

# Vitreomacular Adhesion: Pathology and Treatment

New pharmacologic treatment option is an alternative to surgery or watchful waiting.

BY DAVID S. BOYER, MD

One of the most fulfilling aspects of the science of medicine is participating in new discoveries that lead to improved treatment modalities for our patients. The last few years have led to significant advances in our understanding of the vitreous of the eye. The transparent nature of the vitreous combined with inadequate imaging capabilities resulted in diagnoses of vitreomacular adhesion (VMA) or vitreomacular traction (VMT) based on visual disturbances rather than actual pathology. The evolution from B-scan ultrasound to spectral-domain optical coherence tomography (SD-OCT), however, can be compared to the leap from analog to high-definition television. The improvements in image detail and quality have opened the door to studying the natural pathology.

## UNDERSTANDING THE PATHOLOGY

SD-OCT allows evaluation at the microstructural level of changes that are happening within the retina. It is now possible to view each of the 10 layers of the retina to evaluate deformations of the fovea, cystic changes, or the presence of subretinal fluid. The physician can identify if there is a problem at the inner-segment/outer-segment junction or in the retinal pigment epithelium, as well as measure the size of an adhesion or macular hole. As the vitreous liquefies and goes through the process of detaching from the retina, it may remain

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attached at certain places. If those adhesions are in the area of the macula and causing visual disturbances, we label this pathology symptomatic VMA, which is synonymous with the older term VMT. VMA and VMT were likely grossly underdiagnosed in the past. Now we have the ability to study these adhesions and determine which morphologic characteristics are most likely to lead to spontaneous resolution and which are not. A working group has now convened to classify the severity of VMA based on OCT images, and a manuscript is expected sometime in 2013.

## NEW TREATMENT OPTIONS

The ability to visualize pathology has coincided with the availability of a pharmacologic agent for treating it. Ocriplasmin (Jetrea, ThromboGenics) was approved by the US Food and Drug Administration in October 2012 for the treatment of symptomatic VMA. A single injection of 125 µg of this proteolytic enzyme resolved VMA

in 26.5% of treated eyes compared with 10.1% of eyes that received sham injection ( $P < .001$ ).<sup>1</sup> Nonsurgical closure of macular hole was achieved in 40.6% of ocriplasmin-injected eyes, as compared with 10.6% of placebo-injected eyes ( $P < .001$ ). Subgroup analysis of

this study shows that patients with adhesions smaller than 1500  $\mu\text{m}$  and macular holes smaller than 400  $\mu\text{m}$  had even better results. Improved imaging capabilities even since the inception of the studies on ocriplasmin have shown that accurate measurements of macular

# Ocriplasmin in Practice

## AN INTERVIEW WITH PRAVIN U. DUGEL, MD

### **Q: What are your patient selection criteria for ocriplasmin (Jetrea, ThromboGenics)?**

**Dr. Dugel:** I have the same criteria for treatment with ocriplasmin that I have for surgery. Patients must have vitreomacular adhesion (VMA), and it must be symptomatic. Within that group, the patients shown to have the greatest success with ocriplasmin are those with a VMA of 1500  $\mu\text{m}$  or less and those with a macular hole of 400  $\mu\text{m}$  or less. Because there is level 1 evidence to support the use of this drug in these patients, they represent the first tier of candidates for ocriplasmin.

The second group of patients who are candidates for ocriplasmin includes those with epiretinal membrane or VMA greater than 1500  $\mu\text{m}$ . Ocriplasmin was successful in some of these patients, but not to the same extent as in the first group.

The third group of patients who could potentially benefit from ocriplasmin includes those with neovascular age-related macular degeneration, diabetic macular edema, and retinal vein occlusion. The key word here, however, is “potential,” because although there is some preliminary evidence that VMA may have significant influence on these diseases, the scientific data are lacking. If a relationship between VMA and these diseases is confirmed in larger studies, ocriplasmin may have an important role as a combination agent. We look forward to forthcoming scientific evidence.

### **Q: How do you manage patient expectations for treatment with ocriplasmin?**

**Dr. Dugel:** If patients meet the criteria for ocriplasmin injection, I tell them that they are a candidate for vitrectomy, but that there is a drug with an excellent safety profile that has about a 50% chance of fixing the problem and allowing them to avoid surgery. If the drug doesn't work, they will go on to surgery that they would need anyway, and studies show that the success of surgery will not be compromised. If I were a patient,

there would be no reason for me not to accept this line of treatment.

It is also important for surgeons to understand that this drug mirrors surgery very closely. The immediate impressive effects of anti-VEGF injections make it easy to expect a similar “wow” effect with an injection of ocriplasmin. However, that is not the case. Some patients may even have decreased vision before improving. As with vitrectomy, recovery is gradual, not immediate.

### **Q: Will this drug take away from the surgical procedures that will be performed?**

**Dr. Dugel:** There is a small overlap. Patients with VMA less than 1500  $\mu\text{m}$  and macular hole smaller than 400  $\mu\text{m}$  may no longer need surgery. However, there are also many patients who have symptomatic VMA but who are not candidates for surgery. Although they cannot read or do other near vision tasks, their visual acuity may still be 20/30 or 20/40. They have real symptoms, but the risk-to-benefit ratio of vitrectomy surgery is still too great. We currently watch these patients, which is frustrating to both the patient and the physician. Now we have a medical treatment for this large group of patients who previously had no appropriate treatment, because with a drug the risk-benefit profile is more acceptable than with surgery. This is very exciting. ■

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hole sizes and adhesion spots are directly related to the efficacy of the drug. We are now able to predict that it works best in patients with smaller macular holes and adhesions and no epiretinal membranes.

Although the understanding of the natural pathology of VMA is still in its infancy, ocriplasmin study results are encouraging. The alternative to an injection is vitrectomy, a surgery for which the risk-to-benefit ratio cannot be justified unless visual acuity is significantly decreased. An important finding in the ocriplasmin study was that successful pharmacologic treatment manifested in less than 28 days in the majority of patients, and, in those who did not achieve posterior vitreous detachment (PVD), vitrectomy surgery was not precluded or hindered in any way. In fact, data indicate an improvement in stage gradation of PVD after ocriplasmin administration, perhaps making it less work for the surgeon to achieve PVD with vitrectomy.

In my opinion, the ideal case in which to use ocriplasmin is a younger phakic patient with a small stage 2 macular hole. The potential is high for such a patient to avoid vitrectomy surgery, with a difficult recovery period and the potential side effect of cataract formation.

Effective October 1, 2011, the ICD-9-CM diagnosis code 379.27 was created for VMA and VMT. This code can be used in addition to the code for macular hole, enabling a surgeon to first treat with ocriplasmin and, if the pathology does not resolve, to then perform vitrectomy surgery.

## CONCLUSION

There is still a lot to learn about this pathology; thankfully, many studies are currently under way. The OASIS study (clinical trials.gov: NCT01429441) is one of the largest studies in the public domain that will improve our understanding of the natural history of VMA and improve knowledge regarding who is most likely to respond positively to treatment. Studies have also been initiated to see if treatment with ocriplasmin can help quiet the disease process in age-related macular degeneration. Great progress has been made, and I look forward to continued clinical and study results. ■

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1. Stalmans P, Benz MS, Gandorfer A, et al. Enzymatic vitreolysis with ocriplasmin for vitreomacular traction and macular holes. *N Engl J Med*. 2012;367:606-615.