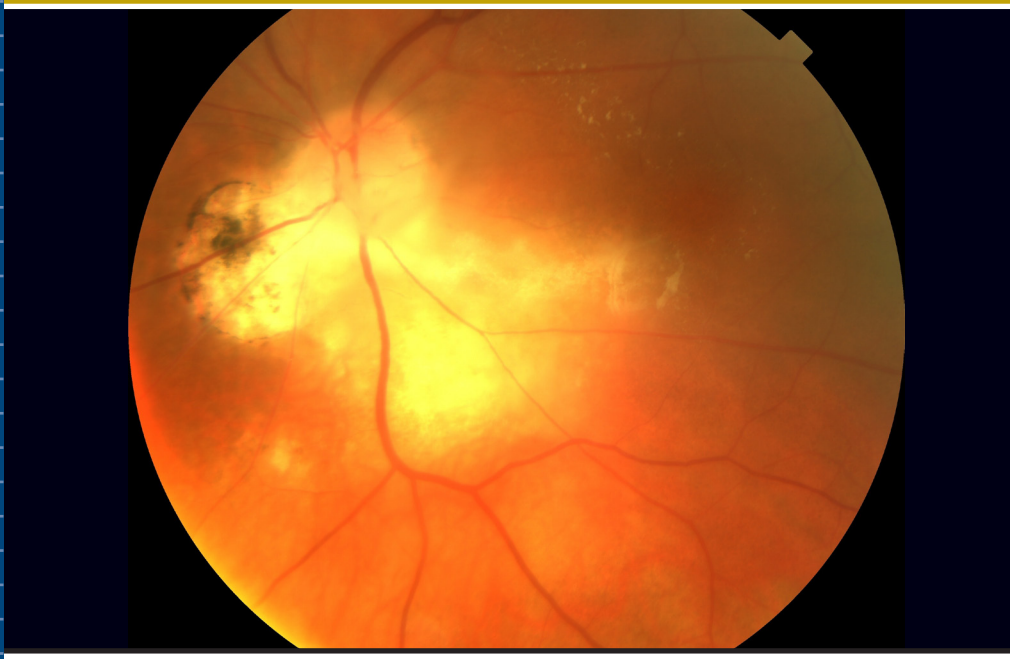
the LIGHT PIPE

Winter 2013



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THE NEWSLETTER OF

GEORGIA RETINA

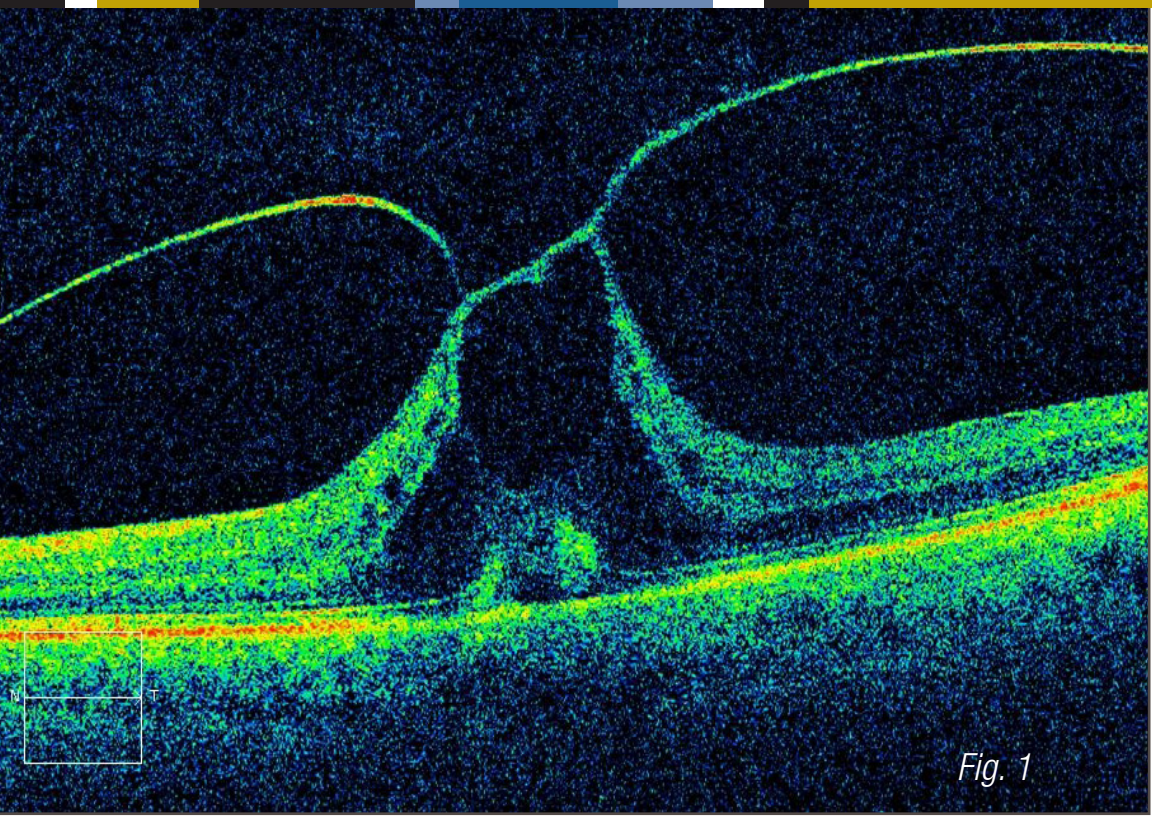


Fig. 1

What is Ocriplasmin?

Pars plana vitrectomy as a technique has revolutionized retinal surgery since its advent and initial report by Machemer. It allowed the removal of traction by an internal method, essential in retinal detachment procedures, as well as provided an active management modality for vitreous hemorrhage, and opened the door for surgical intervention in a myriad of retinal pathologies.

Since that time, the evolution of vitrectomy surgery has seen experimentation and implementation of smaller surgical instruments aimed at greater functionality and minimalization of ocular trauma, as well as shorter operating times, greater patient comfort and quicker recovery times. However, as we all know, the health care system is increasingly stressed with the aging of the population. There is a general trend in medicine to seek the least invasive treatment possible for the benefit of the patient. Whenever possible, it is preferable to avoid surgery and the resulting trauma to the patient and the potential impact of surgery on a patient's life, including post-operative recovery times, need to take off from work, or an added burden on family members. For certain vitreo-retinal conditions, there now may be a paradigm shift in the way these patients are managed.

Everyone's vitreous gel gradually peels away from their retina as they age. This vitreous separation typically occurs in one's fifth or sixth decade of life. In many individuals, there are moments when the gel adheres to and tugs on the macula during posterior vitreous separation. This occurrence is called VMA traction. *(Fig. 1)*

Symptomatic VMA is when the patients experience distortion or metamorphopsia. This can significantly affect a person's ability to carry out everyday tasks such as reading, driving, filling out checks, or computer related tasks. They may even have difficulties with depth perception, making going down a flight of steps hazardous. Peripheral vision generally remains quite good. The Food and Drug Administration recently approved a new drug for the treatment of vitreo-macular adhesion (VMA) and associated macular hole formation. In early November 2012, the FDA announced it has approved ocriplasmin (Jetrea, ThromboGenics) for the treatment of symptomatic VMA, which makes it the first pharmacological agent for the treatment of this progressive retinal condition. Ocriplasmin has been able to meet the objectives of both liquefaction and detachment of the vitreous at the vitreoretinal interface, while maintaining an acceptable safety profile. In preclinical studies, it succeeded in cleanly separating the vitreous from the internal limiting membrane and achieving therapeutic posterior vitreous detachment. It has been shown to be effective and generally well tolerated in two large phase 3 clinical trials, the MIVI-TRUST program.

The program compared a single injection of 125 µg ocriplasmin to a single placebo injection for the treatment of symptomatic VMA in 652 patients in Europe and the U.S. Of the 464 patients who were given a single injection of ocriplasmin, 26.5% achieved VMA resolution by day 28 compared to 10.1% of the 188 patients in the control group. In 74% of the responders, VMA resolution was achieved by day 7. Furthermore, ocriplasmin was shown to be effective in closing full-thickness macular holes (FTMH) in a significant proportion of patients after a single injection. Of 106 patients with FTMH at baseline, 40.6% experienced closure by day 28 and sustained it through the entire 6-month follow-up compared with 10.6% of 47 subjects in the placebo group. For the subset of patients with a stage 2 MH (less than 250 µm, 58.3% of 48 ocriplasmin-treated patients achieved successful closure compared with 16% of 25 subjects in the placebo cohort. Also worth mentioning, the visual acuity and visual outcomes favored the ocriplasmin group. The safety review showed most adverse events were relatively minor and transient. Floaters (13%), eye pain (10.5%), photopsia (10%), and blurred vision (6.5%) were the only adverse events that occurred at a rate >5% in the ocriplamin-treated eyes. There were few serious adverse events in the study and reportedly occurred in both cohorts.

As of January 2013, Jetrea (ocriplasmin) will be commercially available and may provide an option for many patients with symptomatic VMA or early macular hole. Pharmacologic vitreolysis may have a positive economic impact on the health care system by decreasing health care costs related to surgery and reducing surgical rates. In addition, it may have a tremendous impact on the individual patient and/or caregiver by reducing the burden of treatment for the patient, as there is generally a significant amount of lost work time associated with surgery and recuperation and multiple post-operative visits. Time will tell how this new therapeutic will fit into the pharmacologic armamentarium of the vitreo-retinal surgeon.

The sole purpose of this article is to advance the knowledge and understanding of the product. Georgia Retina does not receive any financial compensation.

EMAIL & HIPAA

Tips on Compliance

Electronic communication has greatly improved the flow of information, including the information we use each day in caring for pati ents. Doctors increasingly use email to communicate with their patients and with fellow physicians. Unfortunately, the internet at large is not secure. Neither are most email services. An email message may be read by an unintended recipient through hacking, information theft, or simply sending it to the wrong person. Unintended recipients are the focus of HIPAA. Here are several guidelines to maintain HIPAA compliance:

- **Source of email**
  - Message should be composed on a secure network within the sender's office
  - Virus protection and firewalls provide the network with security.
  - In the eyes of HIPAA, using a secured network to compose the message opens the opportunity to use email for patient-related communication.
- **Subject line of email**
  - Must be intentionally vague.
  - Should never contain specific patient information (name, date of birth, etc).
- **Body of email**
  - Should contain a properly worded "email notice" located at the end of the email.
  - Explains that the content of the email is confidential and private.
  - Notifies the recipient that they should not share or forward the information.
  - Requests that the recipient let the sender know if the email was received in error.
- **Sending of email**
  - Should be via an encrypted email or encrypted attachment to standard email.
  - Recipient opens the email with a password received in a separate communication.

When communicating directly with patients, inform them of the risks. In fact, do not assume the patient is aware of the security risks, even if they initiate email communication. Post visible notices online and in the office warning patients of those risks. Most patients will already understand, but HIPAA requires that the doctor inform the patient anyway.

We at Georgia Retina strive to provide the best care for your patients and to communicate with you as efficiently as possible. We also have a responsibility to protect patients, who trust us with their information. The above guidelines help us do so when communicating through email. More detailed information may be obtained at the HIPAA FAQs page at hhs.gov.

Anti-VEGF:

Therapy for Diabetic Macular Edema (DME)

The role of Lucentis (Ranabizumab) in the treatment of **D**iabetic **M**acular **E**dema **(DME)** has been studied in two phase 3 randomized trials collectively called RIDE/RISE. The three year results have been released and Lucentis 0.3mg is quickly becoming an important drug in the treatment of macular edema related to diabetic retinopathy.

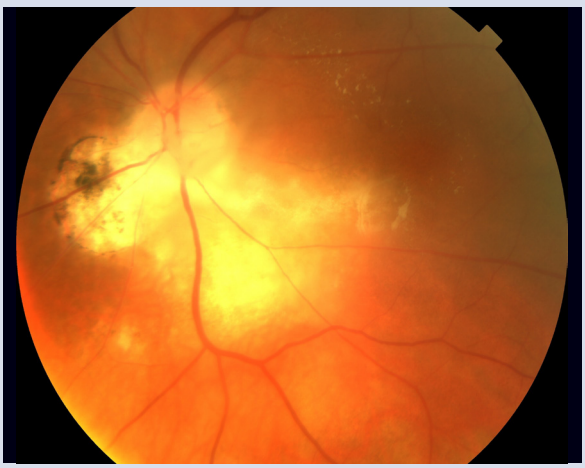
The incidence of diabetes is on the rise in the United States. In 2010 25.6 million people over the age of 20 years in the United States were considered diabetic. By the year 2020 this number is expected to increase to 39 million people, an increase of 15%.

The need for better treatments has been long apparent, particularly for patients with diffuse rather than focal edema related to diabetic disease. Focal and grid type laser treatment is much more effective for focal retinal swelling than in cases of diffuse retinal swelling and has been studied in the **E**arly **T**reatment of **D**iabetic **R**etinopathy **(ETDRS)** trial.

Anti-VEGF therapy for DME is indicated due to the over expression of intraocular VEGF in poorly controlled diabetic patients. Chronically elevated blood glucose levels lead to chronic subclinical microvascular inflammation. This leads to microvascular damage, ischemia, and the liberation of elevated levels of VEGF leading to more damage and leakage.

The RIDE/RISE trial used monthly injections of Ranabizumab in two doses, 0.3mg and 0.5mg, compared to sham injections or laser only treatment, for 24 months. This was followed by

Diagnostic Challenge



A 59 year old Caucasian woman presented to an ophthalmologist for progressively worsening blurriness and floaters in her left eye for one month. She has no past ocular history and her past medical history is unremarkable. The visual acuity was 20/20 OD, and HM OS, with a 2+ rAPD OS.

What's Your Diagnosis?

Examination of the right eye was within normal limits. The anterior segment exam of the left eye was normal, and the left fundus is shown above. Her lab workup, including serum Toxoplasmosis antibodies, were negative.

answer on page 7

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a 12 month crossover arm where sham patients were given the 0.5mg dose. Finally, patients were then enrolled in an open label extension trial using 0.5mg dose. This has resulted in the approval of the 0.3mg dose for the treatment of DME.

The 36 month visual results of the trial are impressive. Almost 40% of patients in the treatment groups had 3-line gains in visual acuity by 24 months. This is compared to 15% sham group. Patients in the sham group received laser only, and the 15% three line gain compares nicely to the ETDRS which previously showed the exact result.

At 36 months, patients in the treatment group had a mean gain of 12.4 letters compared to less than five letters in the sham group. Furthermore, patients in the treatment groups required less macular and pan-retinal laser as well.

The efficacy of the 0.3mg dose and the 0.5mg dose was similar but the rate of serious adverse events possibly caused by treatment was higher for the 0.5mg dose group than the other two groups, leading to approval of the 0.3mg dose by the FDA. Ocular adverse events were similar for the sham and 0.3mg dose groups.

An interesting finding from the trial is failure of the patients in the crossover group at 24 months to achieve the same gains as patients treated with drug from the beginning of the trial. This suggests that earlier treatment is likely better.

When considering this treatment, other factors aside from the presence of macular edema should be considered, including whether or not the patient will benefit from focal laser prior to the initiation of therapy. Patients with focal thickening alone were not considered candidates for anti-VEGF therapy as a primary therapy in the trial unless laser therapy failed. In other words, some patients may do well with laser alone if they have only focal thickening.

Another consideration is the use of Avastin instead of Lucentis for this indication. Although we have been using Avastin for DME for several years, its efficacy in comparison to Lucentis is presently unknown. Patient therapy of course needs to be tailored to the individual patient. However, the evidence that Lucentis treatment is beneficial for patients with DME is now overwhelming.

Personalized Medicine for Your Practice

Now you can identify at-risk Caucasian patients, 55 years of age or older, who may progress to wet AMD, so you can individualize your AMD patient management. RetnaGene™ AMD, available exclusively from Sequenom Center for Molecular Medicine (Sequenom CMM), is a laboratory-developed genetic test designed to evaluate the risk of a patient with early or intermediate AMD progressing to advanced choroidal neovascular disease within two, five, and 10 years.

Sequenom CMM validated the RetnaGene test using 2,415 DNA samples acquired from the National Eye Institute-AREDS Genetic Repository from subjects who were previously enrolled in the Age-Related Eye Disease Study (AREDS). The samples were genotyped in our CLIA-certified, CAP accredited molecular diagnostic laboratory and combined with patient data including clinical, demographic, and environmental criteria to evaluate the risk of progression of wet AMD over a 12-year

Diagnostic Challenge

Diagnosis

Toxoplasma gondii is a parasitic protozoan that is shed in cat feces. Two thirds of ocular infections are acquired after eating undercooked, contaminated meat. The other cases are congenital.

Toxoplasmosis is one of the most common causes of posterior uveitis. The anterior segment is often not involved. Inactive toxo lesions appear as darkly pigmented chorioretinal lesions with sharp borders. Active toxo lesions appear as a whitish, yellow lesion arising adjacent to an old toxo scar. There is often dense vitritis ('headlight in the fog'), which can cause floaters. These lesions are often found in the posterior pole, and can cause significant blurriness if involving the macula. Occasionally, toxoplasmosis can involve the deeper layer of the retina, without significant vitritis.

The diagnosis can be made based on the characteristic focal necrotizing lesion. The presence of anti-Toxoplasma IgG, IgM antibodies can help confirm the diagnosis. The antibody titers may be extremely low in some cases, and PCR of aqueous samples may be required to confirm the diagnosis. Other causes of necrotizing fundus lesion, such as tuberculosis or syphilis, should be excluded.

Not all cases of ocular toxoplasmosis require treatment. However, lesions involving the macula, optic nerve, or cases with significant vitritis usually require treatment. Sulfadiazine and Pyrimethamine have been traditional treatments, but both of these treatments can cause anemia and leukopenia due to folic acid inhibition. Thus, folic acid supplementation is necessary when using these drugs. In recent years, oral Bactrim (trimethoprim/sulfamethoxazole) and intravitreal Clindamycin have been reported to have comparable results to sulfadiazine and pyrimethamine. Oral steroids are often instituted shortly after starting antibiotics to reduce ocular inflammation.

This patient was started on a Bactrim DS and oral prednisone. She responded well after several weeks of treatment with complete resolution of the chorioretinitis. However, she maintained an afferent papillary defect and her final vision only improved to 20/200.

Participating Insurance Plans:

- Aetna U.S. Healthcare
- BCBS of Georgia
- Beech Street
- Blue Choice
- CCN PPO
- Choice Care Network
- Cigna
- Coventry Healthcare
- Evolutions Healthcare System
- First Health
- Great-West
- Humana
- Medicaid
  - Peach State Medicaid
  - Wellcare Medicaid
  - Amerigroup Medicaid
- Medical Resource Network
- Medicare
- Medicare Railroad
- Multiplan PPO
- National Preferred Provider Network
- Novanet
- Private HealthCare Systems
- Southcare PPO
- TriCare PPO, HMO
- State Health
- United Healthcare
- USA Managed Care Organization
- WellCare Medicare HMO

Other plans are pending; please call to check specific participation.

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