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Optimizing Vision Outcomes in nAMD

Announcer:
Welcome to CME on ReachMD. This activity is part of a special series titled "Time is Vision in Neovascular Age-Related Macular Degeneration and Retinal Vein Occlusion" and is provided in partnership with the National Eye Institute of the National Institutes of Health, of the U.S. Department of Health and Human Services, along with Prova Education. It's supported by an independent educational grant from Regeneron Pharmaceuticals. To view this activity or others in the series, please visit EyeHealthAcademy.org/TimeIsVision

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Dr. Do:
Welcome. Age-related macular degeneration [AMD] is the most common cause of vision loss in individuals ages 50 years and older. We know that anti-VEGF therapy has revolutionized the treatment of neovascular age-related macular degeneration. However, can we do better and maximize the long-term vision benefits in our patients?

This is CME on ReachMD. I'm Dr. Diana Do from Stanford University, and joining me today are my two friends and colleagues, Drs. Julia Haller from the Wills Eye Hospital and Dr. Rishi Singh from the Cole Eye Institute. Welcome.

Dr. Haller:
Thanks, Diana. It's great to be here.

Dr. Singh:
Thank you for having me.

Dr. Do:
Let's start with a patient case. This is a 73-year-old gentleman who came to my clinic complaining of new-onset vision loss in the right eye, and his visual acuity dropped to 20/100. The exam showed evidence of new-onset wet age-related macular degeneration. I obtained an OCT [optical coherence tomography] scan which shows both intraretinal fluid and elevation of the pigment epithelial detachment, consistent with wet AMD.

Julia, can you share with us what baseline characteristics might affect prognosis in wet AMD?

Dr. Haller:
Sure, Diana. Of course, we used to spend a lot of time trying to decide exactly what characterized these lesions – you know, whether they were minimally classic, predominantly classic, occult – but these days, what we know is that anti-VEGF therapies are agnostic as to lesion type, so although we may consider prognostic factors like presence of pigment epithelial detachment, whether there's intraretinal fluid or subretinal fluid, we know we're going to be treating them with an anti-VEGF agent, and we know that those drugs work.

Dr. Do:
Rishi, can you discuss with us – there are different dosing regimens a retina specialist can use. Tell us what your thoughts are about these dosing regimens, and which one do you think would benefit this patient?

Dr. Singh:
You know, Diana, when we first started anti-VEGF therapy, we started with monthly therapies in these patients and then we moved to bimonthly and as-needed treatment for some of the patients, as well. And so now we have sort of a – initially potpourri of sort of

approaches to it. And we've all sort of migrated to a format of what we call treat and extend, where we basically dose the patient, continually give them injections on a dry retina to extend the intervals in between the treatments, maximizing the visual benefit and reducing the potential complications. And in fact, if you look at some of the studies and why this treat-and-extend regimen has become popularized is because of some of the 1-year data which shows you there's a relationship between the number of injections and the visual outcome. And even the long-term 5-year data – and this is a paper that a medical student and I authored in *Retina* a few years back where we looked at the long-term studies and saw a complete relationship between the number of injections given and their long-term visual outcome and success in this study.

Dr. Do:
The role of fluid is key to the treatment of wet AMD. I'd like to share with you the photos from the patient who I treated, and we can see that with anti-VEGF therapy, there is some reduction in the fluid, but there's still some persistent CNV [choroidal neovascularization] activity.

Julia, can you share with us what your thoughts are about the different fluid compartments and how they affect disease activity?

Dr. Haller:
Well, Diana, what we are now using to track these patients is, of course, OCT. So OCT has pretty much supplanted fluorescein angiography in terms of our tracking and decision-making as we treat these patients, usually – as Rishi is saying – with a treat-and-extend type of program. So what we're looking for in terms of activity is signs of fluid, leakage, evidence that we need to keep treating that patient and helping us make decisions about intervals between treatments.

There are 3 types of fluid that we are looking at. The one that's the most straightforward to me is subretinal fluid because you can see it most easily, and it's most clearly there. And it is a good sign of activity, and it's not as hard to determine exactly what's causing the fluid. Now there's some thought now that instead of activity, some of that subretinal fluid may be caused by a lack of adhesion, that the damaged cells can't lie back down and stick to the retinal pigment epithelium as well. And so it may be possible to just follow that subretinal fluid because we know prognostically the presence of subretinal fluid, at least with stable vison, is not as bad as the presence of intraretinal fluid.

So the second type of fluid, then, is intraretinal fluid, what you saw as you were treating your patient, and that fluid is a little bit harder to track because it can be a sign of activity of the disease, or it can be due to apoptotic changes, a decay, cellular death, and actually not a sign of active VEGF-stimulated disease progression. So that can be a little trickier to sort out. We know that intraretinal fluid is worse prognostically, and we make a real effort to get rid of it.

Finally, there is sub-RPE fluid, and that can be more difficult to track, particularly on OCTs because it's harder for the OCT to penetrate deeper into the layers in the back of the eye. But in general, we don't know as much about tracking sub-RPE fluid as we'd like to, but we'd like to dry everything out, if we possibly can.

Dr. Do:
For those just tuning in, this is CME on ReachMD. I'm Dr. Do, and joining me today are Drs. Julia Haller and Rishi Singh. We're discussing strategies for long-term success in managing your patients with wet age-related macular degeneration.

Let's move to the next patient case, and I know, Rishi, you'd like to share with us one of your clinical cases.

Dr. Singh:
I'd love to, Diana. So, this is a female that I've been treating in my practice for the last couple of years, and I'll talk about, sort of, her longitudinal course in therapy. She's a 75-year-old woman who has been treated for – or followed for dry macular degeneration for at least 5 years prior to this initial conversion. And she had some vitrectomy surgery and cataract surgery in her right eye for a membrane peel but otherwise was unremarkable from her history. And this picture on the OCT shows you her initial point of transition from non-exudative intermediate AMD to finally the exudative component and, as Julia said, it's really hard to pick up some of these fluid compartments sometimes. This patient really didn't have a manifestation of a lot of fluid, intraretinal fluid in this case, as one would expect to see, and definitely no subretinal fluid here. The fluorescein confirms that there is a neovascular complex, which appears to be occult in nature. And if you look at the slide that shows you the progression of this patient, on the far left side, you can actually see the initial OCT when she first came to see me back in 2012. In the middle, you see the time of the point of conversion, and then following that, you see the graph of the central macular thickness after treatment as a result of receiving anti-VEGF treatment.

And the lessons learned from this patient are innumerably shown to us through some of the clinical studies I'm going to mention in just a moment, but basically, if you look at her anti-VEGF history, you can see in year 1 she received about 5 injections, year 2 she received 4 injections, year 3 and 4 she received only 3 injections, so essentially, more than a quarterly patient. Some patients have been extended for an extended period of time, which is, again, along the treat-and-extend paradigm, a homerun if you can find this sort of patient. And

I think that this has been born out of some of the data that's come out of studies.

In particular, there's been a few studies looking at longer dosing intervals. Brolucizumab was one of those studies. And HAWK and HARRIER, they had a drug, brolucizumab, which is approved for the treatment of neovascular AMD, where they diagnosed and treated patients every 12 weeks versus every 8 weeks given with aflibercept and found some equivalent outcomes after a 2-year study that was done. But more importantly than that, there's been some really good studies that've challenged the treat-and-extend paradigm to the point to see how far out you could really go. And that was the ALTAIR study which was done in Japan which found that 35% to 40% of patients who had a q16-week interval of dosing with almost 50% of patients getting a q12-week or more period of dosing. And the ARIES trial which looked at extending patients either within the first year or the second year and found that q16-week dosing, again, was seen in a good number of patients within this study. And also q12-week dosing or more was seen in a significant proportion; slightly around 50% of patients got q12 week of dosing, as well. So just to show you there's a real durability effect in some of these drugs. And what we see in some of these trials, at least right now according to what we know from the literature, between aflibercept and brolucizumab, we're seeing the longest durability of effect of these anti-VEGF agents in clinical practice.

Dr. Do:
Thank you for sharing that case. Julia, what are your thoughts about achieving dryness and disease control in wet AMD, and which treatment strategy do you employ?

Dr. Haller:
I employ a treat-and-extend treatment strategy, Diana, much as Rishi has outlined so nicely. And I just have to say his case is really a credit to his assiduous follow-up. My policy is to keep at it with monthly doses until I feel like I've got it dry and that we see a stabilization of visual acuity, hopefully at a vastly improved level. And then to back off with a treat-and-extend program, and if I have trouble doing that, I will switch to other drugs if I think I'm not getting the results with drying and stabilization and stretching out of treatments, particularly looking at aflibercept and brolucizumab for those extensions.

Dr. Do:
Those are all excellent points. I think we have to remind our patients that, you know, a lot of them do have apprehension about coming in for intravitreal injections, but we need to be proactive about alleviating their fears. In fact, our colleague Dr. Neil Bressler is creating a video for patients to help explain what to expect in their clinical journey. This video can be found at EyeHealthAcademy.org/TimeIsVision.

In our last few minutes today, I'd like to ask both Rishi and Julia to share with us their take-home messages.

Dr. Haller:
I'd say my message is upfront planning and preparation of patients. When they come in with dry macular degeneration, really get them on target so they know that if they convert to wet, we want to diagnose it quickly and treat it immediately. Our prognosis is much, much better with early therapy.

Dr. Do:
Rishi?

Dr. Singh:
I think that, to echo Julia's points, it's important to consider some of the individual characteristics and preferences of our patients. Having a conversation around what their expectations are following anti-VEGF therapy and trying to tailor our therapy to meet their needs is going to lead to some long-term success with their buy-in. We don't necessarily need to dose patients every month or even every 2 months. There's an opportunity to dose patients even longer and lead to success in those patients.

Dr. Do:
This was a really excellent discussion. I enjoyed learning from both you, Julia, and also Rishi, and I'd like to thank our audience for listening in today. It was a pleasure to have everyone on board with us.

Dr. Haller:
Thank you, Diana, it was great to be with both of you.

Dr. Singh:
Thank you.

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