Supplement to October 2019

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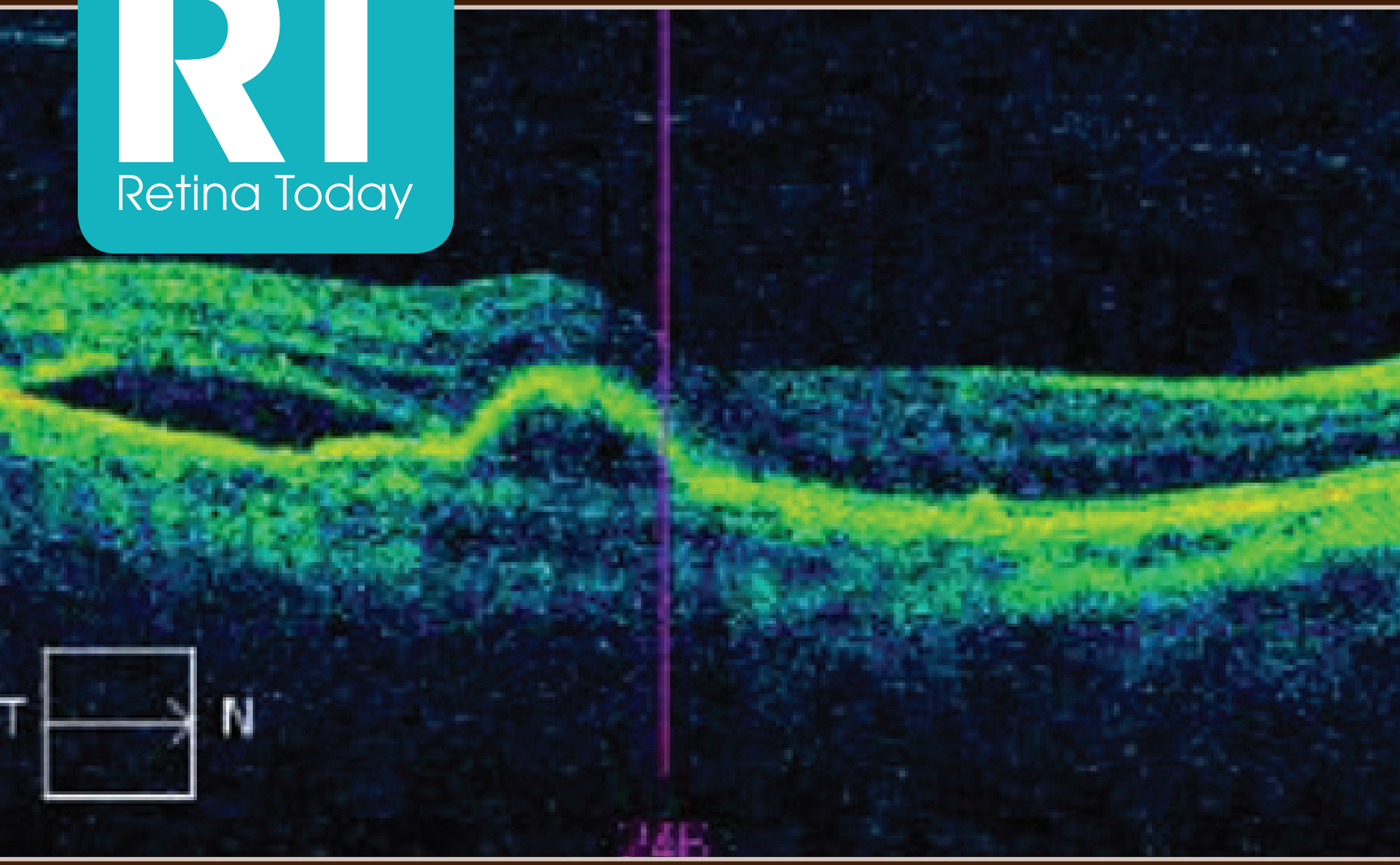

The Role of Imaging in the Diagnosis and Monitoring of Wet AMD: Expert Insights

PART TWO OF TWO: ONGOING MONITORING AND FOLLOW-UP

Rishi P. Singh, MD, Moderator • Michael Singer, MD • Jeffrey S. Heier, MD • Nancy M. Holekamp, MD

The Role of Imaging in the Diagnosis and Monitoring of Wet AMD: Expert Insights

Part Two of Two: Ongoing Monitoring and Follow-up

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The faculty were paid by Novartis Pharmaceuticals Corporation to participate in this supplement.

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Introduction

The leading cause of blindness in the developed world is age-related macular degeneration (AMD).[1] Advanced AMD occurs in two forms: dry AMD, also known as geographic atrophy, and neovascular or wet AMD.[2,3]

Improvements in retinal imaging technology in recent years have enabled significant advances in wet AMD diagnosis and the detection of morphologic biomarkers of disease progression. Imaging techniques comprise an important part of a retinal specialist's everyday clinical practice.

This roundtable gathered a panel of leading retina specialists to discuss the current use of imaging in the management of wet AMD, including the different imaging modalities currently available and their impact on diagnosis, and to provide insights into the role of imaging for clinical decision-making. Personal perspectives and clinical pearls were shared through the presentation of patient cases submitted by the retina specialists.

The resulting discussions will be published in two parts, with this, the second part, focusing on ongoing follow-up and monitoring in patients diagnosed with wet AMD.

Burden for the Patient With Wet AMD

Rishi P. Singh, MD: We know that the loss of vision caused by wet AMD has negative effects on patients' independence, productivity, and quality of life.[4] Compared with age-matched peers, more patients with AMD demonstrate symptoms of depression.[5] What do your patients talk to you about most with regard to the burden of wet AMD?

Michael Singer, MD: Patients talk to me about the need for frequent regular visits, and, depending on the patient, the need for someone else to come in with them. Also, in terms of lifestyle concerns, my patients are most worried about losing the ability to drive.

Jeffrey S. Heier, MD: For my patients, it's having to come in regularly and almost always having to be accompanied by a family member or caregiver. That burden is often hard to overcome.

Nancy M. Holekamp, MD: The burden of losing your vision is very scary to my patients. Many of them don't fully understand that macular degeneration rarely, if ever, makes you completely blind. I'm continually reassuring people that, as bad as this disease gets, they can usually maintain some level of independence. But my patients with advanced macular degeneration need constant reassurance about that.

Dr. Singh: My patients are typically concerned about driving ability and maintaining independence in their own lives.

Monitoring Disease Activity in Wet AMD

Dr. Singh: The definition of disease activity in wet AMD has traditionally been based upon three parameters: a loss of ≥ 5 letters in VA, evidence of new hemorrhage, and the presence of intra- and subretinal fluid as seen on OCT.[6] What do you look for in your patients in terms of monitoring for disease activity during follow-up?

Dr. Singer: Initially, I look at the overall amount of fluid and then evaluate whether the fluid is intraretinal or subretinal. I look at OCT volume scans to see if the overall fluid volume has changed. In addition, I also stress to my patients the importance of coming to see me at the correct intervals, as patients who come back to the clinic after their scheduled follow up appointment may end up losing vision in the long term.

Dr. Heier: To me, it's not just about vision; it's about vision and anatomy. In some cases, I just have to tolerate a certain level of fluid that's never going to go away.

Dr. Holekamp: Even though we call it wet AMD, and we consider it one disease, it's not the same disease in every patient. In fact, it can be a very different disease in two eyes of the same patient. I have to see someone frequently in order to figure out how the disease is manifesting in their eye.

Dr. Singh: I look at the global perspective of where the patient started and compare that with where they are now. I look at the central subfield over time and see if there are changes as a result of disease activity.

Retinal Fluid in Wet AMD

Dr. Singh: As we've just been discussing, the presence of retinal fluid, including intraretinal fluid, subretinal fluid, and sub-retinal pigment epithelium (RPE), is a standard marker of disease activity in wet AMD.[4,6,7] However, are we making too much out of these different fluid compartments? Or do they really resonate to you with regard to your patients?

Dr. Heier: I take the presence of any fluid seriously, but I have found that many patients can have chronic subretinal fluid and still have outstanding vision. In contrast, there aren't many patients who have chronic intraretinal fluid and have outstanding vision, so I worry more about intraretinal fluid in terms of the ultimate prognosis. My strategies for persistent subretinal fluid are probably less stringent than those for persistent intraretinal fluid. There is a growing body of work demonstrating that such fluid can be well-tolerated and is compatible with good vision.

Dr. Holekamp: Intraretinal fluid may distort the normal anatomy, from which patients may not recover. In my opinion, sub-RPE fluid is the least damaging to vision because even when there is sub-RPE fluid present, there is still reasonable apposition of the photoreceptors to the RPE. We are also finding out that subretinal fluid isn't that damaging to vision: many patients with persistent subretinal fluid have good vision. In my experience, persistent long-term fluid is most likely to be subretinal.

Dr. Singh: The recent FLUID study investigated whether patients can tolerate a small amount of subretinal fluid with no adverse effect on visual outcome.[6] Do you tolerate a little fluid in your patients in your practice, or do you have zero tolerance for subretinal fluid?

Dr. Holekamp: The FLUID study is influencing our ideas about retinal fluid. If a patient has persistent intraretinal fluid after 1 year of follow-up, I might do additional imaging at that time. I feel optimistic for the patient if it's subretinal fluid, because we know that persistent subretinal fluid is compatible with good long-term vision. I think the FLUID study and other post-hoc subgroup analyses show that subretinal fluid may be of a different nature compared to fluid in other compartments.

Practical Aspects of Imaging During Ongoing Follow-up

Dr. Singh: When patients attend appointments at different offices, how do you compare OCT scans in order to assess disease activity and progression?

Dr. Heier: I like to have registered volume scans, so I can show two scans on top of one another and do a point-to-point comparison of the scan taken that day with a previous scan. I'm fortunate in that I'm in the same office 5 days a week, so I'm always comparing scans from the same machine. In this manner, patients can easily appreciate changes, both positive and negative.

Dr. Holekamp: I have two different offices with two different machines. It's usually most convenient to have patients keep going to the same office, as otherwise I have to compare two different modalities. Fortunately, all the modalities are good at showing the presence or absence of fluid. Doing a direct comparison between two different machines is a little difficult, but simply knowing if there is fluid or not is not that challenging.

Dr. Singh: Is it your routine practice to perform bilateral OCT?

Dr. Holekamp: Yes, we look carefully at the asymptomatic fellow eye at every visit because we know the high likelihood of developing wet AMD in the second eye.

Dr. Heier: This is something we've recently been discussing in our practice. All OCTs are now a bilateral code, with reimbursement being the same for one or both eyes. Since it's not costing the patient more, why not get scans of both eyes?

Dr. Singer: It doesn't take too many of those cases where you suddenly find an asymptomatic fellow eye with signs of wet AMD to make you want to do bilateral OCT.

Dr. Singh: Considering OCT angiography (OCT-A), what are your recommendations for achieving good images?

Dr. Heier: We use both 3-mm and 6-mm scan protocols. However, the way in which we interpret them is evolving. We used to look at the *en face* images in order to visualize the neovascular complex. Now, we often look at the flow patterns within them. It's a very interesting modality with very important information to be gleaned, but we're still just learning how to use and interpret it.

Dr. Singh: Beyond OCT, what, if anything, do you use with regard to imaging modalities in the ongoing follow-up period?

Dr. Singer: If patients are showing unexplained decreased vision without OCT changes, I'll also repeat fluorescein angiography and compare the results to my baseline images to see how conditions have changed and if there is still active leakage.

Case 1: Follow-up of a Typical Patient With Wet AMD

Nancy M. Holekamp, MD

Case overview:

- A 70-year-old white female presented with a BCVA of 20/40 in the right eye.
- Color fundus photography revealed a lesion superior to the fovea with no hemorrhage, and discoloration suggesting subretinal fluid (Figure 1).
- OCT revealed subretinal fluid, which was not directly subfoveal, hence the good baseline vision (Figure 2).
- Fluorescein angiography (FA) revealed disruption of the retinal pigment epithelium (RPE) (Figure 3).

Follow-up:

- At 1 year, OCT showed good resolution of fluid (Figure 4), and FA confirmed staining rather than leakage (Figure 5).

Discussion:

Nancy M. Holekamp, MD: As a result of the findings at presentation I was convinced that this patient had wet AMD. The lesion looked classic, being small, well-defined, with leakage, and associated with some RPE disruptions.

Rishi P. Singh, MD: Could it be minimally classic? There's a larger component that seems like it might be occult.

Dr. Holekamp: There could be a part of a larger component inferiorly. It could be minimally classic with just a portion of it showing superiorly, in which case the lesion would go through the fovea.

After 1 year, the patient's fellow eye developed wet AMD, and while I was taking a baseline FA for that eye, I performed a

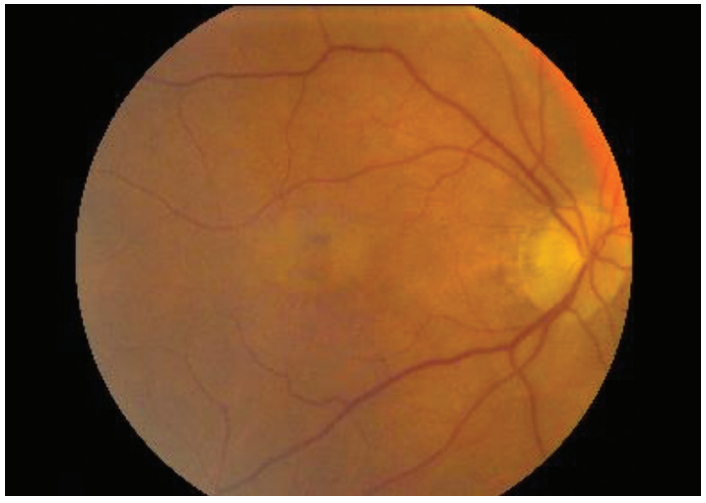

Figure 1. Color fundus photograph at presentation.

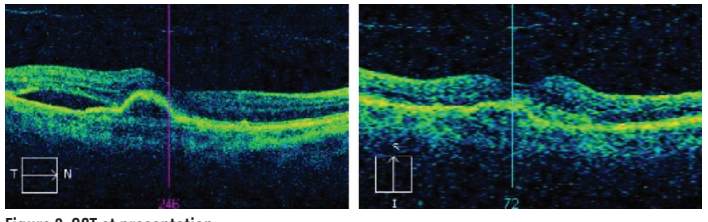

Figure 2. OCT at presentation.

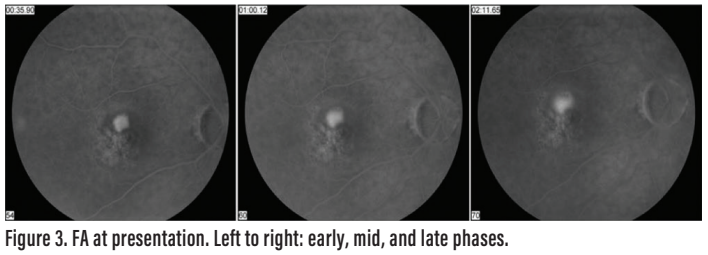

Figure 3. FA at presentation. Left to right: early, mid, and late phases.

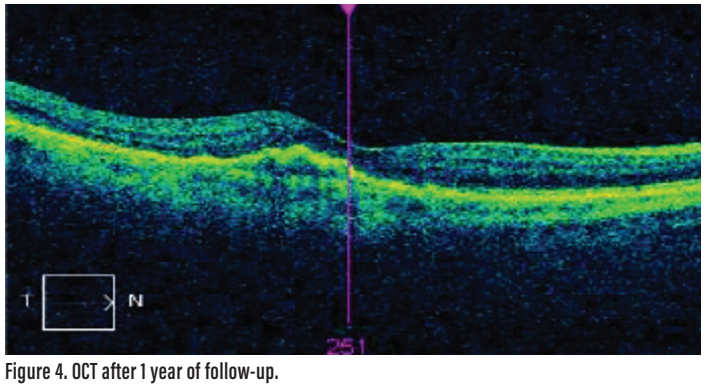

Figure 4. OCT after 1 year of follow-up.

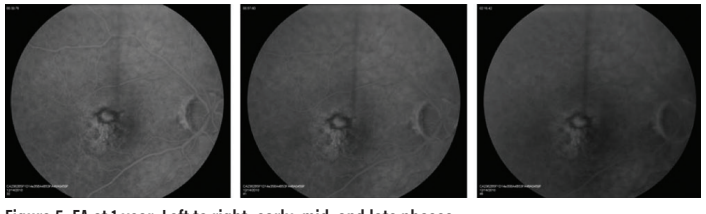

Figure 5. FA at 1 year. Left to right: early, mid, and late phases.

follow-up FA on the first eye, as well as OCT. While the average person doesn't show up in our offices every day, this is a good example of the average case of what we hope to see in our wet AMD patients during follow-up, as well as highlighting the importance of monitoring the asymptomatic eye.

Case 2: Use of OCT Angiography to Confirm Wet AMD

Jeffrey S. Heier, MD

Case overview:

- The patient presented with dry age-related macular degeneration (AMD) and a BCVA of 20/20 in the left eye (Figure 1).

Follow-up:

- After 2 years of follow-up, the patient converted to wet AMD. BCVA was still 20/20, but confluent drusen were visible in the fovea, and subretinal fluid was present (Figure 2).
- After a further year of follow-up, BCVA remained at 20/20, but subretinal fluid was persistent or worsening (Figure 3).
- OCT angiography (OCT-A) confirmed the presence of a neovascular complex (Figure 4).

Discussion:

Jeffrey S. Heier, MD: In this case, the patient had persistent subretinal fluid during follow-up which seemed to wax and wane. This made us wonder what was going on, as it demonstrated components of a central serous type picture, but with drusen present as well. The OCT-A clearly showed a neovascular complex on the upper left, which gave us confidence that we were correct in our

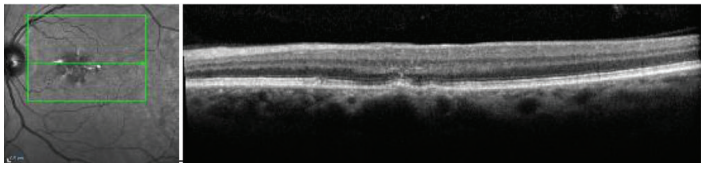

Figure 1. OCT at presentation showing dry AMD.

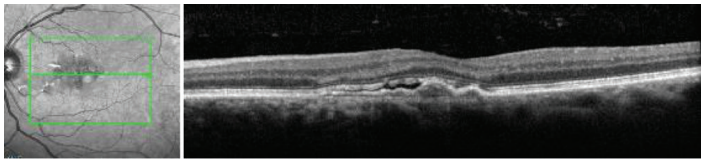

Figure 2. OCT after 2 years of follow-up showing conversion to wet AMD.

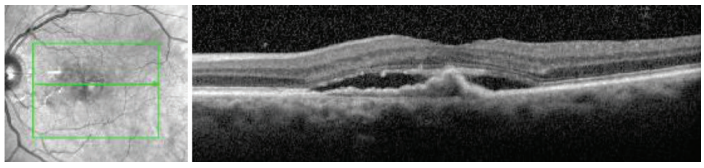

Figure 3. OCT after 3 years of follow-up showing persistent subretinal fluid.

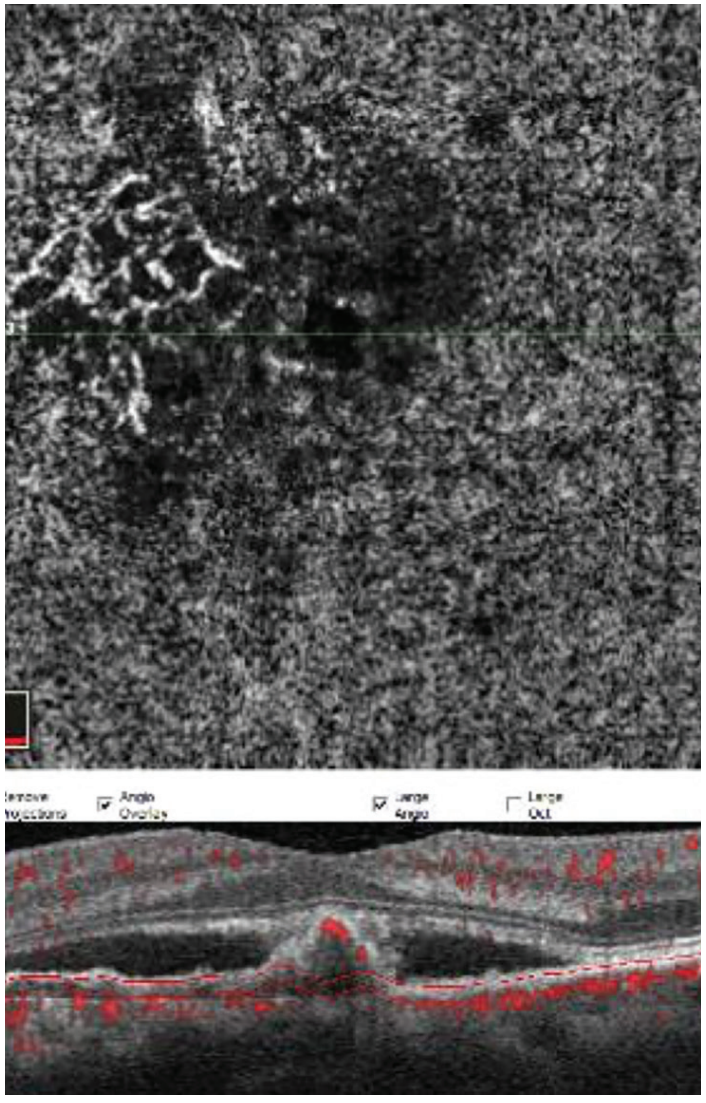

Figure 4. OCT angiography at 3 years.

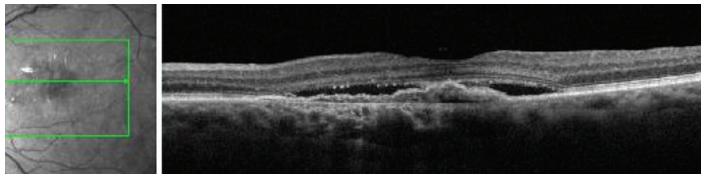

Figure 5. OCT showing long-term follow-up.

belief that we were dealing with a neovascular process. This patient has subsequently maintained very good vision (Figure 5).

Rishi P. Singh, MD: This is a great case because it demonstrates the fluid compartment issue. This patient has predominantly subretinal fluid, which persists throughout follow-up, yet there are other components of fluid in the initial image that are not present in later images, and the patient has an excellent visual outcome.

Case 3: Wet AMD With Stable Residual Fluid

Michael Singer, MD

Case overview:

- An 85-year-old male who had been followed for wet age-related macular degeneration (AMD) for several years presented with a BCVA of 20/40 in the left eye.
- OCT showed persistent, predominantly subretinal fluid (Figure 1).
- Fluorescein angiography (FA) showed leakage (Figure 2).

Follow-up:

- At 8 months, BCVA was 20/40. OCT showed improvements, but persistent subretinal fluid remained (Figure 3), and FA showed residual disease activity, with a 'hot' central area (Figure 4).

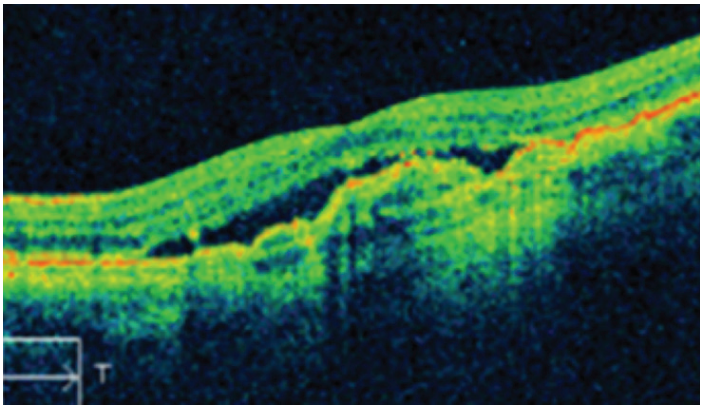

Figure 1. OCT at presentation.

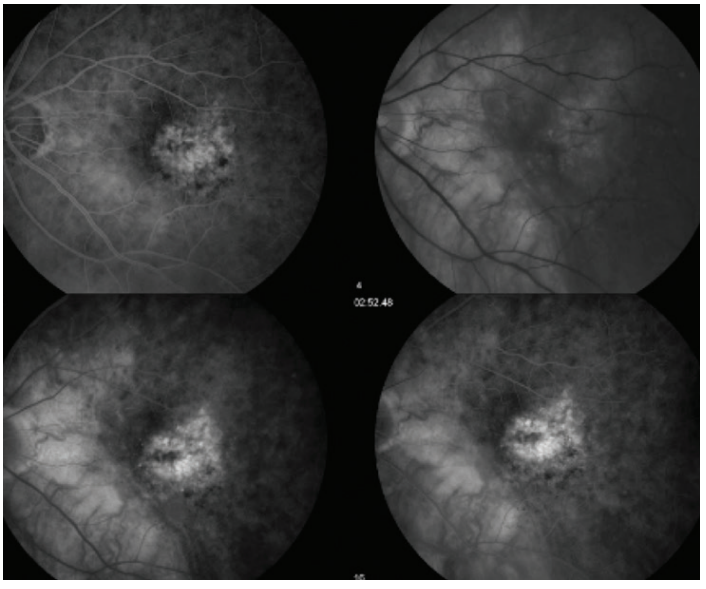

Figure 2. FA at presentation.

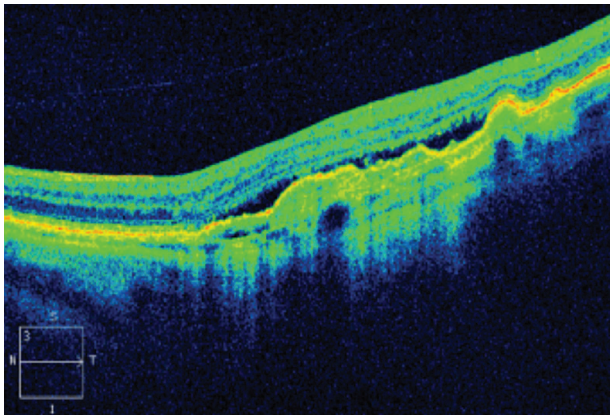

Figure 3. OCT at 8 months.

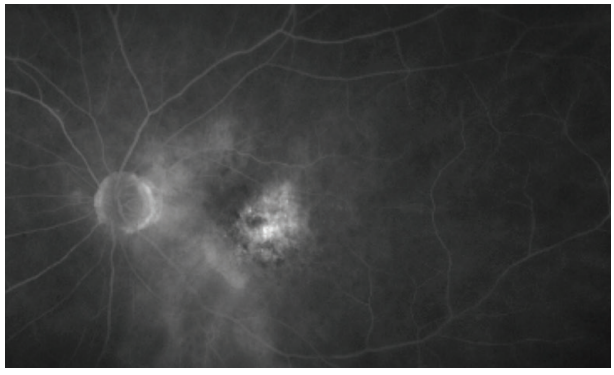

Figure 4. FA at 8 months.

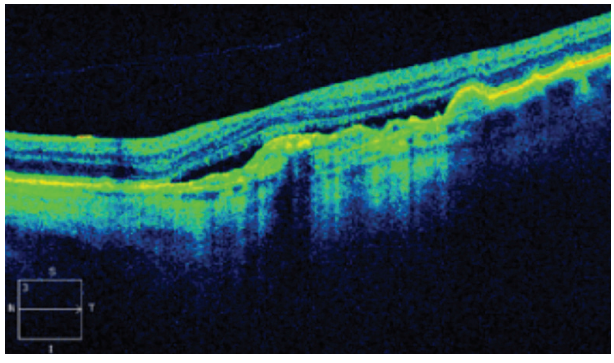

Figure 5. OCT at 24 months.

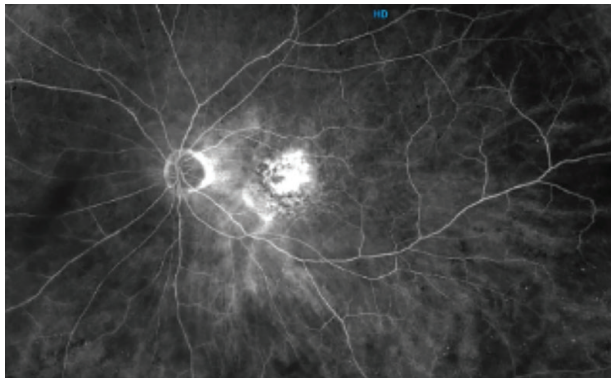

Figure 6. FA at 24 months.

Discussion:

Michael Singer, MD: At 8 months, FA showed an area right in the middle that was still hot, so I thought there was still some disease activity, but while there was staining, it wasn't leaking much. I continued treating this patient for 16 months. During this time the patient remained stable, with persistent fluid but no significant change on OCT or worsening of vision (Figures 5 and 6).

Jeffrey S. Heier, MD: In these chronic patients, I find that FA is often not helpful, due to staining and scarring. It becomes hard for me to really tell what is actually active disease and what isn't.

Case 4: Progressive Macular Atrophy With Persistent Fluid

Rishi P. Singh, MD

Case overview:

- An 82-year-old female presented with dry age-related macular degeneration (AMD) and a BCVA of 20/25 in both eyes.
- OCT showed a small amount of intraretinal fluid in the right eye and no significant fluid in the left eye (Figure 1).
- Infrared (IR) imaging showed macular atrophy in both eyes, with a greater degree of atrophy in the right eye (Figure 2).

Follow-up:

After 4 years, vision was reduced to 20/50-1 in the right eye and 20/40+1 in the left eye, despite therapy. OCT showed residual intraretinal fluid (Figure 3) and fluorescein angiography (FA) (not shown) revealed leakage.

IR imaging showed that atrophy progressed over time in both eyes (Figure 2).

Vision continued to deteriorate over time to counting fingers at 3 feet in the right eye and 20/50 in the left eye at 7 years, though OCT still showed limited fluid present (Figure 4).

Discussion:

Rishi P. Singh, MD: I use the words macular atrophy in the setting of wet AMD instead of geographic atrophy because we think that there's a difference in the pathogenesis and the progression rates between the two types of atrophy.

In this case, the fact that the patient continues to have leakage on the angiogram while there was little activity visible on the OCT image illustrates the disconnect that can sometimes occur between OCT and what can be seen on the FA. Since we didn't see any changes in fluid over time and were concerned about the progressing atrophy, we opted primarily to observe the patient from 4 years onward, although the FA still manifested some mild leakage. The atrophy continued, resulting in severe photoreceptor loss; as a result, the patient's vision deteriorated until she had only counting fingers vision in the right eye.

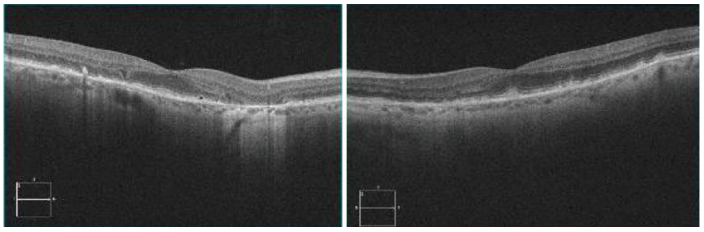

Figure 1. OCT at presentation.

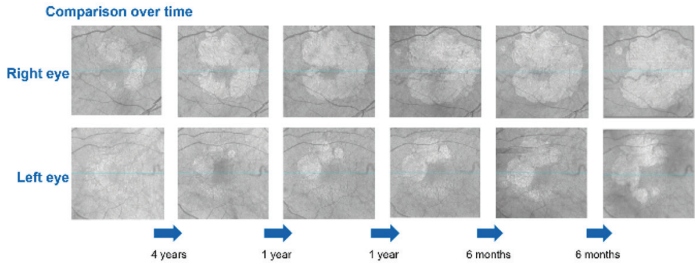

Figure 2. IR imaging showing progression of atrophy over time.

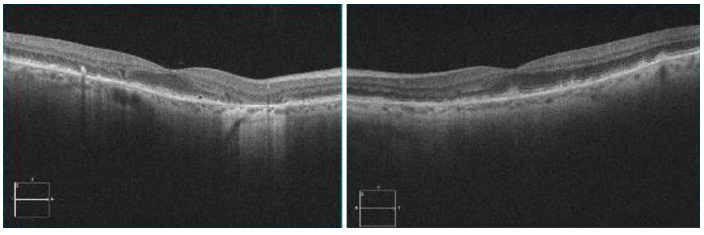

Figure 3. OCT at 4 years.

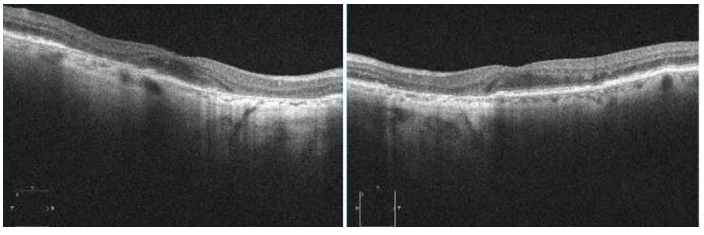

Figure 4. OCT at 7 years.

Jeffrey S. Heier, MD: This is where OCT-angiography (OCT-A) might be interesting, because with OCT-A you may actually see a neovascular complex at least.

Dr. Singh: Yes; this case was from the days before OCT-A, unfortunately.

Nancy M. Holekamp, MD: This looks like the natural history of geographic atrophy along with AMD to me, due to the asymmetric time course where the right eye is certainly more advanced than the left eye. But at the last frame, there is some symmetry.

Conclusion

Dr. Singh: Thank you all for joining me today to discuss the burden of disease in nAMD, the importance of monitoring our patients, and the practical aspects of imaging during ongoing follow-up. What are your key takeaways from our discussion?

Dr. Singer: The monitoring of wet AMD has to be individualized to the patient, as every patient's disease is different.

Dr. Heier: Patients with persistent subretinal fluid can still have excellent vision. When it comes to monitoring a patient, I focus on the anatomy as well as the VA.

Dr. Holekamp: Always be aware of the high likelihood of developing wet AMD in the second eye. It's good patient care to always look at the fellow eye as closely as you look at the eye with active disease.

Dr. Singh: From 2005 until today, we have learned a great deal about morphology: which parameters matter and which don't matter; what are prognostic factors and what are not. Now, more than ever before, I think we are able to individualize clinical practice based upon some of those factors because we have really good data available to enable us to determine what really matters for our patients. ■

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HRT-1377309 Retina Today Roundtable Supplement - Part 2 October 2019

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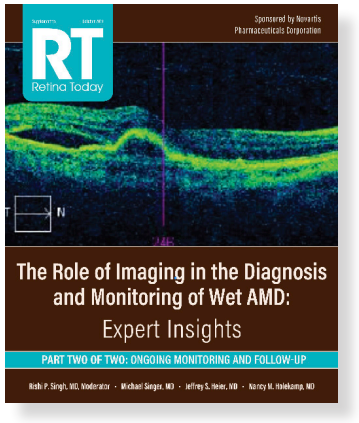
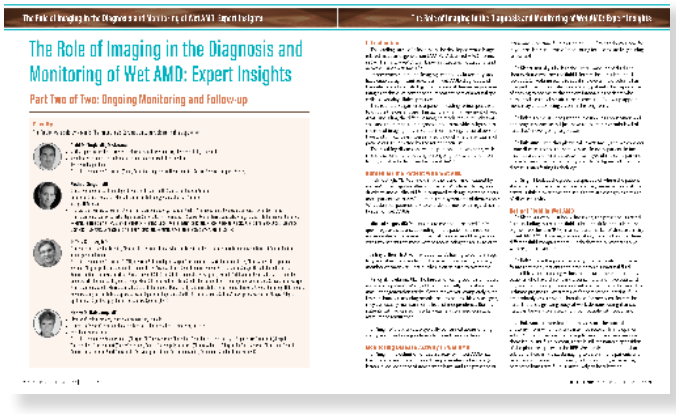
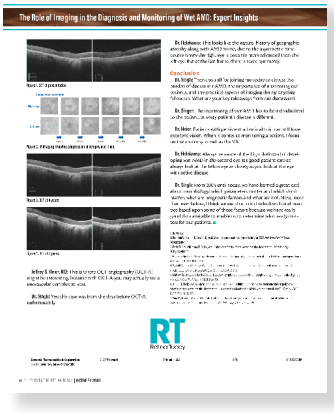


Front Cover (9 x 10.75 inches)



Interior Spread (18 x 10.75 inches)
Pages 2-7



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