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Sharpening the Focus: Identifying Treatment Strategies for Diabetic Retinopathy

Announcer:
Welcome to CME on ReachMD. This activity is part of a special series titled “The Mission Continues: Saving Sight Through Early Referral, Diagnosis and Treatment for DR/DME.” 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/SaveSight

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Dr. Scott:
A main goal in the management of diabetic retinopathy is to intervene before vision loss occurs. But how early is too early? New studies are giving us insight into the management of diabetic retinopathy, and I’m pleased to bring you a discussion today of those new studies and the insights we can take into our clinical care.

This is CME on ReachMD. My name is Dr. Adrienne Scott, and I’m pleased to be joined by Dr. Jennifer Lim and Dr. Raj Apte.

Dr. Apte:
Adrienne, thank you for having me. It’s great to be here.

Dr. Lim:
Great to see you, Adrienne, and great to see you, too, Raj.

Dr. Scott:
So we know that patients with varying degrees of diabetic retinopathy are at differing risks for risk of vision loss. I’d like to present a case of a patient of mine. The 54-year-old man was referred for evaluation of nonproliferative diabetic retinopathy [NPDR] with no vision complaints. Right eye vision measured 20/20 and left eye vision measured 20/25. He’s a type 2 diabetic for 20 years with a hemoglobin A1c 10 years ago of 12%, which he has recently brought down to 6.3%. He has a past medical history of controlled hypertension and hyperlipidemia and takes only metformin for his glycemic control. He is a nonsmoker with 2 drinks daily.

30-degree fundus photos of this patient are depicted. The right eye shows mild juxtafoveal lipid with a few foveal microaneurysms and moderate intraretinal hemorrhages throughout, consistent with moderate NPDR. Given the proximity of lipid to the fovea, this eye likely has DME [diabetic macular edema] as well. The left eye shows a few foveal microaneurysms, and the periphery shows moderate intraretinal hemorrhages, also consistent with moderate NPDR. No neovascularization is present. Fluorescein angiogram shows mild increased foveal avascular zone in each eye with mild leakage from peripheral microaneurysms. There are no leaking aneurysms in the left eye; however the right eye does show a few juxtafoveal leaking microaneurysms. The OCT [optical coherence tomography] in the right eye is consistent with mild center-involving DME [CI-DME], and the left eye also has slightly increased center-involving DME.

So, Raj, I’d like to ask you, what do you consider the risk factors for vision loss in this particular patient?

Dr. Apte:
Thank you, Adrienne. This is a really good case because it highlights the complexity of diabetes. We know that having an accurate diagnosis is important, and this patient has moderate nonproliferative diabetic retinopathy with some ischemia and nonperfusion. The patient also has comorbidities which should be addressed – hypertension, hyperlipidemia – and the fact that their hemoglobin A1c is under much better control than 10 years is also important for prognosis.

We know that with increasing severity of diabetic retinopathy, the risk of blindness is higher. For example, a patient with severe nonproliferative diabetic retinopathy or proliferative diabetic retinopathy [PDR] has a twice higher likelihood of severe vision loss or blindness compared to someone with mild nonproliferative diabetic retinopathy, and so it's important to classify or stratify risk of vision loss based on the severity of retinopathy. If interested, you can also see how your skills stack up in our image-based activity by going to EyeHealthAcademy.org/SaveSight.

Dr. Scott:
That's great. Thank you for that insight.

Jenny, new studies are giving us more and more information about management of nonproliferative diabetic retinopathy and proliferative diabetic retinopathy. Can you please give us your insights into these studies?

Dr. Lim:
Sure, happy to, Adrienne. We're really fortunate that in 2022 we have the PANORAMA and the Protocol W results that can help guide the management of a patient just like you presented. So let's first talk about Protocol W. So Protocol W enrolled about 400 eyes into a study where they were randomized to receive aflibercept or sham for management of moderate to severe nonproliferative diabetic retinopathy. At 2 years, the rate of development of center-involved DME or PDR in the sham group was about 44%, and with aflibercept this was significantly decreased to 16%. So that was essentially a huge improvement there, and essentially for the proliferative diabetic retinopathy arms, it represents about a halving of the incidence, and for center-involved DME, it's about a third. So significant reduction there. In addition, Protocol W also showed that the DRSS [Diabetic Retinopathy Severity Scale] 2-step improvement was markedly higher in aflibercept, about 45% compared to about 14% in sham.

PANORAMA is the other study that also looked at eyes with moderately severe to severe NPDR. So basically, if we look at the Week 100, which would be the equivalent comparison group for Protocol W, we see that the rate here for vision-threatening complications [VTCs] – that is, development of proliferative diabetic retinopathy or anterior segment neovascularization – was 27% in the sham group, and this was decreased to 6%-8% in the 2 aflibercept arms. So again, a significant reduction in the rates of VTCs. Now this next slide shows us the rates of DRSS step improvements of 2 or more steps. And again, we see, similar to Protocol W, that aflibercept showed a significant improvement in this DRSS. And that is compared to a sham group, where at 1 year it was 15% that had this improvement. It was 60%-80%, actually, for the aflibercept arms, and then at Week 100, it was 13% for the sham group and 50%-60% for the aflibercept arms.

So I think this gives us some new information to help guide the management of eyes with moderate diabetic retinopathy in terms of prevention of CI-DME or proliferative diabetic retinopathy, and of course also improving the rates of improvement of 2 steps in the DRSS score.

Dr. Scott:
Thank you for that insight. So in summary, we have a man who has 20/20 vision in his right eye and moderate NPDR with borderline macular thickening from diabetic macular edema, and in his left eye he has 20/25 vision, moderate nonproliferative diabetic macular edema with some leaking microaneurysms in the periphery and center-involving DME. Jenny, what are your thoughts on how to manage this case?

Dr. Lim:
Normally, for a patient who just has moderate nonproliferative diabetic retinopathy of this severity, I would not actually use an anti-VEGF. However, this patient also has macular edema. And you might say, well, he has macular edema, but his visual acuity is good, and we can use the results from Protocol V to inform us as to whether we need to treat this patient. I would say, though, that a further analysis of Protocol V showed that a patient such as this, who already has macular edema where the thickening is over 300 microns and has moderate NPDR severity, is at higher risk for visual loss in their analysis. And so this is actually a patient I would use an anti-VEGF to treat the macular edema.

Dr. Scott:
That's great. Raj, what are your thoughts?

Dr. Apte:

I think Jenny wonderfully summarized the results of Protocol W and PANORAMA and actually brought in the results of Protocol V, and this is a great illustration of how we can distill clinical trial results and talk to individual patients. So I would actually have a conversation with the patient of the level of their macular edema and the fact that they have good vision, their comorbidities, and I would be willing to observe this patient as long as they understand that it's important to be seen fairly frequently. And if there's evidence of progression, worsening in vision, then I would be in agreement that we would treat them with anti-VEGF pharmacotherapy because that's a wonderful option for us.

Dr. Scott:
For those just tuning in, this is CME on ReachMD. I'm Dr. Adrienne Scott, and today I'm speaking with Dr. Jennifer Lim and Dr. Raj Apte about the latest data on the management of patients with NPDR and how physicians are interpreting this data.

I'd like to move to a second case of a man who presented to my clinic. He's 63 years old, referred for diabetic retinopathy evaluation. He's a type 2 diabetic, and his hemoglobin A1c wass most recently 9%. Vision acuity, best corrected, in the right is 20/20 minus 1, and in the left is 20/30 minus 2. His past medical history is significant for end-stage renal disease on hemodialysis. Ultra-widefield fundus exam does show severe nonproliferative diabetic retinopathy in both eyes, with scattered intraretinal hemorrhages and lipid and cotton wool spots through the periphery.

OCT in his right eye shows mild center-involving diabetic macular edema with some preservation of the foveal contour. And in the left eye, more significant center-involving diabetic macular edema with more loss of central foveal contour.

Raj, this is a commonly encountered clinical scenario. How would you manage this patient?

Dr. Apte:
Adrienne, I really like the juxtaposition of this case versus the first one we discussed because it highlights how complex diabetes is. You can see that this patient is on end-stage renal disease and hemodialysis, so you really have to look at the whole patient, not just their eyes, and think about the comorbidities and the ability of the patient to come for follow-ups. Also, their A1c is poorly controlled. They are in a higher quartile, putting their risk of progression of retinopathy higher, and as Jenny pointed out, this patient is in a much thicker group of the central OCT thickness. So there have much more pronounced cystic macular edema, more so in the left eye than the right eye, and the severity of the retinopathy on the wide-field images is also more severe than the first case that we saw.

So there are a lot of factors that would push me more towards treating this patient or at least having a discussion about treating their left eye and potentially their right eye with anti-VEGF pharmacotherapy and discussing, again, the importance of A1c control, their hypertension, potentially their lipids, and other comorbidities.

Dr. Scott:
Thank you, Raj. Jenny, what are your thoughts on this case?

Dr. Lim:
I agree entirely with what Raj has said. You know, despite the fact that the visual acuity is good, this is a patient with severe macular thickening. And in the subgroup analysis of Protocol V, we know that patients who are over 300 have a twofold risk for visual acuity loss compared to somebody who doesn't. And on top of that, this patient has severe NPDR, which also has a twofold risk for progression compared to somebody who has a lesser degree of diabetic retinopathy severity. Lastly, this is a patient who has end-stage renal disease, comorbidities, uncontrolled A1c, and I would get this patient and their family very involved in their treatment, make sure they understand the importance of follow-up so that they're not lost to follow-up. So I would aggressively treat, get this macular edema down. And then one of the benefits that would also happen, as we know from the PANORAMA and the W results, is that when we treat with anti-VEGF, we're also most likely going to get a decrease in the DRSS severity in this patient, and that hopefully, in the long term, that will actually be beneficial for this patient as well.

Dr. Scott:
We need to help patients understand how diabetes can affect their vision and how they can take control of maintaining their vision. We've created a brief 3D video to illustrate the role of diabetes and how it affects vision and also the interaction of anti-VEGF and the retina. Let's take a look.

[VIDEO PLAYS.]

Announcer:
If you have diabetes, you are at risk for diabetic retinopathy.

Even though you can't see it, diabetes and high blood sugar can seriously damage blood vessels.

When that happens, it can cause vision loss or even blindness.

The good news is that regular eye exams and early treatment with anti-vascular endothelial growth factor, or VEGF, can reduce your risk—even before *you* notice a change.

So see your eye doctor once a year or more, because the best chance to save your vision is when you don't have vision problems.

Dr. Scott:
If you are interested in sharing that animation with your patients, it can be found at EyeHealthAcademy.org/SaveSight.

As we conclude our discussion today, we'd like to get some final take-home points from both of our guest discussants. Jenny, what are your thoughts?

Dr. Lim:
Adrienne, it's really been a fun conversation to have with you and Raj. I think my main take-home point from today is that anti-VEGF can actually prevent progression of diabetic retinopathy and prevent the complications of proliferative diabetic retinopathy, center-involved diabetic macular edema in patients who have severe and moderately severe nonproliferative diabetic retinopathy.

Dr. Scott:
Wonderful. And Raj, what do you think? What are your take-home points for the discussion?

Dr. Apte:
I concur with Jenny and you. I think anti-VEGF pharmacotherapy has revolutionized our ability to treat diabetic retinopathy and save vision. And what well-designed clinical trials like Protocol W, PANORAMA, and others have done is, in this era of precision medicine, it's allowed us to customize and titrate therapy to individual patients so that we can have the best outcomes, as illustrated in the 2 cases that we discussed.

Dr. Scott:
I'd like to once again thank our guest discussants, Dr. Jennifer Lim and Dr. Raj Apte, in discussing Protocol W and PANORAMA and the many options we have for treatment for our diabetic patients. It was a joy to speak with you both.

Dr. Lim:
Thanks so much, Adrienne, for having me. I really enjoyed it.

Dr. Apte:
Thank you. It was a pleasure as well.

Announcer:
Thank you for listening! This activity is part of a special series titled "The Mission Continues: Saving Sight Through Early Referral, Diagnosis and Treatment for DR/DME." 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/SaveSight