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Viewpoints on Cases in Diabetic Retinopathy: What the Optometrist Needs to Know

Announcer: This activity is provided in partnership with the National Eye Institute, of the National Institutes of Health, of the US Department of Health and Human Services. The National Eye Health Education Program of the NEI is acknowledged for its important contributions to this initiative.

Dr. Dunbar: You are listening to CME on ReachMD. My name is Dr. Mark Dunbar, and I am joined today with Jay Haynie, who is an optometrist at Sound Retina in Tacoma, Washington. Jay, we have had a lot happening in the area of diabetes and diabetic retinopathy over the last 10-15 years or so. There has really been a complete paradigm shift in when we refer these patients instead of waiting till they develop proliferative diabetic retinopathy, maybe recognizing that we should be referring these patients much earlier, and that maybe even treating these patients at the level of severe non-proliferative disease. Obviously, how we diagnose diabetic macular edema has also changed. Many us now have OCT, so we rely on being able to really pick up early retinal thickening, and then of course how we manage to treat diabetic macular edema has also evolved. We are going to present a couple of cases today, really highlighting some of these shifts, paradigm shifts, and so on. Why do you not lead us through that first case, Jay?

Dr. Haynie: Thank you, Mark. First, we need to understand in the past treatment of non-proliferative diabetic retinopathy really occurred only when it was associated with diabetic macular edema. Based on the data from the RISE and RIDE clinical trials, this study was designed to study diabetic macular edema. The study population contained a mix of patients with both NPDR and PDR. Secondary analysis showed that after treatment with ranibizumab, eyes with diabetic macular edema and diabetic retinopathy were less likely to exhibit worsening of retinopathy. They were also less likely to progress to PDR, and they were more likely to show improvements in retinopathy severity. This is the case of a 57-year-old woman who has been referred for evaluation and treatment of diabetic retinopathy. Chief complaint was blurred vision in each eye for the past six months. Her past medical history is significant for type 2 diabetes of 12 years' duration. Her current medications include insulin glargine and glimepiride. Entering visual acuity was 20/50 in the right eye and 20/60 in the left eye. She had some early nuclear cataract with normal intraocular pressure. These are the fundus phots that we obtained. Mark, why do you not take a look at these fundus photos and help us in how we grade and stage non-proliferative diabetic retinopathy.

Dr. Dunbar: Sure. These are beautiful wide-field images that really give us a nice view of the right and the left eye beyond the arcades. Whenever I am looking at a fundus photo, I start at the beginning. The disc looks clear. There is a moderate-sized cup. You can see as you go along, the vessels along the arcade. It looks like there are hemorrhages in all four quadrants, maybe worse in the left eye than the right eye. You can see some scattered cotton wool spots. It is possible there may even be some IRMA there. I do not think I have quite enough detail or resolution to see that, but I would categorize this patient as probably having at least the left eye severe NPDR. I think the right eye as well. It is interesting. one of the reasons we stage these patients, it is all about their risk of going on to develop proliferative disease in a year. We know the mild and moderate NPDRs, their risk is about 5% to 12%, but that severe NPDR, that risk goes up to over 50%. For that reason, typically we would bring these patients back maybe three months at a time and follow them because we know that risk of going on to proliferative disease is in a year. We have a slide up that really looks at the different grading scales for diabetic retinopathy, and most of us are familiar with that international grading scalethe grading scale that all of us use. I think it is important to know that there are a couple of other grading scales as well. There is the ETDRS grading scale that they use in the

ETDRS study. It starts from 10, which is really no retinopathy, and goes up to 85, which is the end stage of proliferative diabetic retinopathy. There is also a modified ETDRS scale. this is a scale that starts at one and goes up to nine. The reason that is important is because when they are doing these clinical trials, it is important to be able to really have a more sensitive scale. When we talk about the severe NPDR patient, categorically that is a patient who is in that almost level 47-53 on that ETDRS grading scale. That becomes important because I think the paradigm shift is referring these patients earlier and treating these patients earlier. I think you are going to tell us a little bit more regarding the PANORAMA data that looks specifically at that categorization, that by treating these patients earlier, we are actually able to see a regression in the severity of their diabetic retinopathy. When you look at the fundus photos in this patient, that is a patient who has that severe NPDR. As a primary care optometrist, I would send that patient to the retinal specialist.

Dr. Haynie: That is a great point, Mark, and I agree with your classification of this patient. The question became why is the visual acuity diminished at 20/50 in the right eye and 20/60 in the left eye? We obtained spectral domain OCT images, which you can see here, which shows an increase in central macular thickness with an accumulation of intraretinal cystoid macular edema in each eye. This patient was diagnosed with not only severe NPDR but also with center-involved diabetic macular edema.

Dr. Dunbar: I was thinking back to our old ETDRS days, Jay, when a patient would come in who had diabetic macular edema and 20/80 or so visual acuity. The goal of laser of course was to dry up the macula, make the macular edema go away, but there was really no benefit necessarily in getting the vision back. That 20/80 patient, success was keeping him at 20/80.

Dr. Haynie: Yes, Mark, that is correct. This patient was treated with a series of anti-VEGF injections and following the induction treatment, which was three procedures, the follow-up OCT as we see here clearly shows resolution of the intraretinal cystoid changes, reduction in central macular thickness, and a reestablished foveal contour. But an interesting part in this case is it has been shown that patients who receive anti-VEGF injections for treatment of macular edema may also develop regression of the severity in diabetic retinopathy.

Dr. Dunbar: I think that is interesting. As you comment, that retrospective data of the clinical trial was designed to see if the anti-VEGF drugs work for treating diabetic macular edema. Of course, we know the answer to that. As you pointed out, to really look at the level of diabetic retinopathy in those patients that were treated for diabetic macular edema and see, in fact, we were able to improve and make the diabetic retinopathy much better, which really has led to where we are today. The PANORAMA data was looking prospectively at these patients, designing a clinical trial to really see if, in fact, what we saw in RISE and RIDE and some of the other clinical trials of VIVID and VISTA to see in a prospective fashion, do we see the same thing? The reality is that is exactly what happened when we looked at those patients who were in that severe or moderately severe NPDR, that was really the highlight of the PANORAMA, What they found was that those patients who were within that category really did the best in terms of having a regression in the level of their diabetic retinopathy. Almost 80% had a two-step regression in their diabetic retinopathy. If they were level six, for example, they were more likely to go down to level four. that was really the highlight of the PANORAMA, That is really changed the landscape of how we manage and treat these patients.

Dr. Haynie: That is a very good point that you make, Mark. We know that patients with diabetic macular edema will receive treatment with anti-VEGF therapy, but I would like to take a moment to present a case in a patient who had severe non-proliferative diabetic retinopathy in one eye and did not have the presence of macular edema. This patient is a 62-year-old woman who was referred for an evaluation of treatment. Her chief complaint was floaters in the left eye for the past two months, and she had a longstanding history of type 2 diabetes of 34 years' duration. She was also hypertensive and was on medication for elevated cholesterol. Her entering visual acuity was pretty good, 20/20 in the right eye and 20/30 in the left eye. She had some nuclear cataract with normal intraocular pressures. If we look at the imaging that was obtained, the color fundus photographs in the right eye, we can see areas of scattered dot-like hemorrhages, cotton wool spots, but the central macular area actually looks fairly pristine. In the fellow eye, she had a little haze to the photograph inferior, which was the vitreous hemorrhage. If you look at the optic nerve, there are some irregular vessels stemming off the nerve, which was consistent with NVD. The classification for this patient was severe NPDR in the right eye, proliferative diabetic retinopathy in the left eye with vitreous hemorrhage, and OCT imaging confirmed normal macular thickness, normal foveal contour without the presence of macular edema. This patient was treated with serial anti-VEGF injections in the left eye for the complications of proliferative diabetic retinopathy but was also treated with anti-VEGF injections at 12-week intervals in the right eye, which was the eye with non-proliferative diabetic retinopathy. Interestingly, follow-up fluorescein angiography of the right eye, which began as severe NPDR, continues to be classified as severe NPDR without evidence of more proliferative findings. In the left eye you can see regression of the neovascularization, which is indicating a great response to anti-VEGF and laser treatment.

Dr. Dunbar: This is really the classic case where that works very well. She had proliferative disease in the left eye, and you know that the right eye, it is just a matter of time before they progress to that level as well. In this case, it really becomes pretty easy because you have a snapshot of what really the future held for this lady, so by treating her early, you were able to really avoid the potential of going

on to develop neovascularization and proliferative disease, etc. I wonder though, Jay, in light of that, if the left eye did not have neovascularization, what are you guys doing in your practice? Have you guys made the transition of treating these severe NPDR cases or is it just a case-by-case basis?

Dr. Haynie: We have not quite made the leap to treating everybody, but what we do in our clinical practice is we look at other variables. We look at the duration of the diabetes. Systemic conditions will contribute to the progression of retinopathy. It is more about identifying the risk profile for our individual patients.

Dr. Dunbar: Jay, I know these treatments are not without risk. The anti-VEGF drugs are viewed to be very safe, but there are some risks that I think we need to be aware of. Can you discuss that with us?

Dr. Haynie: Most of the complications with intravitreal injections are transient. Patients can develop corneal irritation. They can have a subconjunctival hemorrhage, but as we know, these symptoms are self-limiting. Through the clinical trials in PANORAMA, there were no new adverse events developed or identified.

Dr. Dunbar: When you look at the data, the fact that you can get almost an 80% regression in the level of retinopathy really is pretty powerful. To me, it is interesting to see. This is fairly recent, this data, and so I think it is going to take awhile for retinal specialists to really decide what they want to do with it. Do they want to embrace treating these patients as the study recommends or take a little more of a conservative approach? I am kind of excited to see how this is all going to shake out once the dust settles. I think from the optometric perspective, however, recognizing the severity of the diabetic retinopathy, making sure patients understand, understand the significance of the retinopathy and the importance to make sure they are following up with the retinal specialist. Even though we are not going to be the decision makers on if the patient is going to be treated but more importantly helping them understand what the risk factors are, the risk of progression. Being that go-between on one side of the retinal specialist but also making sure the primary care physician and the endocrinologist are also aware. Echoing the sentiments of what they say in terms of making sure they are controlling their diet, making sure they are following through what their blood sugars are, and their hemoglobin A1c levels are. It really is very much that team approach that we play with the endocrinologist, primary care providers on one side and the retinal specialists on the other.

Dr. Haynie: Those are great comments that you make, Mark. I think some of the take-home points, to reiterate what you said, is the profession of optometry is really on the front line of diagnosis of diabetic retinopathy. A couple of key points that you made were patient education. I think what is also very important is documenting these retinal findings and, as you know, a fundus photograph speaks very highly when we are educating our patients. I really have enjoyed watching the profession grow with better technology and fundus photography, the wide-field imaging systems that we have available to us. One clinical pearl is when looking at fundus photos, I tend to concentrate more on looking at a red-free image because the red-free image highlights the hemoglobin. It highlights more small microaneurysms. To follow up, we can show the patients, we can show them their retinal findings, and we can encourage them to obtain better control of their diabetes. I think it really boils down to us taking a very strong role in trying to educate our patients through the examination, through imaging, and letting them understand what their risk profiles are.

Dr. Dunbar: Well said. Jay, that was an interesting discussion. Thank you for joining me today. I certainly learned a lot. I hope our audience has learned a lot as well. Thank you.

Dr. Haynie: Thank you, Mark, for having me be a part in a great discussion. It is always nice to get together with you.