifoveal PVD with a small vitreofoveolar adhesion (500µm or less) by imparting greater tractional stress, may cause localised cystoid foveal thickening, or one of several macular hole conditions. Lower tractional stress associated with larger adhesion zones may cause a separate group of macular disorders such as VMTS, traction diabetic macular oedema and myopic traction maculopathy, or exacerbate an age-related macular degeneration (AMD).[2,11]

Spaide found a statistically significant correlation between smaller diameters of vitreous attachment and the amount of foveal deformation in early macular hole stages.[14] The hypothesis is that the tractional stress (force per unit area) acting on the fovea increases with decreasing area of vitreous attachment.[11]

In epiretinal membranes (ERMs), there is significant variability in the size, number and presence or absence of vitreomacular attachments.[2,15,16] Ultrastructural studies suggest that ERMs develop from cortical vitreous remnants left on the retinal surface after PVD and play an important role in the pathogenesis of traction maculopathies.[2,11]

ERMs may result from the proliferation and transdifferentiation of hyalocytes contained within vitreous cortical remnants formed by a splitting or schisis within the vitreous cortex after PVD.[12,13,17–24] The fibrocellular proliferation along the retinal and vitreal interfaces in VMT may contribute to the tenacity of vitreoretinal adhesion.[24]

Diagnosis

Biomicroscopy and echography have largely been used to identify partial PVD and associated macular tractional pathologies. These examination techniques, however, underestimate the prevalence of VMA. Since the 1990s, time-domain optical coherence tomography (TD-OCT) – having axial resolution of 15µm and scanning speed of 400 A-scans per second – has been widely used to image the vitreomacular interface, so ameliorating the ophthalmologists' ability to identify VMA and related maculopathies.[25–37]

By using OCT, VMA is defined as adhesion of the posterior hyaloid cortex involving the centre of the foveal region with or without a hyper-reflective signal on the inner surface of the retina. VMT is diagnosed when the inner macular surface slopes steeply, or sharp angulation and localised deformation of the retinal profile is detected at the VMA site. Otherwise, VMA is simply considered to be persistent adherence of the cortical vitreous.[8]

Uchino and colleagues[27] studied the development of PVD in 209 healthy eyes using biomicroscopy, ophthalmoscopy and OCT. Posterior vitreoretinal interface condition was classified as one of five stages, according to biomicroscopic findings and OCT images relative to discrete linear signals indicating a detached posterior vitreous face: stage 0 – no PVD (61 eyes [29.2%]); stage 1 – incomplete perifoveal PVD in up to three quadrants (100 eyes [47.8%]); stage 2 – incomplete perifoveal PVD in all quadrants, with residual attachment to the fovea and optic disc (26 eyes [12.4%]); stage 3 – incomplete PVD over the posterior pole, with residual attachment to the optic disc (four eyes [1.9%]); or stage 4 – complete PVD identified with biomicroscopy, but not with OCT because of instrument limitations (18 eyes [8.6%]). Stages 1, 2 and 3 incomplete PVD without subjective symptoms was not recognisable on contact lens biomicroscopy. OCT demonstrates that healthy human eyes have incomplete or partial PVD beginning as early as the fourth decade of life. The superior quadrant was usually the initial site of incomplete PVD.

Gallemore and colleagues[26] compared the relative incidence of VMAs diagnosed with biomicroscopy versus those diagnosed with TD-OCT. The authors found that the OCT was more sensitive than biomicroscopy in identifying VMAs (30 versus 8%). In addition, using OCT, two patterns of VMA were identified: a focal type, in presence of

a vitreoretinal adhesion attached to the foveal or parafoveal retina associated with a surrounding partial posterior vitreous separation; and a multifocal type, when multiple vitreoretinal adhesions were separated by areas of posterior vitreous separation. Focal type was found in 25 eyes, while multifocal type was detected in 14 out of 132 eyes. Splitting of the posterior vitreous cortex (vitreoschisis) and its relation to VMT have been clearly documented by OCT.[30,31]

In the last few years, OCT techniques have evolved to spectral-domain OCT (SD-OCT), which features a higher speed and improved resolution, presenting an axial resolution of 3–7µm and a scanning speed of up to 40,000 A-scans per second in commercially available systems.[38–40]

Most importantly, these advanced OCT systems are based on a raster scanning method and provide a 3D reconstruction of the entire macular region, substantially contributing to a better understanding and spatial perception of the pathophysiologic features of the vitreoretinal interface and helping surgical planning as it reveals the manner and direction of ERM traction on the retina.[41–43]

Recently, in an observational, cross-sectional study,[44] Mojana and colleagues used simultaneous SD-OCT and SLO imaging instruments to image both eyes of patients with symptoms of PVD. A partial PVD was detected more frequently by SD-OCT/SLO than by biomicroscopy examination (45 versus seven eyes). SD-OCT/SLO allowed improved visualisation of the vitreoretinal relationship, reliably visualising the effects of PVD, including vitreoretinal traction, paravascular lamellar holes and fine changes at the fovea.

Therapy

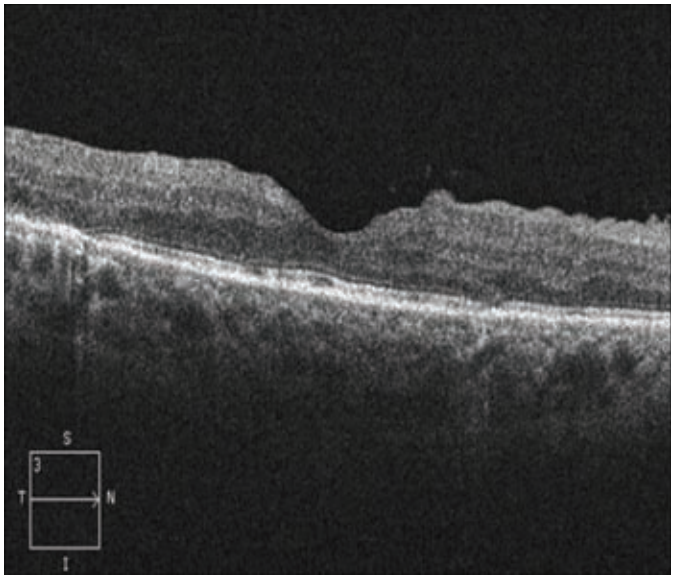
The current standard of care of vitreomacular interface pathologies is vitrectomy and membrane peeling – a procedure that is thought to relieve epiretinal traction – followed by regeneration of the retinal architecture (see *Figure 3*) and recovery of visual function.[45]

A complete vitrectomy combined with the induction of a posterior hyaloid detachment releases both static, trampoline-like traction anteriorly to the foveola due to the elastic properties of the hyaloid and the dynamic vitreous traction forces generated during ocular rotations in the early stage of PVD.[46] Then, a careful removal of the ERM and ILM is performed.

Since the advent of vitrectomy in the early 1970s, there has been a continuing evolution in vitrectomy techniques, indications and instrumentation.[47,48] Three-port system pars plana vitrectomy (PPV) remained the standard of care for over 30 years. Twenty-gauge (0.89mm) vitrectomy has been both well tolerated and effective, with high rates of successful outcomes and low rates of complications. Over the last few years, with the introduction of 25-gauge (0.50mm) and 23-gauge (0.72mm) instruments, there has been another major shift toward transconjunctival microincisional vitrectomy surgery (MIVS).[49–52]

The advantages of a transconjunctival, sutureless approach include increased patient comfort, decreased corneal astigmatism and decreased operative times.[53–56] In addition, there is less conjunctival scarring, which may benefit patients who have had multiple previous surgeries, or where preserving the conjunctiva is paramount (as in glaucoma patients who may require filtering surgery).[57] The advantages must be weighed against the potential drawbacks of post-operative hypotony and a possible increased risk of endophthalmitis.[58]

Figure 3: The Same Case in Figure 2 After Surgical Resolution of Vitreomacular Traction Syndrome



As instrumentation for MIVS continues to evolve, the indications for transconjunctival sutureless vitrectomy continue to increase, with low rates of complications.[57] Recent enhancements in MIVS include an ultra-high-speed vitrectomy system to decrease vitrectomy times, new trocar blade design to ease incision creation, valved cannulas to prevent fluid leakage, a lighted infusion or chandelier light to perform bimanual surgery and collagen plugs to aid closure of sclerotomy sites.

The concept of 'minimally invasive vitreous surgery' has to be referred not only to the size of the pars plana sclerotomy entry site, but also to what extent the vitreous gel needs to be vitrectomised[59–61] and the number of sclerotomies.[62–64]

Sakaguchi et al.[65] have further reduced the size of two sclerotomies to accommodate 27-G micro-instruments to perform a non-vitrectomising technique, only for epiretinal membranes.

More recently, Gualtieri[66] reported preliminary results of a pilot study of minimally invasive vitrectomy through one-port pars plana sclerotomy, by 25-G instruments for selected vitreous, macular and vitreomacular interface disorders.

Since 2000, the so-called 'chromovitrectomy' has become a common approach among vitreoretinal surgeons.[67–80] It concerns the use of vital dyes or crystals to improve the visualisation of intraocular tissues, thereby improving the surgical outcome. In macular hole surgery, after vitrectomy procedure, indocyanine green (ICG) was injected in the vitreous cavity over the macular area to stain the ILM and facilitate membrane peeling.[67,68,70] Trypan blue was used as a helpful tool to identify the several types of ERM,[69] while the intravitreal triamcinolone acetonide has been very useful for improvement of vitreous identification.[71] Recently, several other dyes, including infracyanine green, patent blue, bromophenol blue and brilliant blue have been proposed as possible tools in chromovitrectomy.[72–80]

Although intra-operative application of vital dyes has facilitated surgical techniques and outcomes in recent years, controversy still remains

around various issues, mainly potential toxicity and safety. Besides, during vitrectomy procedure, the mechanical induction of PVD can result in a higher incidence of intra- or post-operative retinal breaks, or both.[81,82]

The ability to treat and even prevent the complications of early-stage PVD will expand as safe and effective pharmacological methods for inducing PVD become available.[10]

The goals of pharmacological vitreolysis are to induce liquefaction of the vitreal gel and promote complete dehiscence of the vitreous from the retina.[83]

The migration toward 25-gauge and 23-gauge vitrectomy surgery encounters the difficulty in obtaining the adequate suction to create a surgical PVD. Therefore, an agent that induces vitreous liquefaction and facilitates posterior vitreous separation from the retina may make more cases amenable to less-invasive vitrectomy via small-gauge instrumentation. Increasing the number of cases potentially approached with small-gauge surgery may decrease both patient discomfort and recovery times after vitrectomy surgery.[84]

In vitro assessments of plasmin and microplasmin demonstrate activity against substrates important in vitreous structure and the vitreoretinal interface, including collagen type II and fibronectin (Kindt N, unpublished data, ThromboGenics, 2009). A prior clinical study supports the hypothesis that microplasmin may have beneficial characteristics in eliminating VMT.[85]

Results from a phase II study evaluating the safety and efficacy of intravitreal microplasmin in facilitating the creation of total PVD before vitrectomy are intriguing and warrant further investigation.[84,86]

Conclusion

In conclusion, the improvement of diagnostic tools, especially OCT, makes diagnosis and follow-up of VMA easier. However, despite the advent of dyes and minimally invasive vitrectomy surgery, VMT has still to be managed with caution. Due to the risk of heavy complications, surgical indication has to be reserved to cases showing morphologic findings of progression of the disease together with functional signs of worsening of the visual function. We do believe that pharmacological induction of PVD can become a further step toward a real 'minimally invasive vitreous surgery' for VMTS. ■

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