Because diabetes and complications related to the disease can cause damage to blood vessels in the retina, patients with diabetes are at increased risk for developing ocular complications. Diabetic retinopathy (DR) is the most common reason for vision loss in patients with diabetes. Diabetic macular edema (DME) is a consequence of DR characterized by swelling in the macula and blurred vision.

DR is not usually treated until it progresses to proliferative DR or when DME occurs. New treatments continue to emerge, adding to the armamentarium and promising to improve patient outcomes. How and when to use new and existing treatment options is not an exact science. In fact, physicians commonly differ in their approaches to managing patients with diabetic eye disease. Reviewing the patient cases of experienced retina specialists can provide helpful insights into treatment decisions for individual patients. That is where the DME Resource Center (www.retinatoday.com/dme-resource-center) comes in handy.

At the DME Resource Center, clinicians will find videos, articles, and news pertaining to the topic of treating patients with DR and DME. The DME Resource Center print series explores the evolving landscape of managing patients with DME through patient cases and the experiences of other retina specialists. In Part 11 of this series, Maria H. Berrocal, MD, an assistant professor in the department of ophthalmology at the University of Puerto Rico, details her management of three patients with DME.

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There are an estimated 30 million Americans with diabetes and more than 560,000 Americans with diabetic macular edema (DME). The pathogenesis of DME includes retinal capillary damage, disruption of the blood-retina barrier, and vascular leakage, which causes edema. VEGF inhibitors, although useful, target only one of the mediators of DME. Many systemic and local inflammatory cytokines also contribute to DME. The concentration of inflammatory factors correlates with disease activity.

EVALUATION AND DIAGNOSIS
Steroids and other antiinflammatory agents can be useful in the treatment of patients with DME. In the past, fluorescein angiography (FA) was the mainstay for diagnosis of patients with DME, but it is not useful in the assessment of response to treatment. It is not quantitative, but it is useful in the assessment of ischemia, nonperfusion, and associated neovascularization.

Optical coherence tomography (OCT) is the new gold standard for the management and follow-up of these patients. It is ideal for diagnosis, quantitative assessment, and determining response to treatment. It should be performed at every visit.

TREATMENT
The Diabetic Retinopathy Clinical Research Network’s Protocol I study showed that anti-VEGF agents are useful in the treatment of patients with DME. In that study, in 60% of eyes treated with ranibizumab (Lucentis, Genentech), visual acuity improved by 5 letters or more at 3 months, and the response at 1 year correlated with the response at 3 months.

However, this leaves 40% of eyes improving less than 5 letters with anti-VEGF treatment. What do we do with these patients? Other treatment options, namely steroids, laser, and vitrectomy, may be beneficial in this population. For this article, sterile treatment will be discussed in this context.

Using steroids in the treatment of patients with DME makes sense because this class of drug targets most of the inflammatory cytokines that play a significant role in the pathology of poorly controlled diabetes. We know that dexamethasone can reduce edema, capillary leakage, and fibrin deposition in DME; however, it has a short duration of action once inside the eye. The sustained-release dexamethasone intravitreal implant 0.7 mg (Ozurdex, Allergan) solves this issue.

In the MEAD study, after 3 years of treatment, eyes treated with the dexamethasone intravitreal implant 0.7 mg gained 15 letters or more of visual acuity at double the rate of those receiving sham treatment (19.5% vs. 10.7%). Steroids can be useful in eyes with DME that do not respond to VEGF inhibitors and/or that have significant inflammation (eg, in patients with long-standing DME, poorly controlled diabetes, or both diabetes and concomitant renal disease). Additionally, the treatment regimen with the durable steroid implant is less burdensome than that with injected anti-VEGF drugs. With the dexamethasone intravitreal implant 0.7 mg, patients can be treated every 4 to 6 months, rather than monthly or bimonthly.

There are certain cases (eg, vitrectomized eyes) in which treatment of patients with DME can be particularly challenging. In eyes that have undergone vitrectomy, the half-life of VEGF inhibitors is significantly reduced, making it necessary to administer injections at intervals shorter than 4 weeks. In some such cases, injections may be necessary every 2 weeks, which poses a significant burden to the patient and to the health
system. The dexamethasone intravitreal implant 0.7 mg is ideal for these eyes because its 4-to-6-month duration of effect is not affected by vitrectomy. Several cases that illustrate this point are discussed below.

**PATIENT CASES**

**Case No. 1**

A 57-year-old man with a 25-year history of poorly controlled insulin-dependent diabetes mellitus presented for treatment. At the first visit his HbA1c was 10%, and visual acuity was 20/400 in his right eye (OD) and 20/200 in the left (OS). He was treated with focal laser three times with no response and was then treated with bevacizumab (Avastin, Genentech) six times at 1-month intervals, also with no response (Figure 1).

The patient was treated four times OD with triamcinolone acetonide intravitreal injections at 6- to 10-week intervals. He showed some reduction of edema in response to this treatment approach but not complete resolution (Figure 2). Additionally, although his visual acuity improved to 20/200, the patient developed elevated intraocular pressure in response to the triamcinolone steroid treatment.

Next, treatment was initiated with the dexamethasone intravitreal implant 0.7 mg. After one injection, the patient’s visual acuity improved to 20/100, and OCT imaging revealed complete...
resolution of edema (Figure 3). His IOP is controlled with one glaucoma drop, and he continues to be treated with the dexamethasone intravitreal implant 0.7 mg every 4 to 5 months.

Case No. 2
This case profiles a patient with DME and proliferative diabetic retinopathy (PDR), a common combination. This 68-year-old woman has insulin-dependent diabetes mellitus of 35 years’ duration. She had been treated with laser panretinal photocoagulation (PRP) and focal laser therapy but showed no response. Her visual acuity was 20/400 despite treatment in the left eye, and multiple areas of capillary nonperfusion were evident on FA (Figure 4).

The patient received seven monthly injections of anti-VEGF therapy, but her visual acuity did not improve, remaining at 20/400. Her edema was also unchanged (Figure 5). She was then treated with the dexamethasone intravitreal implant 0.7 mg, and her visual acuity improved to 20/100. Both FA and OCT showed reduced edema (Figure 6).

Case No. 3
A 73-year-old woman presented with a 30-year history of diabetes mellitus with PDR and vitreous hemorrhage in the left eye. The patient underwent vitrectomy due to the vitreous hemorrhage, and her visual acuity improved to 20/200. Both FA and OCT showed significant edema in the vitrectomized eye (Figure 7). The patient’s edema had significantly decreased 2 months after the first injection of the dexamethasone intravitreal implant 0.7 mg (Figure 8).
was 3/200. FA showed significant edema in the area of the macula (Figure 7).

After the vitrectomy, four monthly injections of bevacizumab were administered, but no improvement in edema was noted. However, 2 months after receiving a dexamethasone intravitreal implant 0.7 mg, the patient’s visual acuity had improved to 20/400 and the edema had significantly decreased (Figure 8).

CONCLUSION

Anti-VEGF therapy is typically the first line of treatment for patients with DME, but this approach does not target inflammatory cytokines. Furthermore, as many as 40% of eyes show minimal response to this treatment modality. In many cases, particularly those involving vitrectomized eyes and those with minimal response to VEGF inhibition, a sustained-release steroid can produce better outcomes.


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