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Source of a Vitreous Hemorrhage:
When a Clinician Becomes a Detective

Some of the most exciting cases that come though the eye clinic involve the opportunity for the clinician to play the role of detective. One common clinical presentation of loss of vision in a retina practice can also prove to be quite a mystery to solve – vitreous hemorrhage. While the diagnosis is straightforward, uncovering the 'culprit' can be challenging. It is critical, however, to identify the causative etiology, as this dictates the best management plan. Approaching this diagnostic conundrum in a stepwise process can facilitate a swift and accurate diagnosis. The first step is to consider the different mechanisms of intraocular bleeding (Figure 1).

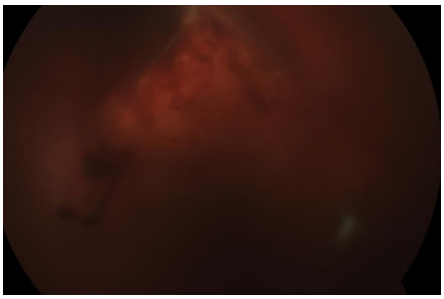

Figure 1:
A dense vitreous hemorrhage

Blood vessels that have released their contents are often fundamentally flawed and, therefore, deemed 'abnormal.' Abnormal vasculature is the result of either ischemic or non-ischemic processes.

In the setting of ischemia, the production of angiogenic factors initiates neovascularization. Abnormal, fragile blood vessels develop. These friable vessels bleed easily. Even the slightest traction from adherent vitreous can result in an eye full of blood. Falling into this category are patients with proliferative diabetic retinopathy (Figure 2), ischemic vein occlusions, ocular ischemic syndrome, sickle cell retinopathy, or adult retinopathy of prematurity (ROP). Complicating this clinical picture, the patients that are most prone to retinal ischemic events are often on systemic anticoagulation. In these patients, even a focal area of bleeding can lead to significant loss of vision. Furthermore, even a remote history of an ischemic injury must be considered. For example, an ischemic vein occlusion can result in proliferative vessels many years after an antecedent event, an event that in some cases may be unbeknownst to the patient. Vitreous hemorrhage more commonly occurs in the setting of a prior branch retinal vein occlusion, and less often in the setting of a central retinal vein occlusion (CRVO). Anterior segment neovascularization is more coming with ischemic CRVO than posterior segment neovascularization. Consequently, CRVO should always be considered in the setting of neovascular glaucoma.

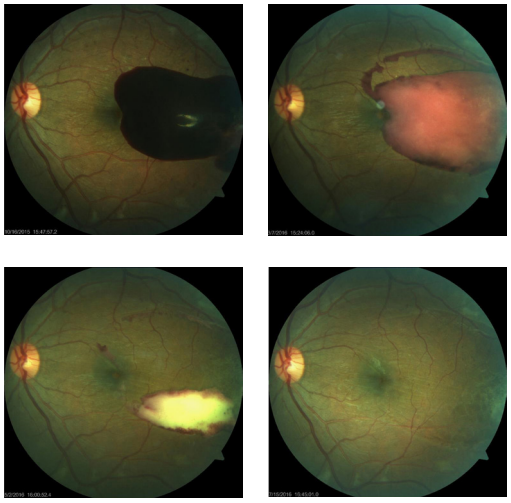

Figure 2:
Vitreous hemorrhage due to diabetic proliferative retinopathy treated with anti VEGF therapy over consecutive months

Abnormal blood vessels that result from non-ischemic etiologies refer to structural alterations in the vasculature that might allow for a bleeding event. In this category, the culprit might be a macroaneurysm (Figure 3), retinal angiomas, or congenital peripapillary arterial loops.

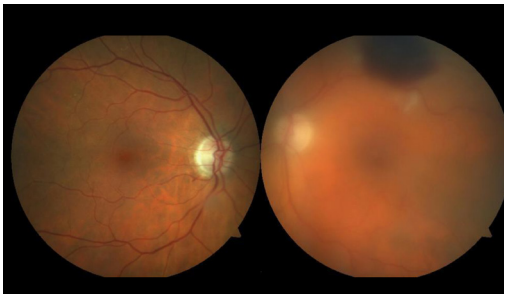

Figure 3:
Normal right eye compared to the left eye with mild vitreous hemorrhage emanating from a macroaneurysm along the superior arcade.

This can be a difficult diagnosis to make if there is poor visualization of the retinal features. If there is a high suspicion of this category, a plan for 'watchful waiting' can be implemented. Advising minimal activity and elevated head position can allow for overlying blood to clear with gravity. As long as bleeding does not recur, direct visualization can eventually be accomplished with some patience.

After abnormal vessels, one must consider the rupture of normal vasculature. The mechanism for this is usually due to a tractional force. Most commonly, posterior vitreous detachment, either spontaneous or caused by blunt trauma, can result in the tearing of vessels as the retina, itself, is torn (Figures 4 and 5). Traction on areas of retinoschisis can result in vitreous hemorrhage as well as hemorrhage directly into the schisis cavity. Intercranial processes such as Terson's syndrome can result in the rupture of normal vasculature through pressure gradients. One must also take into consideration the extravasation of blood from normal vasculature in the clinical setting of hematological disorders. Here, it is critical to consider anemia, leukemia, or blood dyscrasias due to prolonged bleeding time.

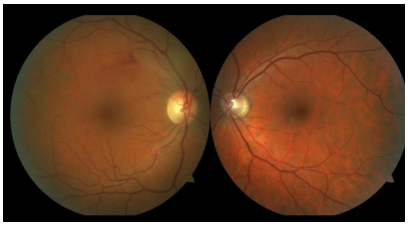

Figure 4:
Normal left eye compared to the right eye with mild vitreous hemorrhage resulting from a torn retina.

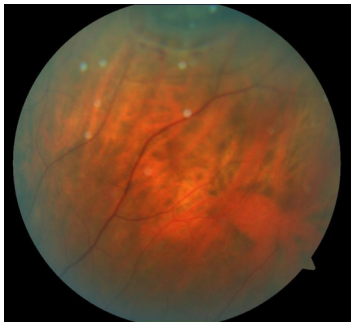

Figure 5:
The causative superior retinal tear

The final category to consider is breakthrough bleeding from a subretinal hemorrhage or choroidal hemorrhage that dissects directly through intact retina without an associated defect. Instances of exudative age-related macular degeneration (Figure 6), idiopathic polypoidal choroidal vasculopathy and choroidal melanoma must be considered.

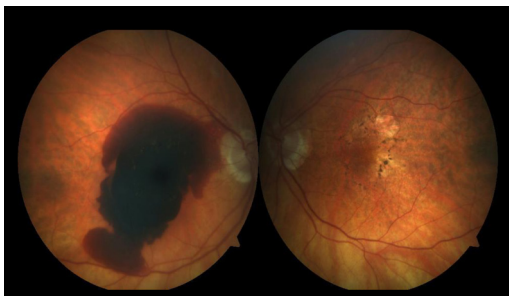

Figure 6:
Massive subretinal hemorrhage in the right eye with mild breakthrough bleeding. This is the result of exudative age related macular degeneration.

Clues to discovering a causative event can often be gleaned from the clinical exam. If an eye is hypotonus, one should consider the possibility of a retinal detachment hiding underneath the vitreous hemorrhage. Chronic retinal detachments often result in hypotony. Surgical wound leaks are an obvious cause of hypotony, and these leaks can also be associated with vitreous hemorrhage and a poor posterior view. Of course, hypotony with vitreous hemorrhage can also be indicative of an open globe injury which would be dependent on the patient's history. Conversely, an elevated intraocular pressure would be suggestive of neovascular glaucoma, hemolytic glaucoma or even tumor invasion into the angle.

If the examiner is unable to visualize any part of the retina, scleral depression can be a useful tool to elevate the retina into view. Ultrasound is mandatory if adequate visualization cannot be achieved. Dynamic B- scan can detect underlying retinal tears, detachments, areas of vitreous traction or mass lesions (Figures 7 and 8).

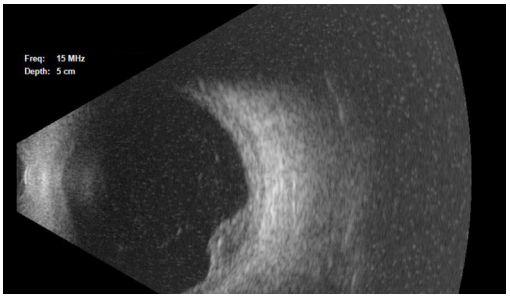

Figure 7:
Ultrasound reveals a mass lesion

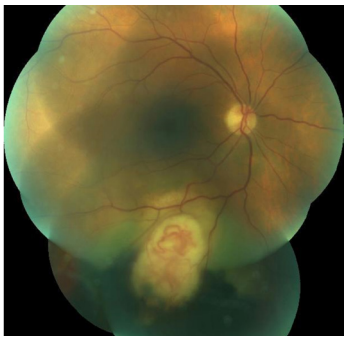

Figure 8:
This vascular choroidal melanoma caused significant vitreous hemorrhage. After the tumor was treated with radiation plaque therapy, a vitrectomy was performed.

One should maintain the highest suspicion for underlying pathology that has the potential to result in permanent loss of vision in a short period of time. The presence of a retinal tear or detachment hiding beneath a vitreous hemorrhage that is obscuring a clear view of retinal details is always a possibility. Most interestingly, in the setting of an acute posterior vitreous detachment, the presence of vitreous hemorrhage can portend vision threatening pathology even if it is not present on initial exam. In this scenario, the clinician moves from the role of detective to one of fortune teller. Studies suggest a 70-95% incidence of a retinal tear in the presence of a hemorrhagic PVD compared to a 2-4% incidence of a tear when a vitreous detachment does not involve a bleeding event. Every patient who experiences a hemorrhagic PVD should be warned of this future risk, and the need for appropriate follow up should be emphasized. When the index of suspicion for a retinal tear is high but cannot be directly visualized and therefore treated, a diagnostic and therapeutic vitrectomy may be considered.

Vitreous hemorrhage is a manifestation of serious ocular pathology that can have systemic associations. With an incidence of 7 cases per 100,000, vitreous hemorrhage is a mystery that every vitreoretinal clinician should be comfortable managing. Timely and accurate diagnosis is crucial. If vitreous hemorrhage does not clear rapidly enough to allow for adequate visualization, diagnosis and treatment of underlying pathology, early surgical intervention is often warranted. As a consequence, primary eye care specialists should maintain a low threshold for vitreoretinal consultation in the case of vitreous hemorrhage of unknown etiology.

References:

1. Coffee RE, Westfall AC, Davis GH, Mieler WF, Holz ER. Symptomatic posterior vitreous detachment and the incidence of delayed retinal breaks: case series and meta-analysis. Am J Ophthalmol. 2007;144(3):409-413. doi:10.1016/j.ajo.2007.05.002
2. Johnson BB. Vitreous Hemorrhage. American Academy of Ophthalmology, EyeWiki. January 2020. http://eyewiki.aao.org/Vitreous_Hemorrhage.
3. Melamud A, Pham H, Stoumbos Z. Early Vitrectomy for Spontaneous, Fundus-Obscuring Vitreous Hemorrhage. Am J Ophthalmol. 2015;160(5):1073-1077.

NJRetina Welcomes Our Newest Physicians

Akosua Nti, MD

Akosua Nti, MD is a vitreoretinal surgeon at NJRetina. After completing her undergraduate degree in Neuroscience and Behavior at Wesleyan University in Connecticut, she earned her medical degree from the University of Pennsylvania School of Medicine as a Willis Scholar.

Dr. Nti completed her residency in ophthalmology at the Scheie Eye Institute at the University of Pennsylvania in Philadelphia, followed by a two-year fellowship in vitreoretinal surgery at the Wilmer Eye Institute at Johns Hopkins in Baltimore.

Dr. Nti is married, and enjoys spending time with family, traveling, and hiking.

Harris Sultan, MD, MS

Harris Sultan, MD, MS, is a vitreoretinal surgeon at NJRetina. After completing his undergraduate and Master's degrees at the University of Connecticut where he was inducted into the Phi Beta Kappa Honor Society, he earned his medical degree from the University of Connecticut School of Medicine in Farmington.

He completed his residency in ophthalmology at the University of Texas Medical Branch – Blanton Eye Institute in Houston followed by a two-year fellowship in vitreoretinal surgery at Washington University in St. Louis.

Dr. Sultan is fluent in Urdu, proficient in French, and enjoys playing tennis, badminton, and traveling.

To learn more about Dr. Nti and Dr. Sultan, visit njretina.com.

At the **Forefront** of **Clinical Research**

NJRetina currently conducts clinical trials at key locations. Our clinical research coordinators who conduct the trials will be happy to discuss the inclusion/exclusion criteria or any other aspect of these studies with you or your patients. If you have any questions, please feel free to contact:

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Dina Christodoro - Toms River: 732-797-3984

Amy Leviton - Edison: 732-906-1887

NOTE: ENROLLMENT IS ON HOLD FOR ALL STUDIES UNTIL FURTHER NOTICE.

Enrolling Studies:

Dry AMD

Teaneck & Edison

A Genetic Screening and Registry Study to Evaluate Long-term Clinical Outcomes and Disease Progression in Subjects with Non-Central Geographic Atrophy (GA) Who Are Carriers of High-Risk Genetic Complement Variants Associated with Dry Age-related Macular Degeneration (AMD)
A Prospective Natural History Study to Evaluate Clinical Characteristics and Disease Progression in Subjects with Non-Central Geographic Atrophy (GA) Who Are Carriers of High-Risk Genetic Variants of Complement Factor H (CFH) (Gemini)

Teaneck

Phase II, Randomized, Double-Masked, Placebo-Controlled Clinical Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of Subcutaneous Injections of Elamipretide in Subjects with Age-Related Macular Degeneration with Geographic Atrophy (SPIAM)

Teaneck & Toms River

A Phase II, Multi-Center, Randomized, Single-Masked, Sham Injection Controlled Study of the Safety, Tolerability, and Evidence of Activity of Intravitreal Injection of R7171009 in Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration (Gallego)

Vauxhall

A Study of Disease Progression in Genetically Defined Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration

Wet AMD

Edison and Teaneck

A Randomized, Single-Masked, Active-Controlled Phase 2 Study of the Safety, Tolerability, and Efficacy of Repeated Doses of Hight-Dose Aflibercept in Patients with Neovascular Age-Related Macular Degeneration(Candela)

Teaneck

A Phase 2, Prospective, Randomized, Double-masked, Active Comparator controlled, Multi-center Study to Investigate the Efficacy and Safety of Repeated Intravitreal Administration of KSI-301 in Subjects with Neovascular (Wet) Age-related Macular Degeneration

Soon to Enroll Studies:

- A Phase III, Multicenter, Randomized, Visual Assessor Masked, Active Comparator Study of the Efficacy, Safety, and Pharmacokinetics of the Port Delivery System with Ranibizumab in Patients with Diabetic Macular Edema (PAGODA)
- A Phase 2, Randomized, Multicenter study to assess the dose level of multiple THR-149 injections and to evaluate the efficacy and safety of THR-149 versus aflibercept for the treatment of diabetic macular oedema (DME)- (Oxurion study)
- A Phase 2 Multicenter, Randomized, Double-Masked, Sham-Controlled Study of the Safety and Efficacy of Intravitreal Injections of NGM621 in Subjects with Geographic Atrophy (GA) Secondary to Age-Related Macular Degeneration (AMD) (NGM study)
- A Multicenter, Open-Label Extension Study to Evaluate the Long-Term Safety and Tolerability of the Port Delivery System with Ranibizumab in Patients with Neovascular Age-Related Macular Degeneration (Portal)
- A Multicenter, Open-Label Extension Study to Evaluate the Long-Term Safety and Tolerability of Faricimab Iin Patients With Diabetic Macular Edema (Rhone)
- A Phase 2, Randomized, Dose-escalation, Observation-controlled Study to Evaluate the Efficacy, Safety, and Tolerability of RGX-314 Gene Therapy Delivered via One or Two Suprachoroidal Space (SCS) Injections in Participants with Diabetic Retinopathy (DR) Without Center Involved-Diabetic Macular Edema (CI-DME) (ALTITUDE)
- Serum Anti-AAV8 Neutralizing Antibody Assessment Study of Patients with Neovascular Age-related Macular Degeneration or Diabetic Retinopathy
- A 64-week, Phase 3b, Multicenter Study Assessing the Efficacy and Safety of Brolucizumab 6mg Compared to Aflibercept 2mg in a Treat to Control Regimen in Patients with Neovascular Age-Related Macular Degeneration (Talon)
- A Randomized, Double-Masked, Active-Controlled Phase 3 Study of the Efficacy and Safety of High -Dose Aflibercept in Patients with Neovascular Age-Related Macular Degeneration (Pulsar)
- A Randomized, Double-Masked, Active-Controlled Phase 2/3 Study of the Efficacy and Safety of High-Dose Aflibercept in Patients with Diabetic Macular Edema (Photon)
- Phase III, Multicenter, Randomized Study of the Efficacy, Safety, and Pharmacokinetics of the Port Delivery System with Ranibizumab in Patients with Diabetic Retinopathy (PAVILION)