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Macular Leakage: Indicator of Vascular Stability

Dr. Lim:
This is CME on ReachMD. I'm Jennifer Lim, and I'm joined by Justis Ehlers today. Today, we'll discuss drying of the retina.

So drying of the retina is our primary goal in managing retinal disease, but we are reacting to the presence of fluid. Are there now ways, Justis, that we can be more proactive in our approach to disease control?

Dr. Ehlers:
Thanks so much, Jenny. It's great to chat with you today. As we look at opportunities for disease control, particularly, I think in diabetic eye disease and retinovascular disease, looking at macular leakage is something that we're starting to look at in more and more ways, particularly as new treatments come available. There have been multiple studies that have helped inform us in terms of what the potential complications are related to untreated leakage. For example, in the PANORAMA post hoc analysis, increased areas of leakage and retinal nonperfusion indicated a greater risk for NPDR worsening.

In the PRIME study, there was actually an analysis that looked at treatment based on leakage compared to treatment based on DRSS, and what that study identified was that leakage seemed to be sort of a leading indicator, even more significant and quicker to be identified than DRSS changes.

And then lastly, when we looked at the RUBY study, this was an analysis of a Phase 2 trial in diabetic macular edema looking at a correlation of visual acuity as well as ultrawide field angiographic features. And with that, there was actually an association with increased leakage area with overall risk to vision loss.

And so, with that in mind, I'd like to share a case with you. Here when you think about often the way that we treat patients, OCT is really front and center. It's really the workhorse that we use on a day-to-day basis. But as we, again, have more and more therapeutic options as we move maybe toward precision medicine, looking at other imaging modalities, including ultrawide field angiography, may be a unique opportunity.

Here, we see an eye at baseline with really extensive leakage, areas of nonperfusion, significant leakage not only in the macula, but out into the retinal periphery, and even a small area of neovascularization. This patient was then treated with aflibercept over the course of 6 months with 4 treatments. And really, what you are drawn to is this dramatic improvement in leakage and in resolution of the neovascularization, and this is really quite striking. When you really zoom in, what you also see is some true disease remodeling and modulation taking effect. We see here on the left at baseline, areas of multiple microaneurysms and at that month 6, we actually see microaneurysm resolution.

So, one of the questions with this for me that I've really tried to understand is should we be using more angiography in the way that we manage some of these patients?

Dr. Lim:
Justis, I completely agree with you. I think in an ideal world, we would definitely do angiograms, if you will, almost every other visit, so that we can really see how the drugs are modulating the disease process and see how these patients are responding with regards to the fluid that's leaking out. Because as we know, the anti-VEGFs really do dry up the neovascularization, but they also prevent the leakage, and if we could modulate the treatment based upon how much leakage there is, and as you said, we're really doing personalized medicine. However, as you know, our clinics are really overbooked. And, in my clinic, we have uveitis patients that frequently need angiograms, and so we don't have the bandwidth to do angiograms. And also, patients don't like having to have angiography done because of the need for a needle stick.

I think in an ideal world it would be great. I think we probably underutilize this really helpful test. And hopefully, in the future, we can help modify that by maybe unburdening our clinics with more durable therapies.

Dr. Ehlers:
No, it's definitely a great point. And I don't know if this varies a little bit state to state. I mean, one of our challenges is even, we have to have a specific type of provider be able to push the fluorescein and that's a limiting factor, too, in terms of what resources we have in our given clinics.

Some of the exciting opportunities also could be things like artificial intelligence, generative AI for taking things like OCT angiography. Can we actually predict what the leakage patterns would be? So I think the future is really exciting to see how we can continue to use these tools for our patients.

Dr. Lim:
Justis, those were great points. Unfortunately, we're out of time today. Thanks to the audience for tuning in, and thank you, Justis, for joining me today.

Dr. Ehlers:
Thanks, Jenny.