SURVEY OF OPHTHALMOLOGY VOLUME 57 • NUMBER 6 • NOVEMBER–DECEMBER 2012

MAJOR REVIEW

Vitreomacular Adhesion and Neovascular Age-Related Macular Degeneration

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Abstract. We explore the hypothesis that vitreomacular adhesion (VMA) and vitreomacular traction (VMT) play a role in the pathogenesis and clinical course of neovascular ("wet") age-related macular degeneration (AMD). Several biological theories are offered to explain this possible association, including direct tractional force, altered vitreous oxygenation, altered diffusion coefficients of intravitreal molecules, and alterations in the pharmacokinetics of intravitreal drugs. Release of VMT may improve the clinical course of neovascular AMD, and a few case series suggest that vitrectomy can lead to both a functional and anatomic improvement. A large, randomized, controlled clinical trial is underway, investigating pharmacologic release of VMA in eyes with neovascular AMD. (**Surv Ophthalmol 57**:498–509, 2012. © 2012 Elsevier Inc. All rights reserved.)

Key words. age-related macular degeneration • vitreomacular adhesion • vitreomacular traction • vitreous

I. Introduction

Age-related macular degeneration (AMD) is associated with significant visual morbidity and is the leading cause of irreversible blindness in the developed world.[5,27,53,56] AMD accounts for 54% of cases of visual loss in the white population of the United States.[27] In the UK, AMD accounts for 57% of all persons registered as blind. Unsurprisingly this proportion increases with advanced age (42% of cases aged 65–74 years; 66% of those aged 75–84 years; and 74% of those over age 85 years).[12]

Anti-vascular endothelial growth factor (VEGF) agents have transformed the treatment of neovascular ("wet") AMD (nAMD). Following the widespread introduction of ranibizumab (Lucentis; Genentech, South San Francisco, CA) and bevacizumab (Avastin, Genentech), retinal specialists have been able to maintain or improve vision in a disease with an otherwise poor natural history. Many patients, however, do not respond well, if at all, to anti-VEGF therapy. Responder analysis in the SUSTAIN (Study of Ranibizumab in Patients With Subfoveal Choroidal Neovascularization Secondary to Age-Related Macular Degeneration) trial indicates that 47% of patients either lost vision despite anti-VEGF treatment or failed to maintain the visual gains that they achieved at the start of treatment.[42] Some of these patients may have genetic or lifestyle factors that predispose them to more aggressive disease or antagonize the effect of intravitreal agents; there may be other factors, such as

0039-6257/$ - see front matter
doi:10.1016/j.survophthal.2012.01.011

tachyphylaxis,[25,96] that influence the clinical course, however. One possibility is that vitreomacular adhesion (VMA) or vitreomacular traction (VMT) play a role, either in the pathogenesis of the disease or its clinical course.[99]

Historically the vitreous was thought to be an inert structure that had little effect on retinal and, more specifically, macular disease. Using traditional slit-lamp biomicroscopy, the transparent vitreous was hard to assess and only recently, with the development of diagnostic tools such as optical coherence tomography (OCT), our understanding of the link between the vitreoretinal interface and retinal disease has advanced.[9,75,84,127,128] OCT has enabled the visualization of this interface in disorders including epiretinal membrane, macular hole, maculoschisis, VMT syndrome, and diabetic macular edema (DME).[75] A growing number of studies provide evidence that the vitreous plays a role in nAMD.[58,65,76,80,90,99,134] We review the current literature on the interaction of VMA and nAMD.

II. Definitions

A. POSTERIOR VITREOUS DETACHMENT

Posterior vitreous detachment (PVD) describes the separation of the posterior vitreous face from the internal limiting membrane (ILM) of the retina. Throughout life there is gradual liquefaction of the vitreous so that by age 70 approximately 50% of the vitreous is liquified.[24] This vitreous liquefaction, in combination with the progressive weakening of the adhesion between the posterior vitreous face and the ILM,[101] leads to the commencement of a PVD as early as the forth decade of life, with a mean age of onset of complete PVD around 60.[17,138] Uchino et al examined the posterior vitreous face in 209 healthy patients between ages 31 and 74 years.[131] They discovered that PVD usually starts with a focal detachment of the vitreous in one quadrant of the perifoveal area (with a superior predilection), with persistent attachment to the fovea and optic nerve head. They found that that the detachment extended slowly for years, eventually resulting in complete PVD. Further longitudinal studies provide evidence that the progression of a PVD can be slow.[13,48,132] One such study was an observational case series performed by Johnson that showed that only 3 out of 31 (9.7%) patients with perifoveal vitreous detachment progressed to a complete PVD over an average follow-up period of 30 months.[48] Risk factors for the development of PVD include age, sex (Women have approximately a two-fold increase in risk.), and myopia (three- to four-fold increase).[17,138]

Vitreous liquefaction and the weakening of the adhesion between the posterior vitreous face and the ILM do not always occur at the same rate. An anomalous PVD may occur if the extent of vitreous liquefaction exceeds the degree of weakening at the vitreo-retinal interface, leading to abnormal tractional forces being exerted on the macula.[103] If this occurs in the peripheral retina, particularly in the context of firm vitreoretinal adhesion, then retinal tears and detachment may develop. This may underlie the increased incidence of retinal tears in disorders with abnormal vitreous liquefaction, such as Marfan, Ehlers-Danlos, and Stickler syndromes, and to a lesser degree myopia.[103]

B. VITREOMACULAR ADHESION

Because the posterior vitreous face usually lies in apposition to the ILM of the macula, the term vitreomacular adhesion (VMA) describes the normal anatomic state, but the term VMA is often used clinically to describe a situation where there is focal macular adhesion, often centered on the fovea, with surrounding separation of the hyaloid face from the neuroretina. Therefore, VMA may be defined clinically as focal adhesion of the vitreous face within the macular region. In this sense VMA is a type of incomplete PVD.

C. VITREOMACULAR TRACTION

VMA may exist without any structural distortion of the macular architecture (Fig. 1); if VMA exerts focal traction that distorts the macula, however, then this may be defined as VMT (Fig. 2). It can be an arbitrary distinction as to whether the degree of distortion constitutes significant VMT, versus VMA with minor traction. For this reason we have selected a photographic standard (Fig. 3), such that traction greater than or equal to this degree might be classified as VMT.

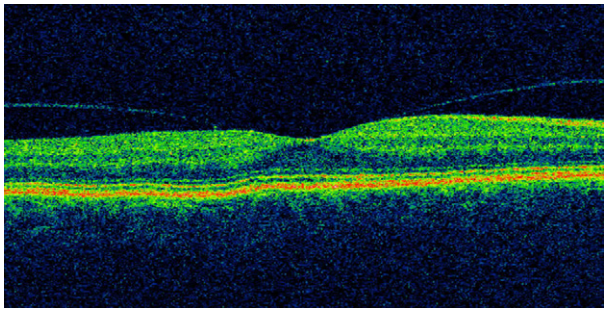

Fig. 1. Vitreomacular adhesion (VMA). The posterior vitreous face is separated from the perifoveal retina and attached to the central macula, without causing retinal distortion.