BY IVAN J. SUNER, MD

Taking a Broader View of Diabetic Macular Edema

How ultra-widefield angiography is changing diagnostic and therapeutic approaches to DME.

When initiating therapy for clinically significant diabetic macular edema, we typically start with focal or grid laser treatments. If unsuccessful, we usually progress to pharmacologic therapy with corticosteroids or vascular endothelial growth factor (VEGF) inhibitors. If the problem persists, we may perform a vitrectomy with or without membrane peeling. Regardless of the intervention algorithm we ultimately settle on, this type of "cookbook" approach may not be practical or targeted to the underlying etiology of each patient's macular edema.

With the emergence of sophisticated and elegant imaging technologies, we are better equipped to classify the etiologies of diabetic macular edema into traction on the retina, focal vascular leakage, inflammatory and cellular swelling, peripheral nonperfusion and ischemia. It stands to reason that different treatments are required for these different causes.

The emergence of ultra-widefield angiography shows more clearly than ever why we need to classify patients better and customize treatments to address varying causes. Here, I will discuss how we have used this new technology to achieve these goals.

COMPARING TREATMENTS

Based on the DRCR.net results, we know that using the macular laser has been fairly effective, at least in a trial comparing the laser to corticosteroid therapy.[1] The laser treatment offers durability, safety and effectiveness. When that approach fails, and we need to decide between corticosteroids and anti-VEGF therapy, the choice can pose a considerable challenge. We must consider factors such as presence of glaucoma, cataracts or history of cardiovascular disease. We must acknowledge and anticipate that patients will respond differently to these treatments. The critical piece is determining which treatment will succeed, thereby sparing patients unnecessary injections and complication risks.

The ultra-widefield imaging technology can help provide the answers we are seeking by complementing what we see clinically. Just as optical coherence tomography (OCT) helped us better diagnose and distinguish various pathologies, this technology is helping us discern the manifestations of different types of diabetic patients, enabling us to treat with the latest in targeted, alternative therapies.[2]

For these reasons, the OCT and ultra-widefield angiography have become a starting point for me when I am caring for diabetic patients with macular edema. The information I obtain helps me offer treatment recommendations and better educate patients.

SPECIFIC CASES

Some of the treatments that are more clearly indicated by the use of this instrument include:

- Macular laser, possibly complimented by an intravitreal corticosteroid and anti-VEGF, for discrete areas of leakage (**Figure 1**)
- Vitrectomy for retinal traction (**Figure 2**)
- Laser and anti-VEGF for nonperfusion/ischemia, (**Figure 3**), which may have been treated unnecessarily with vitrectomy surgery before the introduction of ultra-widefield angiography.

When selecting treatments in the past, we typically have relied on a montage of images, representing photographs from different temporal sequences, instead of a dynamic study. Now, using the maximum resolution modality of this new instrument, we can flip the view back and forth from the macula to the ultra-widefield image, capturing a brush-

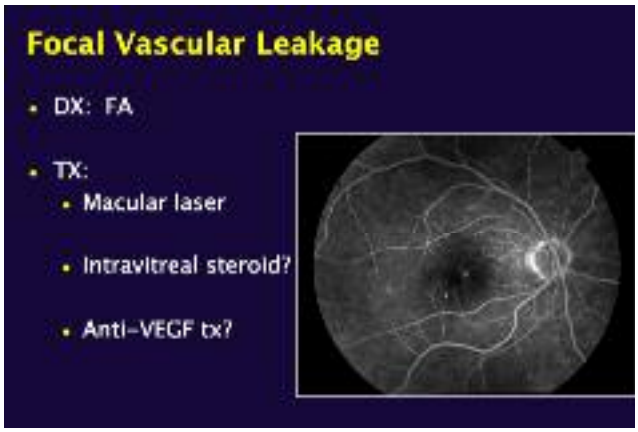

Figure 1. Fluoroscein angiography is used to diagnose and plan a treatment course for focal vascular leakage.

Figure 2. OCT is used to diagnose and treat retinal traction.

guide treatment. In our paradigm, we postulate that a significant component of the macular edema is the result of VEGF is causing vascular permeability in the macula. It makes sense in this case to focus on the ischemic component of the disease by using an antagonist to block existing VEGF and ablating the peripheral areas of ischemia to shut down VEGF production.

This will give us durability and immediately dry the macula, suppressing the permeability of the vasculature. In our practice, I have found that 20% to 30% of our patients have some component of peripheral nonperfusion, which we classify by using OCT and ultra-widefield angiography.

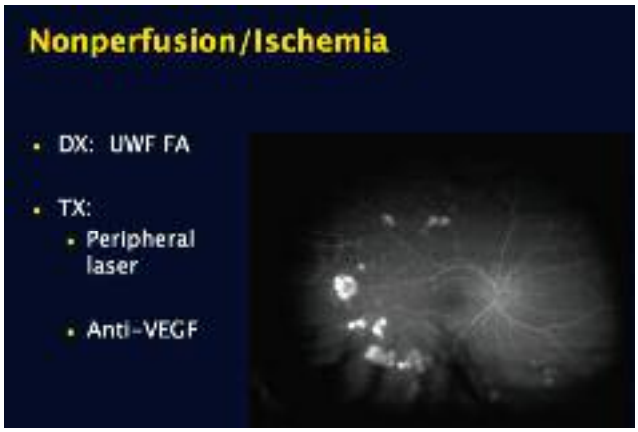

Figure 3. Ultra-widefield angiography helps us see that laser and anti-VEGF treatment may be sufficient to treat this case of nonperfusion/ischemia.

We are evaluating treatment of patients with diabetic macular edema associated with predominantly peripheral nonperfusion in a randomized, prospective, single-center pilot trial.

In the treatment, patients are receiving peripheral laser treatment and pharmacotherapy with ranibizumab (Lucentis, Genentech). We are using an ultra-widefield widefield angiography-guided laser treatment to target peripheral areas of nonperfusion. We are trying to straddle some of the healthy part of the retina and getting that brushfire edge within our range of therapy. This is intended to block VEGF production. Another goal is to enhance durability of the laser therapy while providing immediate relief of the diabetic macular edema.

In the control group, we are performing conventional macular laser in conjunction with intravitreal triamcinolone acetonide.

BILATERAL MACULAR EDEMA CASE

One patient had bilateral macular edema. He was randomized to a different therapy for each eye. The left eye, receiving conventional therapy, began with a wet-looking

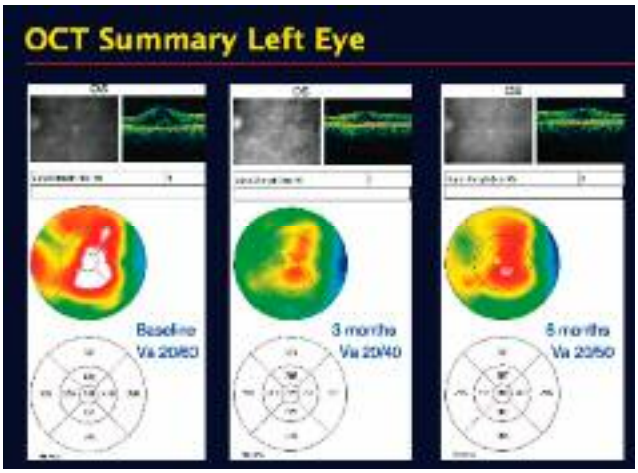

Figure 4. OCT shows a typical cycle of improvement and relapse in a patient with bilateral macular edema.

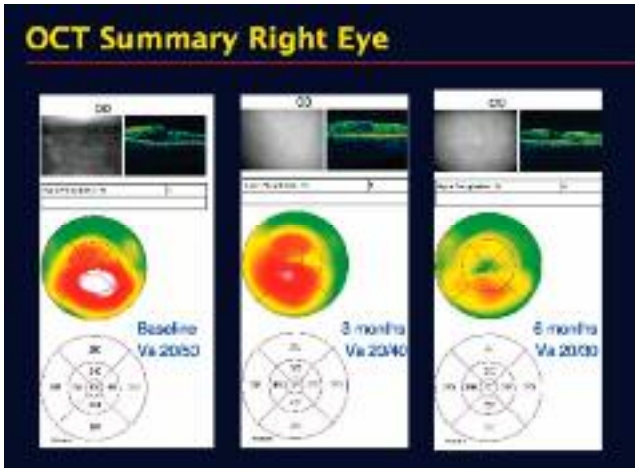

Figure 5. Combining conventional macular laser and intravitreal triamcinolone shows promise for treating bilateral macular edema.

macula at 20/60. The macular laser and the corticosteroid produced some response, improving his vision to 20/40 at 3 months, but then we saw recurrence at 6 months, when his vision dropped to 20/50. (**Figure 4**) This is a typical cycle of improvement and relapse for patients undergoing this regimen.

The right eye began at 20/50 and responded to 20/40 at 3 months. After 6 months, we saw continuing improvement to 20/30 (**Figure 5**). This is just one patient, obviously, but the findings illustrate how we are striving to achieve durability, as well as effectiveness, with more advanced combinations.

As I mentioned, we are straddling some of the perfused retina while trying to cover that brushfire and nonperfusion. Are we going out far enough? We do not know at this point. Some patients have returned with leakage, but usually in spots within the laser treatment area, perhaps indicating more treatment is needed. We have not extended treatment to the periphery, unless we have found proliferation as well.

STEADY GAINS

With ultra-widefield angiography, we believe we can improve treatment of diabetic macular edema, using the peripheral laser, the effects of which we can monitor better, and the mixed use of treatments, including anti-VEGF therapy. Most significantly, we can monitor revascularization or continued dropout of vessels from anti-VEGF.

We also have the opportunity to watch for vascular occlusions involving tumors and other types kinds of diseases — uveitis, for example — as we use this instrument to complement the diagnostic capabilities of OCT. This evolving approach will provide multiple levels of objective measurements over time. RP

Dr. Suñer is in private practice at Retina Associates of Florida in Tampa.

References

1. Diabetic Retinopathy Clinical Research Network. A randomized trial comparing intravitreal triamcinolone acetonide and focal/grid photocoagulation for diabetic macular edema. *Ophthalmology*. 2008;115:1447-1449, and 1449:e1-10.
2. Kumar V, Ghosh B, Raina UK, Goel N. Comparative therapy evaluation of intravitreal bevacizumab and triamcinolone acetonide on persistent diffuse diabetic macular edema. *Am J Ophthalmol*. 2008;146:974.
3. Friberg TR, Gupta A, Yu J, Huang L, Suner I, Puliafito CA, Schwartz SD. Ultrawide angle fluosrescein angiographic imaging: a comparison to conventional digital acquisition systems. *Ophthalmic Surg Lasers Imaging*. 2008;39:304-311.