

DME RESOURCE CENTER: BEYOND THE CLINICAL TRIALS

An educational series on managing the ocular manifestations of diabetes in real-world settings.

Diabetic eye disease is a group of conditions that includes diabetic retinopathy (DR) and diabetic macular edema (DME). DR is the most common reason for vision loss in people with diabetes; DME is a consequence of DR characterized by swelling in the macula and blurred vision. In 2010, an estimated 285 million people worldwide had diabetes, and a third of these individuals had signs of DR.¹ Another third of this population had signs of vision-threatening DR including DME.¹

Fortunately, early detection, timely treatment, and appropriate follow-up care of diabetic eye disease can prevent or delay vision loss. DR and DME can be detected with a comprehensive dilated eye exam that ideally involves the use of optical coherence tomography (OCT) and even OCT angiography. DR is not usually treated until it progresses to proliferative DR, in which case a retina specialist will treat with laser surgery or an anti-VEGF drug, or when DME occurs, in which case treatment consists of one or a combination of the following: anti-VEGF therapy, laser surgery, and corticosteroids.

The DME Resource Center (www.retinatoday.com/dme-resource-center) is a place to find videos in which retina specialists provide insights into the ever-changing landscape of DME management through their own patient cases. There are also articles, such as this one, that complement the videos, articles relevant to the subject matter that have appeared in previous issues of *Retina Today*, and related news. In Part 10 of the DME Resource Center print series, Andre Witkin, MD, an assistant professor at Tufts Medical Center, shares two cases in which he had to change his strategy for treating patients with DME.

1. Yau JW, Rogers SL, Kawasaki R, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care*. 2012;35(3):556-564.

Adventures in Treating Refractory DME

BY ANDRE J. WITKIN, MD



Diabetic macular edema (DME) is one of the leading causes of vision loss in individuals with diabetic retinopathy, and DME can occur in diabetic retinopathy of any severity. Over the past few years, drugs that target VEGF have become the mainstay for treatment of DME, as they have been shown

to improve visual acuity outcomes in the majority of patients with DME. However, some patients with DME continue to have persistent macular edema despite anti-VEGF injections, and alternative treatments may be helpful in treating these cases of refractory DME.

Treatment options for refractory DME include switching anti-VEGF agents, administering intravitreal corticosteroid medications, or performing focal laser treatment or pars plana vitrectomy (PPV) surgery. Patients with refractory DME can experience significant improvements in visual acuity with alternative treatment options, but treating DME that has been resistant to previous treatment attempts can take time, patience, and a willingness to switch one's approach. In this article, I review the details of two cases in which I needed to alter my treatment plan for patients with refractory DME.

PATIENT CASE NO. 1

A 67-year-old woman had long-standing proliferative diabetic retinopathy (PDR) and DME that had been treated with multiple rounds of panretinal photocoagulation and focal laser in the right eye (OD). The patient had also previously received six monthly injections of intravitreal bevacizumab (Avastin, Genentech) by a retina specialist at another center. When she presented to me, her

visual acuity was 20/400 OD, and she had dense macular edema associated with an epiretinal membrane (ERM) (Figure 1). Initially, I switched her to intravitreal aflibercept (Eylea, Regeneron), which was given monthly for 3 months.

After 3 months there was no change on optical coherence tomography (OCT); hard exudates were still visible, there was no change in macular thickening, and an ERM persisted (Figure 2). Additionally, the patient's visual acuity had not changed.

Based on these observations, I decided to switch her to the dexamethasone intravitreal implant 0.7 mg (Ozurdex, Allergan), which resulted in some improvement in macular edema 6 weeks after the first injection. The macular thickness map (Figure 3) showed a significant decrease in macular thickness, but her visual acuity improved only to 20/200. At this time, we discussed with

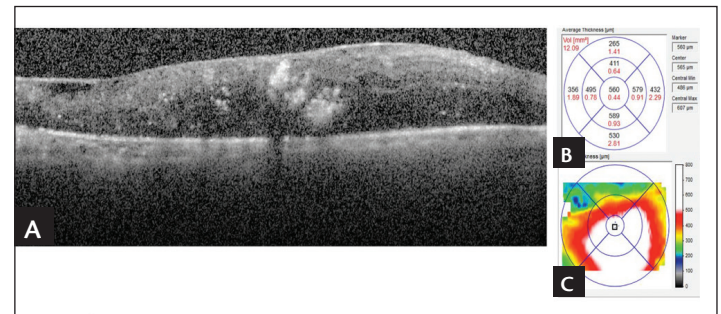


Figure 2. Case 1: The patient's OCT showed no change in macular edema despite three monthly aflibercept injections (A). Visual acuity remained 20/400. Central foveal thickness was 560 µm (B), and the contour map showed extensive macular edema (C).

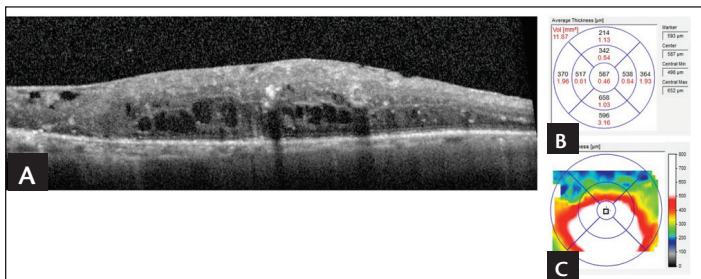


Figure 1. Case 1: The patient's OCT showed dense fovea-involving macular edema and an associated ERM (A). Visual acuity was 20/400 despite six monthly bevacizumab injections. Her central foveal thickness was 587 µm (B), and the macular map showed the extent of macular edema (C).

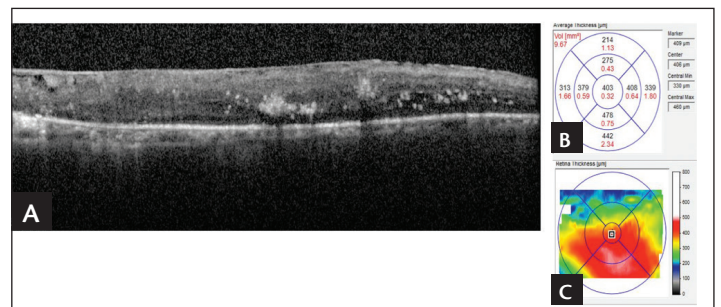


Figure 3. Case 1: The patient's OCT showed improved but persistent macular edema 6 weeks after intravitreal injection of a dexamethasone implant (A). Visual acuity improved slightly, to 20/200. Central foveal thickness improved to 403 µm (B), and the contour map showed improved but persistent diffuse macular edema (C).

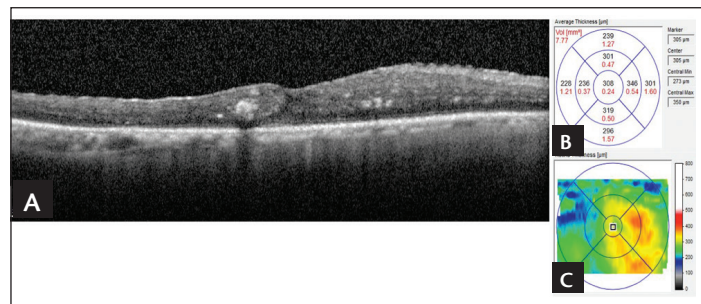


Figure 4. Case 1: The patient's OCT showed absence of the ERM 3 months after vitrectomy with membrane peeling (A). The foveal contour had become evident, and macular edema resolved. Visual acuity improved to 20/50 3 months after surgery. Central foveal thickness improved to 308 μm (B), and the contour map demonstrated that macular edema has almost completely resolved (C).

the patient the option of PPV surgery with membrane peeling, and she chose to proceed with surgery.

Six weeks after vitrectomy surgery, the patient's macular thickness map showed a significant decrease in macular thickness, and her visual acuity had improved to 20/80. The cross-sectional OCT scan showed a reappearance of normal foveal contour, and by 3 months after surgery her visual acuity had further improved to 20/50, her macular thickness had continued to decrease, and she had a much more normalized macular contour (Figure 4). The patient was extremely happy with the outcome, and over the next several months she did not require any additional injections. At her most recent visit, she continued to have good visual acuity.

PATIENT CASE NO. 2

A 43-year-old man with poorly controlled diabetes mellitus and no insurance presented with bilateral PDR and macular

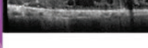
Watch the Video

Dr. Witkin explains the treatment approach for two patients with DME.



bit.ly/witkin0916

Case 1



- 67-year-old woman
- s/p 6 monthly bevacizumab, previous focal lesion
- VA = 20/400

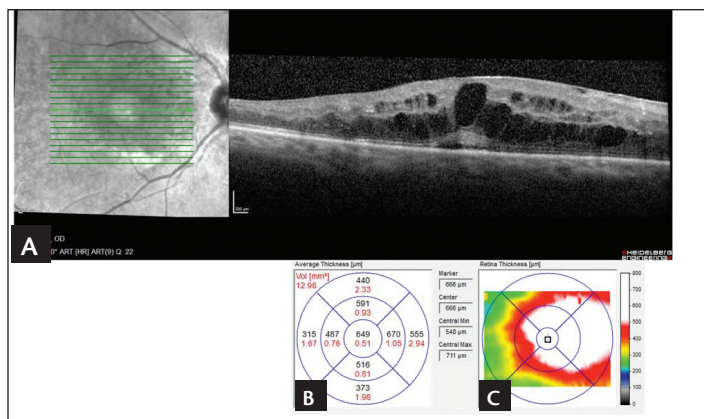


Figure 5. Case 2: The patient's OCT showed dense macular edema despite 4 months of intravitreal bevacizumab injections (A). Visual acuity was 20/80. Central foveal thickness was 649 μm (B), and the contour map showed diffuse macular edema (C).

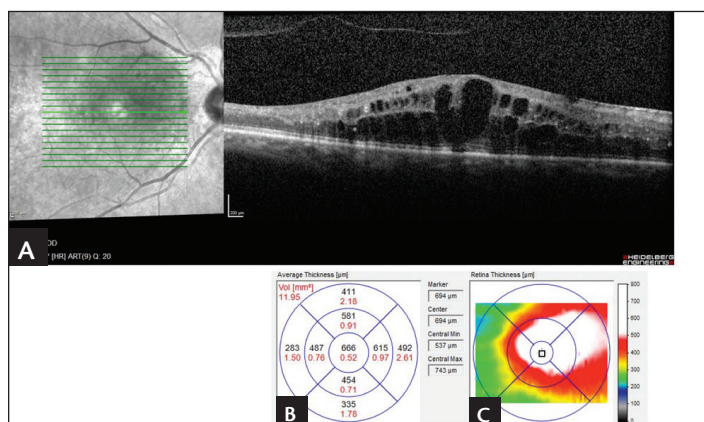


Figure 6. Case 2: The patient's OCT showed no change in macular edema 6 weeks after intravitreal injection of 2 mg triamcinolone (A). Visual acuity remained unchanged. Central foveal thickness was 666 μm (B), and the macular map showed persistent diffuse macular edema (C).

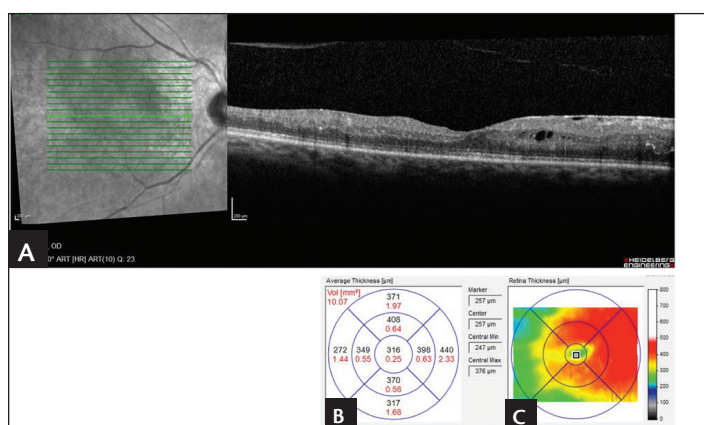


Figure 7. Case 2: The patient's OCT showed that macular edema had resolved 1 month after a single intravitreal injection of aflibercept (A). Visual acuity improved to 20/50. Central foveal thickness improved to 316 μ m (B), and the contour map showed much improved macular edema (C).

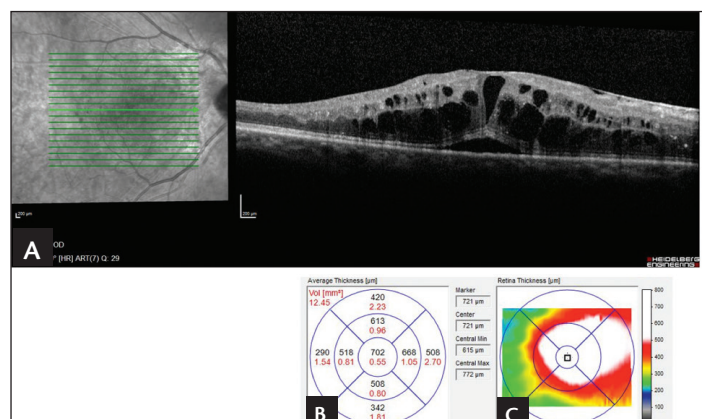


Figure 8. Case 2: The patient's OCT showed recurrent macular edema 1 month after switching back to intravitreal bevacizumab (A). Central foveal thickness increased to 702 μ m (B), and the contour map showed recurrent dense macular edema (C).

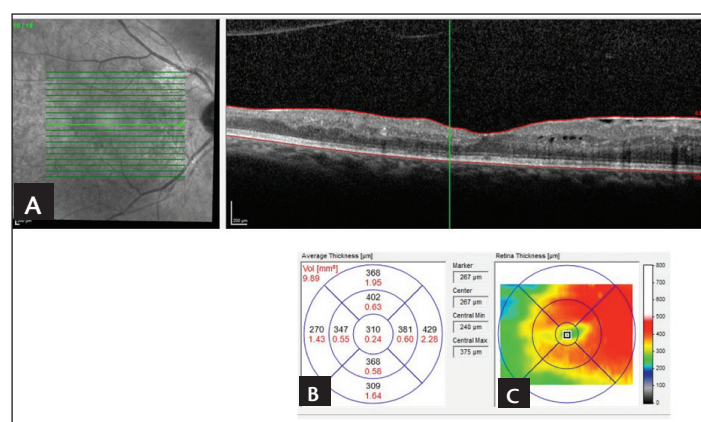


Figure 9. Case 2: The patient's OCT showed resolution of macular edema 1 month after switching back to intravitreal aflibercept (A). Central foveal thickness improved to 310 μ m (B), and the contour map showed that macular edema was much improved (C).

edema. Visual acuity OD was 20/80, and he had significant diffuse macular edema involving the fovea (Figure 5). He received an intravitreal injection of bevacizumab. After 1 month there was no change in macular thickness and no change in visual acuity.

Despite four additional monthly injections of bevacizumab, the patient's macular thickness remained unchanged. He had a slight improvement in visual acuity, although he did not report a change. We decided to switch medications, and I gave him an injection of intravitreal triamcinolone acetonide. One month later, there was still no change in macular thickness (Figure 6) or in visual acuity.

At this point, I decided to try injecting a sample of intravitreal aflibercept (Eylea, Regeneron), which produced a dramatic response 1 month after the first injection (Figure 7). Because the patient was uninsured, however, we switched him back to bevacizumab. One month later his macular edema recurred (Figure 8); there was a significant increase in thickness on the macular thickness map, and his visual acuity had also worsened. We gave him another free sample injection of aflibercept,

Although most patients with DME respond to anti-VEGF injections, some patients continue to have persistent macular edema and require alternative treatments. These patients may benefit from switching to another anti-VEGF agent or from use of intravitreal corticosteroid injections, focal laser treatment, or PPV with membrane peeling.

which resulted in complete resolution of his macular edema (Figure 9). His visual acuity improved to 20/30 OD, and he has continued to receive monthly free samples of aflibercept.

DISCUSSION AND CONCLUSION

Although most patients with DME respond to anti-VEGF injections, some patients continue to have persistent macular edema and require alternative treatments. These patients may benefit from switching to another anti-VEGF agent or from use of intravitreal corticosteroid injections, focal laser treatment, or PPV with membrane peeling. The first case presented here highlights the benefit of PPV with membrane peeling in some cases of DME when an ERM is visible; such patients may not require further intravitreal injections after surgery. The second case highlights an example in which switching from one anti-VEGF agent to another (bevacizumab to aflibercept) led to a drastic improvement in anatomy and visual acuity. ■

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