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Seeing Eye to Eye: Case Series on Treatment Strategies for RVO

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. Scott:
Retinal vein occlusion or RVO is one of the most common retinal vascular disorders. Today, we’re joined by Drs. Rahul Khurana and Dr. Peter Campochiaro to discuss this condition. Peter, Rahul, thank you so much for joining us today. I’d like to welcome you to the program.

Dr. Campochiaro:
Thank you for having me.

Dr. Khurana:
Great to be here.

Dr. Scott:
Let’s review for a minute what we know about retinal venous occlusive disease and how early treatment makes a difference. Rahul, what can you tell us about this?

Dr. Khurana:
Adrienne, we’ve been very fortunate in the past decade to have multiple treatments for the management of macular edema, secondary to venous occlusive disease, including anti-VEGF therapy and intravitreal steroids. What this data has also consistently shown us is that there are better visual acuity outcomes with earlier treatment. When we looked at the SCORE clinical trial and the COPERNICUS and GALILEO studies, they showed that longer duration of macular edema at baseline, those patients had poor visual acuity outcomes. And the univariate SCORE2 analysis, a more recent study, also showed that a longer duration of macular edema at baseline, greater than 2 months, had worse anatomical outcomes and worse visual acuity outcomes. And it really affirms this principle that there are better outcomes with earlier treatment.

Outside of these clinical trials, when we looked at the real world, we’ve seen very similar findings. A recent study that came out that looked at patients who had central retinal vein occlusions and poor visual acuity, even in this group, a simple delay of nearly 30 days, those patients had worse visual acuity outcomes and had a higher rate of neovascular complications and other ocular complications. And it really affirms that with our patients with macular edema, we want to treat them earlier to really achieve the best visual acuity for our patients.

Dr. Scott:
Thank you, Rahul. Peter, what can you tell us about early treatment of RVO?

Dr. Campochiaro:
Well, Adrienne, I'd just like to first illustrate a patient who presented with a hemi-retinal vein occlusion. This patient had a sudden reduction in vision and this fluorescein angiogram shows several areas of retinal nonperfusion. After 6 injections of ranibizumab, we noticed this fluorescein shows a marked improvement in the retinal nonperfusion. The patient was then treated with PRN treatment for 6 months, and after 6 months, there was a recurrence in retinal nonperfusion. So this illustrates that patients with retinal vein occlusion can have the areas of nonperfusion that is improved by anti-VEGF treatment. And it illustrates what we've seen from clinical trials.

In the SCORE trial the natural history was demonstrated in the sham group in which it was shown that patients with CRVO had a 4-fold increase in retinal nonperfusion between baseline and month 4 and had a 37-fold increase between baseline and month 12. The, the CRUISE and BRAVO studies showed that this can be interrupted by anti-VEGF injections. This slide shows the percentage of patients who had no retinal nonperfusion. And you can see that it decreases over the first 6 months in patients in the sham group, whereas it improves in patients treated with ranibizumab. After 6 months, both groups received PRN treatment and the lines came together. And this similar pattern occurred in patients with BRVO. These data were confirmed in the COPERNICUS and GALILEO trials in which patients were treated with monthly aflibercept. And it showed that they looked at wide-angle fluorescein angiograms and measured total areas of retinal nonperfusion. And the percentage of patients who had greater than 10 disc areas of total retinal nonperfusion was 24% at baseline and in the aflibercept group decreased by more than half, whereas it increased somewhat in the sham group. So it illustrates that in patients with retinal nonperfusion, there can be progressive worsening of retinal nonperfusion that is improved by anti-VEGF injections.

Dr. Scott:
Thank you so much, Peter, for that. Yes, this is a chronic disease, and it seems patients need treatment pretty much indefinitely. Peter, what are your thoughts on patient treatment regimen, and what can we do to decrease dependence on anti-VEGF or even laser?

Dr. Campochiaro:
That's a really important question, Adrienne, because as you point out, a large percentage of patients require injections long term. Data from the RETAIN study in which a cohort of patients from BRAVO and CRUISE were followed up for at least 4 years – and the outcomes were quite good. With BRVO, there was a mean improvement of 20 letters, at 4 years, but about 50% of the patients were still requiring injections to control edema. Now this panel with the dots shows the time of last injection for patients who resolved, which are shown in blue and other patients shown in other colors. And one thing you note is that most of the patients who do resolve declare that within the first 2 years. You know by 2 years whether or not a patient is going to need long-term injection.

And the same is true for CRVO. This shows that the mean outcomes were not quite as good, about 14 letters improvement in 4 years, and about 50% of patients were still requiring injections at 4 years. But just like with BRVO, they declare themselves early so that by 2 years, you know who those patients are who are going to require long-term injections.

Now, one of the hypotheses was that scatter photocoagulation to the periphery could decrease the need for injections because the thought was that you would be reducing the amount of ischemic retina. The RELATE study looked into that hypothesis and randomized patients to either ranibizumab alone or ranibizumab plus scatter photocoagulation. And as you can see from these graphs, after 5 years, there was no difference in visual outcome, and there was also no difference in the percentage of patients who had resolution. Those that had PRP still required injections just as much as those that did not. So scatter photocoagulation is not the answer to reduce the burden of injections.

Dr. Scott:
Thank you, Peter. For those just tuning in, this is CME on ReachMD. I'm Dr. Adrienne Scott, joined by Drs. Rahul Khurana and Dr. Peter Campochiaro, and we're discussing management of retinal vein occlusion.

Rahul, I'd like to turn to you and talk a little bit about cystoid macular edema as it pertains to CRVO. Can you give us a little information about your thoughts on macular edema and retinal vein occlusion?

Dr. Khurana:
In the SCORE2 clinical trial, we can see in the bevacizumab-treated arm, after 6 treatments, those who had persistent CME were then switched to aflibercept. And you can see that not only are there improvements in the retinal anatomy, but more impressively, there are improvement in the visual acuity. These patients gained nearly 10 letters of vision. And it illustrates an important principle that if the CME is not responding to your current treatment, it's really important to either shorten the duration of the treatment or to either switch in class as in between anti-VEGF agents or even switching out of class to an intravitreal steroid. Really, the goal is to resolve the macular

edema to really optimize the visual acuity outcomes for your patients.

Dr. Scott:
Great. Thank you so much, Rahul. So I'd like to switch gears a little bit, Rahul, and talk about the strategies for patient education. How best can we relate to the patient that central retinal vein occlusion and other retinal vascular diseases such as this are a chronic condition that requires ongoing treatments? Rahul, what are your go-to strategies for communicating this to the patient to ensure compliance with treatment regimens?

Dr. Khurana:
I think it's a very important point, Adrienne, and I think a lot of times when we thought of our vein occlusive disease, we think of an acute event, and I think our thoughts on management really thought this was an acute process. But I think Peter has done some really phenomenal work that has really showed that the macular edema can be a chronic process, and we need to really watch these patients very closely and they need to be regularly treated. And so part of that patient education is explaining the chronicity and also just explaining the importance of why we want to be proactive, why we want to treat these patients before we can do other things that are there. And so I think part of that education is explaining to the patients that even though they're doing well with current treatment, it really requires buy-in and they have to keep coming back for their treatments and making sure they stick with the treatment plan. And many of our patients do see this because they know if they go longer than their intervals, then the macular edema comes back and their vision worsens. And so that does also further reaffirm what we're saying. But really it requires long-term management and having both the physician and patient engaged in that process.

Dr. Scott:
In our last few minutes, I would like to go ahead and kind of summarize what we've learned today and talk about any take-home messages for our audience regarding treatment of RVO. Peter, why don't you go first. Can you tell us what take-home messages you would advise for our audience about RVO?

Dr. Campochiaro:
Well, Adrienne, I think an important take-home message is illustrated on this schematic, and that is that retinal vein occlusion, just like diabetic retinopathy, is a chronic disease. And that's because both of them are driven by retinal nonperfusion. And in vein occlusion, the nonperfusion occurs abruptly at the onset of the disease. And it's minimal in some patients who have minimal arterial disease, but those patients who have significant preexisting arterial disease develop significant retinal nonperfusion right from the outset. Those that have minimal retinal nonperfusion still have ischemia, and they require anti-VEGF injections to control edema, but at some point, they may have resolution and no longer require injections. But that's generally the minority of patients. Most of those of the patients have significant retinal nonperfusion, and they have high levels of VEGF that promote leukostasis. And the leukostasis plugs retinal vessels, causes further increase in VEGF levels that leads to a positive feedback loop that causes worsening over time. We know that that can be interrupted by aggressive and frequent anti-VEGF injections, and with that we can have good outcomes, but most of those patients still require injections long term. We know that scatter photocoagulation is not the answer to interrupt that, but in the future, there will be sustained delivery of anti-VEGF agents that will improve the burden and probably improve outcomes in these patients.

Dr. Scott:
Excellent points, Peter, thank you. Rahul, what are your take-home messages about RVO?

Dr. Khurana:
I think what it comes down to it, Adrienne, is that we always have to remember that macular edema is the main cause of vision loss, and we really have to do everything to minimize its effects on the vision, on the retina. And that involves before treatment, minimizing treatment delay. That includes during treatment, that they do have persistent macular edema, switching therapies so you do get resolution. And finally, in the long-term management, really preventing recurrences of macular edema which, over time can harm the vision long term. And so, I think, being aware of this at all three levels, before treatment, during treatment, and during maintenance, are really essential to having good outcomes long term for our patients with venous occlusive disease.

Dr. Scott:
Thank you, Rahul. Yes, I think it's clear that retinal venous occlusive diseases are chronic, definitely require buy-in from the patient to understand that they need treatment over the long term, and that early treatment and frequent and aggressive treatment, usually with an anti-VEGF agent, possibly even combined with steroid, can oftentimes improve our vision outcomes.

Well, that's all the time we have for today. I'd like to thank Drs. Campochiaro and Khurana for their time and thank you for your attention.

Dr. Khurana:

Thank you, it's great being with you.

Dr. Campochiaro:
Thank you, Adrienne.

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