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LIGHT PIPE

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IN THIS ISSUE:

Imaging Corner	pg. 2
Clinical Case Study: Medication Toxicity	pg. 3-4
Clinical Case Study: Bilateral Serous Retinal Detachments	pg. 5-7
Update From our Clinical Trials Section	pg. 8
Spotlight Feature: Dr. David S. Chin Yee	pg. 9-10

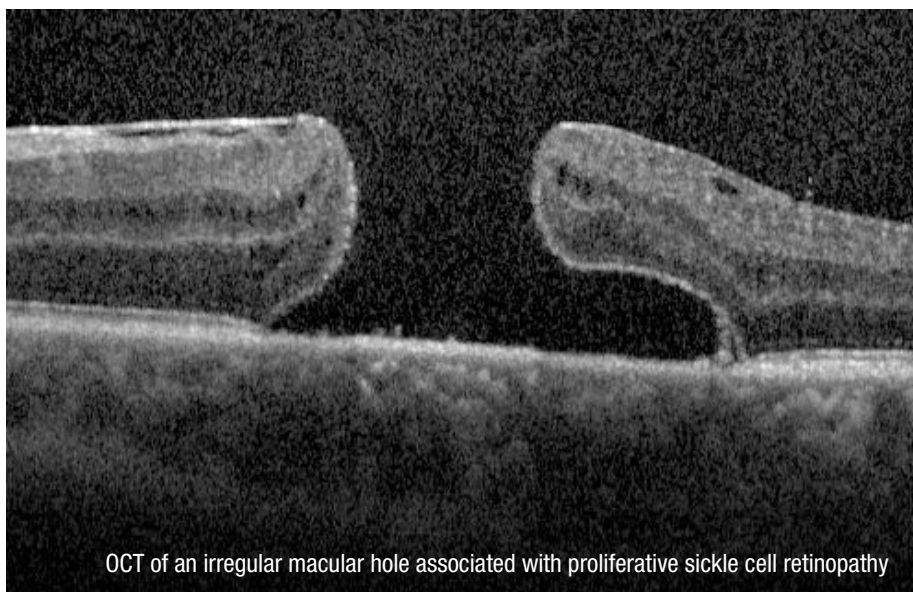
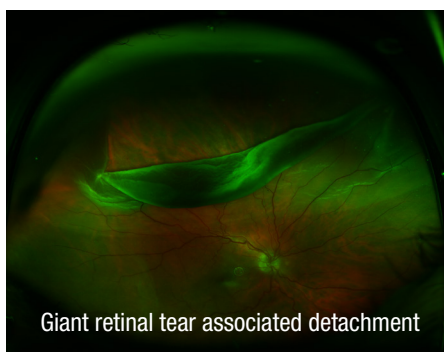
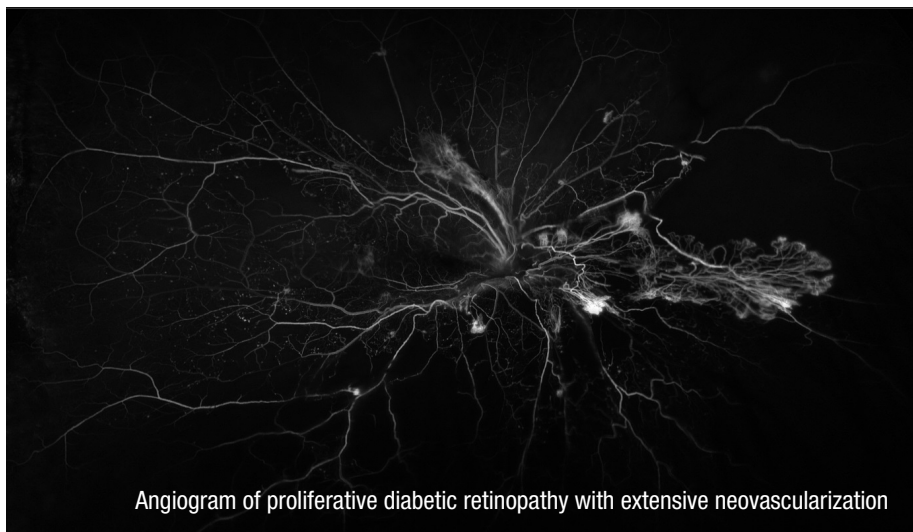
THE NEWSLETTER OF



GEORGIA RETINA

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Imaging Corner



Clinical Case: Medication Toxicity

Krishna Mukkamala, MD

A 59-year old female presented with complaints of difficulty reading and adjusting to darkly lit situations. Her medical history is significant for interstitial cystitis (IC) for which she has used Elmiron (Pentosan Polysulfate Sodium) for twenty years. It is suspected that she may have developed IC as a complication of her mother's use of diethylstilbestrol (DES). DES is a synthetic estrogen what use used until early 1970s to reduce the likelihood of miscarriage.

Her visual acuity is excellent at OD: 20/25 and OS: 20/20 though she does have some mild paracentral AMSLER changes OD. Anterior segment, optic nerve, and peripheral retinal are normal and there was no APD or color plate abnormalities.

In the macula, there is a bilateral and roughly symmetric pattern of RPE and pigmentation changes that can be seen in the fundus photos. The OCT images show parafoveal RPE changes and areas of subretinal pigment. The differential diagnosis for this pattern of findings is MTTL1 (A3243G mitochondrial mutation seen in MELAS / MIDD), age-related dry macular degeneration (AMD), pattern dystrophy, and drug toxicity.

In this particular case, I suspect Elmiron (Pentosan) related macular toxicity. Pearce, et al recently published a case series of six patients with similar findings to the patient above. The patients presented in the study maintained good visual acuity but complained of difficulty reading and dark adaptation. Their fundus revealed macular RPE changes and pigmentation. No evidence of CNVM were seen and no genetic correlation was found.

Interstitial cystitis (IC) is a painful inflammatory disease of the bladder and can be a debilitating. Patients have symptoms including pain/pressure in their pelvis. They can suffer from urinary frequency which can be disruptive to their daily routine and work life.

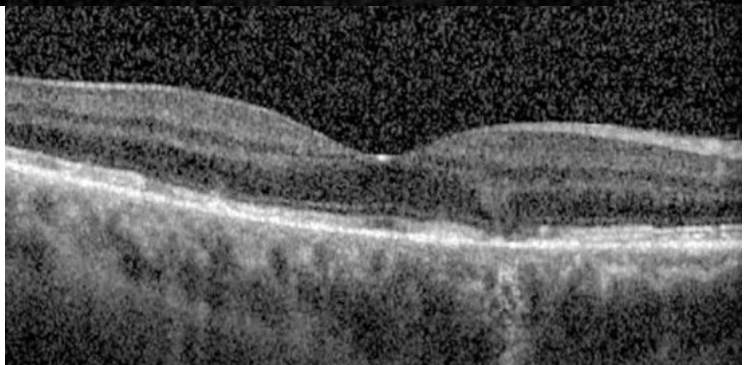
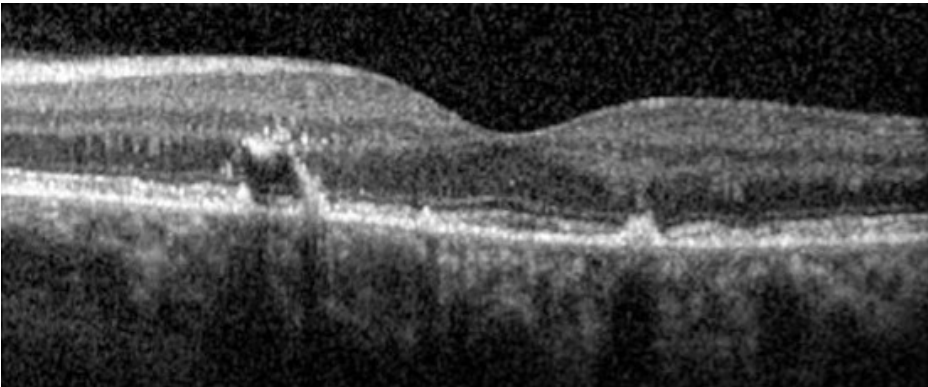
There are several classes of medications that are used for IC, some off-label. They include NSAIDs, antihistamines, and some antidepressants. However, the only FDA approved medication (approved in 1996) for IC is Elmiron (Pentosan polysulfate sodium - PPS). Oddly, the mechanism by which it alleviates the symptoms of patients with IC is not known. There is speculation that it restores the inner lining of the bladder, reducing the impact of irritants on the bladder wall.

If you examine a patient who has a history of IC or chronic PPS use, examine their macula carefully. If pigmentary changes are present, it would be advisable to speak to the patient's urologist to discuss these findings.

It is important to note that the association between chronic PPS use and macular changes is not definitive. But there is growing evidence to suggest it. In this particular case, I advised reducing the dose to the lowest tolerable dose possible. Discontinuing the medication might be best. However, IC is very debilitating and stopping the medication all together may not be tolerated.

REFERENCE

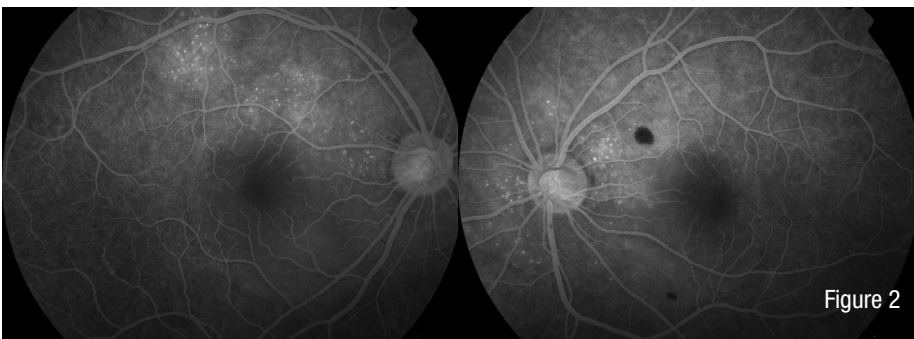
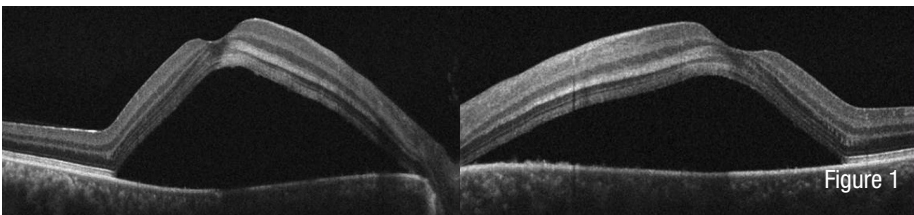
Pearce WA, Chen R, Jain N. Pigmentary Maculopathy Associated with Chronic Exposure to Pentosan Polysulfate Sodium. Ophthalmology. 2018 Nov;125(11):1793-1802.

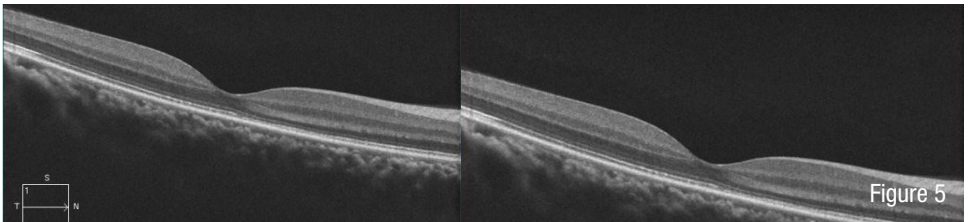
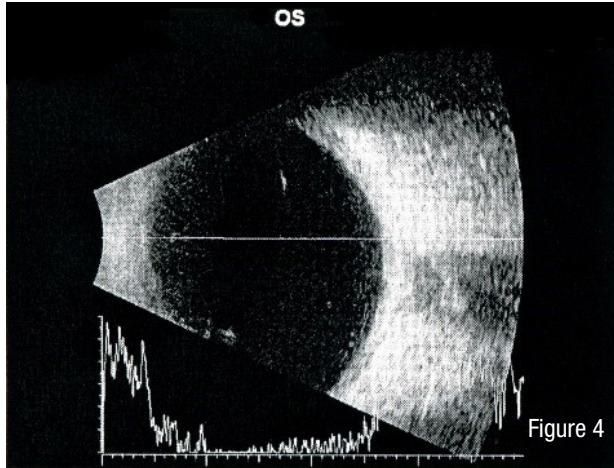
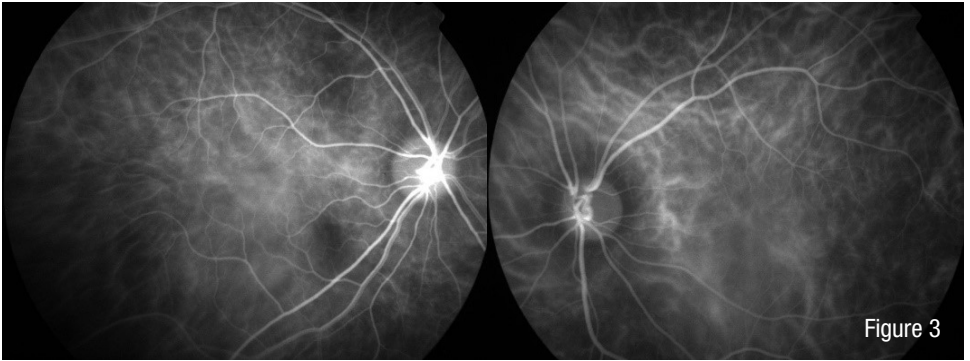


Clinical Case: Bilateral Serous Retinal Detachment

Hyung Cho, MD

A 33 year old asian male with no medical history presents with a sudden onset of blurry vision, mild headaches and low grade fever for two days. On presentation, his vision was 20/200 in both eyes. No evidence of inflammation was observed in the anterior chamber or vitreous. Fundus examination revealed bilateral serous retinal detachments involving the fovea with scattered intraretinal hemorrhages and cotton wool spots. Optical coherence tomography disclosed a large amount of subretinal fluid in both eyes with a thickened choroid (Figure 1). Fluorescein angiography showed multifocal spots of hyperfluorescence centered around the optic nerve and beneath the detachment (Figure 2). The indocyanine green angiography was within normal limits (Figure 3). The B-scan ultrasound showed a thickened choroid (Figure 4). The white blood cell count was 50.8 with 87% lymphoblasts. A blood smear showed a monomorphic white blood cell population with no cytoplasm or vacuoles. A bone marrow aspiration showed blast forms (86%) positive for CD34, HLA-DR, CD10 and CD19 and negative for T-cell, myeloid, monocyte, and mature B-cell markers confirming the diagnosis of precursor B-cell acute lymphoblastic leukemia (Ph+ 9;22). Cytogenetic analysis revealed Philadelphia chromosome (9;22 translocation) as well as 2 novel translocations. Imaging of the head did not detect a tumor or bleed. After induction, there was a rapid resolution of the subretinal fluid and decrease in choroidal thickness (Figure 5) and his vision three weeks later returned to 20/20 bilaterally. His induction regimen comprised of Vincristine and Daunorubicin on days 1, 8, 15, and 22 in addition to L-asparaginase, methotrexate, and prednisone (60mg/m² daily).





Leukemias are systemic hematologic disorders that may affect all the organs of the body. The posterior manifestations of leukemia could be attributed to the associated hematological abnormalities such as anemia, thrombocytopenia, hyperviscosity states, or opportunistic infections.¹ Intraretinal hemorrhages, leukemic infiltrates, white-centered hemorrhages, central retinal vein occlusions, and vitreous hemorrhages can be seen in persons with leukemia.³ Optic nerve head infiltration with acute lymphoblastic leukemia has also been described.⁴

The detachment of the macula in leukemia is typically reported to be shallow in the posterior pole. The mechanism is thought to be due to leukemic infiltration into the choroid, which causes decreased blood flow in the choriocapillaris, resulting in ischemia to the overlying RPE and disruption of the intercellular tight junctions, leading to the SRD.² The involvement of the choroid by leukemic cells tends to be perivascular, and may be patchy or diffuse.⁵ The choroid at the posterior pole may be significantly thickened, as it was in our case.

The differential diagnosis of bilateral SRD includes Harada's syndrome, central serous choroidopathy, posterior scleritis, uveal effusion, age-related macular degeneration, and metastatic neoplasm. With no signs of tumor by imaging, the fluorescein angiographic findings would support Harada's syndrome as the most likely diagnosis. However, the absence of inflammation in the anterior chamber and vitreous, and the absence of other systemic signs such as vitiligo and poliosis are not consistent with Harada's syndrome.

It is unusual for visual complaints to be the presenting symptom of acute lymphoblastic leukemia. Serous detachment of the macula as a presenting sign of acute lymphocytic leukemia has rarely been reported.² Furthermore, reports of patients with visual symptoms are rare. The intraocular manifestations of leukemia are usually treated with systemic chemotherapy, and when this fails, ocular radiation is recommended.¹

In conclusion, serous retinal detachment may be seen in acute lymphoblastic leukemia and may be the first sign of the disease. A sudden appearance of SRD, even in an adult, warrants a thorough systemic screening for underlying leukemia. Prompt recognition of the disease leads to early systemic treatment and may help restore visual function.

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Study Update

Georgia Retina has a long tradition of commitment to and participation in clinical trials in order to provide our patients access to new, state-of-the-art preventative, or therapeutic treatments. We partner with the National Eye Institute, some of the nation's top pharmaceutical companies, and other clinical practices to explore the causes and cures for many retinal conditions.

We take special care to ensure that our study patients experience the best medical care possible. This past year we have been active in 10 clinical trials for wet age-related macular degeneration, geographic atrophy secondary to dry age-related macular degeneration, retinal vein occlusion, diabetic macular edema, and non-proliferative diabetic retinopathy.

We hope that as you consider where to refer your patients for retinal care, you will keep in mind that Georgia Retina not only provides exception care but can also offer your patients the opportunity to enroll in clinical trials thereby offering them new vision saving treatments. If you have any questions about whether your patient might be eligible to participate in one of our ongoing clinical trials, please call any one of our doctors or contact our research coordinator, Leslie Marcus (lmarcus@garetina.com).

ONGOING STUDIES

Ophthotech OPH2003: A Phase 2B Randomized, Double-Masked, Controlled Trial to Assess the Safety and Efficacy of Intravitreal Administration of Zimura® (Anti-C5 Aptamer) in Subjects With Geographic Atrophy Secondary to Dry Age-Related Macular Degeneration. Recruitment began in 2016 and is still enrolling. Dr. Sharma is the principle investigator.

Ora TLC399A2002: Indication: Macular Edema due to RVO. The protocol is to evaluate three different doses of ProDex (Dexamethasone sodium phosphate (DSP) with lyophilized lipid cake). Recruitment is active. Dr. Stoltz is the principle investigator.

Genentech GR39821: A Phase I, Multicenter, Open-Label, Single-Dose, Dose-Escalation and Multiple – Dose Study of the Safety, Tolerability, Pharmacokinetics, and Immunogenicity of Intravitreal Injections of RO7171009 in Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration. Recruitment began in August 2017 and is still enrolling. Dr. Stoltz is the principle investigator.

KalVista KVD011-201:: A randomized sham-controlled double-masked Phase 2a study of the efficacy, safety and tolerability of the intravitreal plasma kallikrein inhibitor, KVD001, in subjects with center-involving diabetic macular edema (ciDME) who have had prior anti-vascular endothelial growth factor (VEGF) treatment. Recruitment began Spring 2017 and is still enrolling. Dr. Stoltz is the principle investigator.

Spotlight with a Georgia Retina Doctor:

Dr. David S. Chin Yee

This month we interview David S. Chin Yee, MD. Dr. Chin Yee joined Georgia Lightpipe Retina in 2015 and has grown a strong presence providing high quality retinal care to patients in Macon, Georgia. Additionally, he has a robust clinical practice in Peachtree City. With his sharp clinical acumen and jovial personality, we are very fortunate to have him in our practice. Despite his busy schedule he was able to sit down with the LightPipe for this month's Spotlight Interview.



LightPipe: What made you choose retina surgery?

Dr. Chin Yee: I decided to choose Retina Surgery at a somewhat early age, growing up in Jamaica I volunteered at a home for the blind in Jamaica and was humbled by the tasks I helped them complete, such as helping them shave, reading to them, and assisting them with their finances. Their dependence and trust in others, inspired me to help the visually impaired. Following up from that desire I specifically choose Retina due to the wide, reaching, and complex pathology of the specialty that enables him to touch a multitude of lives thereby having a far reaching impact in the visually impaired.

Lightpipe: What is the most rewarding part of your practice?

Dr. Chin Yee: The most rewarding parts of my practice is having the ability to try and save someone's sight. When someone loses their sight, it is a devastating event for the patient and being tasked with the challenging role in their recovery is a privilege and it truly is rewarding knowing that I can assist in the restoration of a patient's sight and it is humbling having patient's trust throughout their treatment.

Lightpipe: What has changed the most since you have started practice?

Dr. Chin Yee: Since I started practicing we have seen the introduction and development of better treatment options for the myriad of disease that we treat. With these modalities making breakthroughs in assisting diseases we had no options for and also improving on what we already had, enabling faster and more sustained visual improvement.

Lightpipe: What do you anticipate changing in retina in the next decade?

Dr. Chin Yee: I believe we are facing exciting times in our field. With us being on the cusp of furthering gene therapy. I believe in the next decade with Gene therapy we will be able to make a much bigger dent in preventing

visual impairment and also possibly restoring vision, which is one the most challenging issues we have in our field.

Lightpipe: What do you do for fun?

Dr. Chin Yee: I have multiple outside interested primarily I enjoy sports and cars. In my free time I play ALTA tennis, and recreational soccer. In regards to cars, in the past I have tinkered and modified a handful of cars and still try to find the time to keep up with this hobby. I also enjoy spending my time with my wife, son, and daughter.

Lightpipe: Where was your last vacation?

Dr. Chin Yee: My last vacation was actually back home in Jamaica over the Christmas break, which is my favorite time of the year to visit as the weather is perfect then. I spent time catching up with family and then spent some time on the North Coast of the Island with my family on the beach enjoying some well needed rest and recuperation.

Lightpipe: Where do you want to visit for your next vacation?

Dr. Chin Yee: I would love to travel to Europe, specifically Italy. I have only been to Europe once when I was a teenager and as such have been looking forward to go back. Italy's historic art and architecture, being known as the home of some of the most famous structures in the world is what specifically intrigues me.

Thank you for reading our 2019 Light Pipe Newsletter!

If you have time, please take a moment to answer a few questions about this year's publication.

By doing so, you're helping Georgia Retina become an even better practice.

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