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Neovascular AMD and RVO: Distinguishing the Differential

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. Kaiser:
Correctly identifying retinal diseases early on is essential for preserving patients' vision. So how do we distinguish key pathologic features to identify early neovascular age-related macular degeneration and retinal vein occlusion before macular edema leads to permanent vision loss?

This is CME on ReachMD, and I'm Dr. Peter Kaiser. I'm joined today by my good friend Dante Pieramici.

Dr. Pieramici:
Peter, thanks for having me today. I look forward to our discussion. Retinal vascular diseases and choroidal diseases present with various pathological features that can be challenging to differentiate because there is some clinical overlap between these diseases. Peter, would you mind reviewing for us the normal outer retinal anatomy and tell us why these structures are important to consider in a patient with age-related macular degeneration?

Dr. Kaiser:
Absolutely. You know, we're talking about RVO and macular degeneration, and interestingly, they really work on different parts of the retina. So when we're talking about vein occlusion, the problems are mainly in the inner retina. When we're talking about macular degeneration, it's mainly in the outer retina. So if you look, for instance, at a normal optical coherence tomography [OCT] image, where we're looking at for macular degeneration is the outer retina layers – the RPE [retinal pigment epithelium], Bruch's membrane, choriocapillaris – those outer retinal layers are where we see most of the changes in macular degeneration.

Dr. Pieramici:
When I think about macular degeneration, I look at a classification of the disease process, and I use sort of the simplified classification that was derived from the AREDS [Age-Related Eye Disease Study] studies – the AREDS2 study in particular. We start to get into the diagnosis of early AMD when we see a little bit larger drusen – drusen that are kind of medium-sized, somewhere around 63 microns to 125 microns, but still no pigmentary changes. When they start to get larger drusen or pigmentary abnormalities or both of these things, we call this intermediate AMD. And this is an important thing to find, I think, in patients because, you know, at this point, I'm talking to them about AREDS supplementation of vitamins and watching them more carefully and having them monitoring at home for any visual changes with an Amsler grid, for instance. And that then brings us to late AMD, and these are the stages that we're trying to prevent. And when they do occur, either wet AMD, neovascular AMD, or geographic atrophy [GA], we're going to be looking at treatment. And it's going be important to identify these conversions, to particularly wet AMD, as early as we can since we can institute treatments.

Peter, I have a slide here. It's a patient with some changes. What do you think about this patient? Is this someone you would call early

or intermediate AMD findings?

Dr. Kaiser:
So, Dante, this is a patient who has both drusen as well as some of those pigmentary changes that you mentioned – those little black dots, right around the center of the fovea. So this is a patient that when we look at from the AREDS classification, we would be more concerned about progression. And if you are not versed in following these patients, you probably want to consider referring this patient to a retina specialist for follow-up thereafter.

Dr. Pieramici:
Yeah, I agree completely. This patient has pigmentary changes and some hypopigmentary changes and larger drusen. I have a case here – this is the patient. One eye has large, confluent drusen. They're greater than 125 microns, and I often use the venule at the optic disc – the diameter of that is about 125 microns. I did a fluorescein angiogram here, and it does show that there's just staining of the drusen. And I think the OCT is real helpful to identify these drusen. And there's another kind of drusen here called reticular pseudodrusen [RP]. It's a little bit different. There's these little, peg-like things that are in front of the RP, but they're also an indication of a more advanced AMD.

Peter, I'm thinking about what to look for on a patient who might have wet AMD. What are the kind of things that you're looking for when you're examining a patient, just with a slit lamp and a 90 diopter lens? What sort of things highlight potential CNV [choroidal neovascularization] in this patient?

Dr. Kaiser:
So obviously, the hallmark of CNV is going to be leakage or bleeding. So the easiest way to see this is with a dilated examination, so you can get stereoscopic view of the retina to see if there's any elevation of the RPE, any elevation of the retina. Look for any hemorrhages around the retina. You could also use some imaging to help you with this – optical coherence tomography is very useful to differentiate a patient who has dry macular degeneration versus those who have converted to the wet form. If you're really lucky, you have OCT angiography, which is a form of OCT that allows you to actually look at the vasculature in a little more detail. And it's exciting technology that allows us to really find CNV and differentiate dry versus wet very easily.

But, Dante, there are also patients who develop decrease in vision from just dry macular degeneration. And how do you figure out those patients?

Dr. Pieramici:
Yeah, that can be difficult. You know, you look in the back of the eye and you don't see blood or you don't see lipid or elevation in the back of the eye. But what you might start to see is this hypopigmentary patches, where maybe you're seeing what looks like the choroidal vasculature underneath that. This is a patient who's got this subretinal fluid, kind of a dome-like shaped elevation with blood. And whenever you see blood, it's helpful to try to think about how deep is that blood? And this blood is behind the retinal vasculature, so it's probably subretinal blood. But on OCT, you could see where the pigment's elevated here, and there's subretinal fluid and retinal edema on the OCT. And here's how it looked a couple of months after an injection in the eye.

But this second picture is a picture of a patient with something called geographic atrophy, which is another end-stage part of AMD. And in this patient, I'm not seeing any blowout. I'm seeing these well-demarcated areas where the pigment changes quite dramatically, in both of the eyes. I also see the hallmarks of drusen in this patient – a pigment change. And if I do autofluorescent images, you can see very well the dark areas here. So a fundus autofluorescence can be helpful to do this. And OCT images are very helpful. I'll show the OCT on a patient with atrophy here. So, I'm not seeing any blood or fluid in this patient. There's no fluid on the OCT, but what we actually have is a loss of the cells, so atrophy – loss of the pigment epithelial cells, the choriocapillary cells and the outer retinal cells. So that's the other end-stage disease that we look for. And it can sometimes go overlooked.

Dr. Kaiser:
So for me, when you oftentimes have subtle atrophy, where the patient has developed late macular degeneration – the dry form – oftentimes, as you mentioned, getting a fundus autofluorescence really highlights these areas. But I think we are highlighting the fact that, you know, using both clinical exam and imaging is sort of necessary for oftentimes deciding if a patient has moved from interm~~m~~ediate to late macular degeneration.

For those of you just tuning in, this is CME on ReachMD, and I'm Dr. Peter Kaiser. And I'm joined today by Dr. Dante Pieramici. We are discussing how to differentiate between the pathophysiological features of macular degeneration and retinal vein occlusion.

Retinal vein occlusion is a potential contributor to visual impairment. So, Dante, when someone looks at a retina, can you kind of describe some of the differences between a patient who has a retinal vein occlusion and those with a normal inner retina?

Dr. Pieramici:
Yeah, with retinal vein occlusions – we talked earlier – AMD is sort of an outer retinal problem. With the retinal vein occlusions, it's an inner retinal problem because the backup is going to be in the retinal vasculature. And you know, when you look in the back of the eye, typically you'll see a pattern of intraretinal hemorrhages. They may be flame-shaped hemorrhages; you might see cottony wool spots. You might appreciate thickening of the retina, and there's some patterns to it. I mean, if you see hemorrhaging in all the quadrants, it's probably a central retinal vein occlusion [CRVO], whereas if you see it in just branch of the vein, it would be a branch retinal vein occlusion [BRVO] in that case.

Peter, what can you tell us about the pathophysiology of the central retinal vein and the branch retinal vein that gives us these typical findings that we see on clinical examination?

Dr. Kaiser:
Yeah, so if you look at sort of the cross section of an artery versus a vein, oftentimes patients who develop retinal vein occlusions have hypertension, for instance, so the lamina gets thickened. In particular, the arteries start to get thickened, and so when the artery crosses over a vein, which is a little weaker, that's usually the site of a retinal vein occlusion. So if you see hemorrhages on clinical exam, follow those hemorrhages backwards, and if you can find a crossing point where an artery crosses over a vein or sort of like a pie-shaped area where the hemorrhages have occurred, that's usually a branch retinal vein occlusion. In general, if you see hemorrhages, as you mentioned, all over the place, and you can't really find a point where it comes together, that's oftentimes a central retinal vein occlusion.

Why do we sort of differentiate between the two? Well, they have different natural history. So for instance, branch retinal vein occlusion, some of these patients may actually get better. It's thought that about a third of patients just by itself may get better, whereas with central retinal vein occlusions, oftentimes they don't get better over time. So the prognosis between these two different diseases is actually very different.

You know, if you look at a patient, for instance, with branch retinal vein occlusion, on clinical exam, there are extensive hemorrhages, cotton wool spots, and on the fluorescein, blocking from the hemorrhages. And if you were to do an OCT in this patient, the cross section shows the appearance of macular edema. So you have intraretinal fluid, you oftentimes have cystic changes, and you oftentimes will have increased retinal thickening. Now, the interesting thing of a branch vein occlusion versus a central vein occlusion on an OCT is oftentimes there's a point where things appear totally normal on an OCT, and the part that's actually where the retinal edema is, and you can tell that. Whereas a central retinal vein occlusion, oftentimes, no matter how you cut the OCT image, you're going to see the swelling on the clinical exam.

Now, when it comes to central retinal vein occlusion, another thing you're going to want to figure out is, is this an ischemic central retinal vein occlusion or a non-ischemic central retinal vein occlusion? And the historic definition is based on 10 disc areas of nonperfusion in the periphery – that's considered an ischemic central retinal vein occlusion. And why is it important to differentiate those two things? Well, patients who have an ischemic central retinal vein occlusion are much more likely to develop neovascular complications. So a patient who has ischemic changes on their clinical exam, you're going to want to watch that patient much more closely than those that are non-ischemic. Now unfortunately, the non-ischemic can actually become ischemic, so it's not like you could ignore those patients with a non-ischemic vein occlusion. But one of the things that we almost always get at baseline when a patient comes in with a vein occlusion is a fluorescein angiogram. And nowadays, that fluorescein angiogram is usually wide-field fluorescein angiogram to specifically look for ischemia, oftentimes looking for also early neovascularization which would be a very, very bad sign.

Now there are other things that can tell you if it's ischemic or not. For instance, if you have an afferent defect, that's ischemic. If you have really poor visual acuity, that's more likely to be ischemic than non-ischemic. So there are other features, but the definition is really based on the amount of nonperfusion we see on the fluorescein angiogram.

So, Dante, what are some of the practice pearls that you could give us about identifying early signs of a retinal vein occlusion?

Dr. Pieramici:
When you see these patterns of hemorrhaging in the back of the eye, even in good vision, I think it's probably important to get them in in a timely fashion for further evaluation and potential treatment because we do have good treatments for these nowadays, be it anti-VEGF injections or lasers. So the earlier the better, and it will reduce further complications and improve vision for patients.

Dr. Kaiser:
I agree totally. For those of you who are interested, you can find out more about the specifics surrounding treatment of neovascular macular degeneration and macular edema secondary to retinal vein occlusion at EyeHealthAcademy.org/TimeIsVision.

As we conclude our talk today, Dante, what is your key take-home message for our listeners?

Dr. Pieramici:
I think when you're looking at the macular degeneration patient, couple of things to look for. One, do they have large drusen greater than 125 microns? Do they have RP pigmentary changes? If they have either of those, then they're an intermediate AMD patient. We need to follow them more closely. And then, looking, do you see hemorrhage in the eye or fluid in the eye, or do you start to see areas of geographic atrophy, because those are patients, certainly, that we want to get in. For the neovascular patients, there's treatment. For the GA patients, there's probably going to be treatment soon, and there's certainly a lot of clinical work being done that they might be eligible for. So, you know, timely referral is important, and if you're not sure, we're always happy, as retina specialists, to see these patients and determine whether or not treatment is needed.

Dr. Kaiser:
Thanks for those points there, Dante. When I think about key points for a retinal vein occlusion, I really think if you have a patient who comes in with a sudden decrease in vision and you do a clinical exam and start to see hemorrhages, really look at the pattern of those hemorrhages. If it's a pie-shaped pattern, start thinking branch vein occlusion. If the hemorrhages are all over the place, in all quadrants, start to think of a central retinal vein occlusion.

And the other thing to really think about is hemorrhages from vein occlusion are usually in the inner retina, whereas hemorrhages from macular degeneration are in the outer retina or even in the subretinal space, so really try to figure out the level of the hemorrhages. And if you're unsure of where the hemorrhages are, please refer that patient to a retinal specialist.

So thank you so much for joining me today, Dante, and providing such valuable insight into the pathologic features between macular degeneration and retinal vein occlusion. It was absolutely a pleasure having you join us.

Dr. Pieramici:
The pleasure was mine, Peter. I hope this is helpful for folks.

Annnouncer:
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