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Retina Today

PART VII

DME RESOURCE CENTER: BEYOND THE CLINICAL TRIALS

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

Diabetes, also known as diabetes mellitus, is a chronic metabolic condition that affects nearly 10% of the US population.[1] Specifically, in 2012, the number of people (all ages) with diabetes was 29.1 million, according to the Centers for Disease Control and Prevention (CDC).[2] That number includes those diagnosed with the disease (21.0 million) and those who have not yet been diagnosed (8.1 million).[2] It is well known among retina specialists that diabetic retinopathy and diabetic macular edema (DME) are leading causes of vision loss in patients with diabetes.

The ultimate goal in managing patients with DME is to treat them as effectively as possible while minimizing their cost and burden. In order to accomplish this, retina specialists would be wise to familiarize themselves with every treatment option available and those yet in the works. Although information from key clinical trials is undeniably helpful in directing clinicians toward the most ideal course of treatment, learning how other retina specialists manage the condition can also be valuable.

Each installment of this informational series provides insights from experienced retina specialists into the developing landscape of managing patients with DME. In Part 7 of the series, Daniel Kiernan, MD, of Ophthalmic Consultants of Long Island in Long Island, N.Y., details his use of anti-VEGF therapy and sustained-release corticosteroids in the treatment of patients with DME. In the patient cases he shares, he also includes a short recap on the cost to maintain each patient's vision with the chosen treatment.

1. American Diabetes Association. Fast facts: data and statistics about diabetes. http://professional.diabetes.org/admin/UserFiles/0%20-%20Sean/14_fast_facts_june2014_final3.pdf. July 2014. Accessed November 5, 2015.
2. Centers for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, 2014. Atlanta, GA: U.S. Department of Health and Human Services; 2014.

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Treating DME Economically While Reducing Burden

Balancing care with cost.

BY DANIEL KIERNAN, MD

Diabetes is a chronic disease and a major cause of morbidity. Anti-VEGF injections are effective, but monthly injections are expensive and diabetic macular edema (DME) has more pathologic factors than VEGF alone. Intravitreal anti-VEGF injections such as ranibizumab (Lucentis, Genentech), aflibercept (Eylea, Regeneron), and bevacizumab (Avastin, Genentech) offer effective treatment options, but many patients with chronic DME develop refractory disease that requires additional therapies such as intravitreal corticosteroids. Steroids are helpful, but their use comes with the risk of side effects. The dexamethasone intravitreal implant 0.7 mg (Ozurdex, Allergan) is expensive, but it offers longer efficacy than bolus injections, thus reducing costs per treatment for this chronic disease. Given all of this, how do we best treat macular edema?

Improving and maintaining visual function is the ultimate goal, but we often treat DME based on other factors such as clinical trial recommendations, US Food and Drug Administration labeling of drugs, the presence of edema on optical coherence tomography (OCT), and other exam findings. In this article, I present several case studies taken from my own practice that suggest another factor to consider in making treatment decisions: maintaining the best treatment efficacy while also considering treatment cost and burden on the patient.

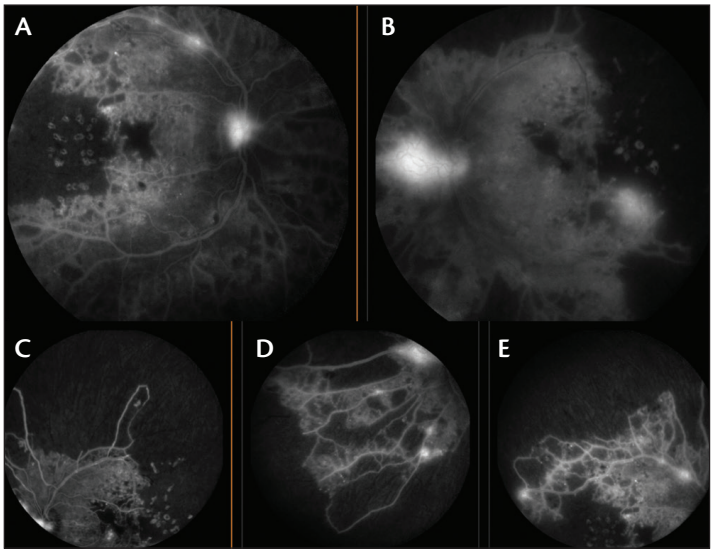

Figure 1. Fluorescein angiography demonstrated severe peripheral and macular ischemia and neovascularization of the optic nerve and elsewhere in the setting of proliferative diabetic retinopathy (A-E).

CASE STUDIES

CASE NO. 1

In September 2014, I saw a 30-year-old male with type 1 diabetes and a history of nephropathy. The patient complained of blurred vision in both eyes (OU) for the past 5 years, he had "had some laser in the past," and he was in my office for a second opinion. His visual acuity was counting fingers in the right eye (OD) and 20/60 in the left (OS). I also noted that the patient had cataracts; proliferative diabetic retinopathy with severe peripheral ischemia on angiography (Figure 1); and diabetic retinopathy in both eyes, as seen on OCT (Figure 2).

Treatment Approach

Macular ischemia was present OD, which limited the patient's best possible visual acuity in that eye. Thus, treating and maintaining useful vision OS was critical. The treatment path chosen (Table 1) resulted in many appointments, procedures, and medications, which

TABLE 1. CASE NO. 1: 4-MONTH TREATMENT SUMMARY

Date(s), 2014	Treatment(s)
Sept. 10	0.3 mg ranibizumab sample OS
Oct. 21	0.3 mg ranibizumab OU
Oct. 14 and 28	panretinal photocoagulation OU
Nov. 18	0.3 mg ranibizumab OD, 0.7 mg dexamethasone OS
Dec. 30	0.3 mg ranibizumab OU
Abbreviations: OD, right eye; OS, left eye; OU, each eye	

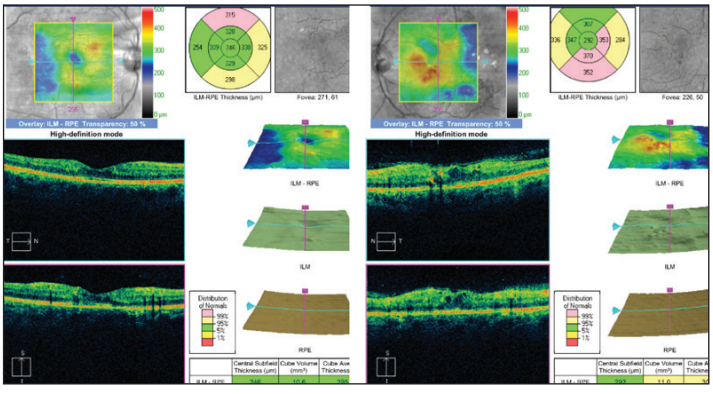

Figure 2. DME is present OD (left panel) and OS (right panel). An ERM is also present OS.

TABLE 2. CASE NO. 1: LEFT EYE PROGRESSION					
Date (2014)	**VA OD**	**VA OS**	**IOP (mm Hg: OD/OS)**	**Treatment (OS)**	**Drug Cost (OS)**
Sept. 10	CF	20/60	18/16	0.3 mg ranibizumab	$1150
Oct. 21	CF	20/400	16/20	0.3 mg ranibizumab	$1150
Nov. 18	20/200	20/70	15/15	0.7 mg dexamethasone	$1300
Dec. 30	20/150	20/80	17/19	0.3 mg ranibizumab	$1150
Abbreviations: CF, counting fingers; IOP, intraocular pressure; OD, right eye; OS, left eye; VA, visual acuity					

led me to examine the fixed drug costs (often the highest percentage of amount billed, collected, and floated within a retina practice's budget) over the 4-month treatment period OD and the visual and anatomic changes noted as a result (Table 2, Figure 3).

Cost of Maintaining Vision

Over the 4-month treatment period, I calculated the cost of maintaining the patient's better-seeing OS to be $4750 for injectable medications. Following the Diabetic Retinopathy Clinical Research Network protocol, this would extrapolate to $14 250 per year per eye in drug costs alone. Because monthly injections are not always possible, a longer-lasting solution that does not lead to functional loss is desirable to lower the treatment burden and cost of care. The question this case left me with was, "If DME is absent, will it stay away if an injection is deferred?" The answer likely depends on the agent administered and the duration of therapeutic effect.

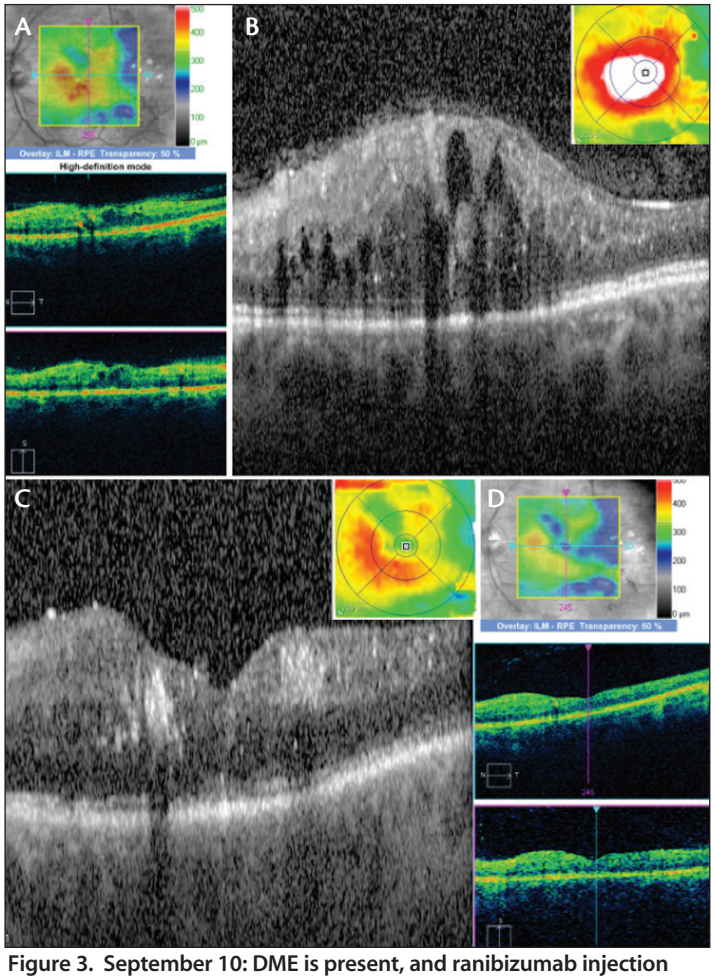

Figure 3. September 10: DME is present, and ranibizumab injection is given (A). October 21: Because edema had worsened, another ranibizumab injection was administered (B). November 18: The edema had decreased, and a dexamethasone implant was administered (C). December 30: edema had completely resolved (D).

CASE NO. 2

A 77-year-old man with a history of type 2 diabetes mellitus presented with blurred vision. He was diagnosed with DME.

Treatment Approach

Because the patient's DME was severe OS, I decided to treat with a dexamethasone implant. I opted to use aflibercept OD, which had a smaller volume of edema. I kept him on this treatment regimen for 4 months. Visual and anatomic changes are shown in Table 3 and Figure 4. Essentially, four treatments with aflibercept were given OD, and the eye still had persistent DME. Conversely, better vision and a dry retina were obtained and maintained OS with a single dexamethasone implant.

Cost of Maintaining Vision

Over the course of 18 weeks (4.5 months), the patient received one injection of dexamethasone ($1300 per dose) and four injections of aflibercept ($1850 per dose). When this cost is broken down per month based on each drug's length of effective treatment, it cost $325 per month to use dexamethasone and $1644 per month to treat with aflibercept. Thus, the cost of using dexamethasone was

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TABLE 3. CASE NO. 2: 4-MONTH TREATMENT SUMMARY				
Date	**VA OD**	**VA OS**	**Treatment (OD/OS)**	**Drug Cost (OD/OS)**
Sept. 12, 2014	20/30	20/25	aflibercept/0.7 mg dexamethasone	$1850/$1300
Oct. 24, 2014	20/20	20/25	aflibercept/none	$1850/$0
Dec. 5, 2014	20/40	20/25	aflibercept/none	$1850/$0
Jan. 29, 2015	20/40	20/25	aflibercept/none	$1850/$0
Abbreviations: OD, right eye; OS, left eye; VA, visual acuity				

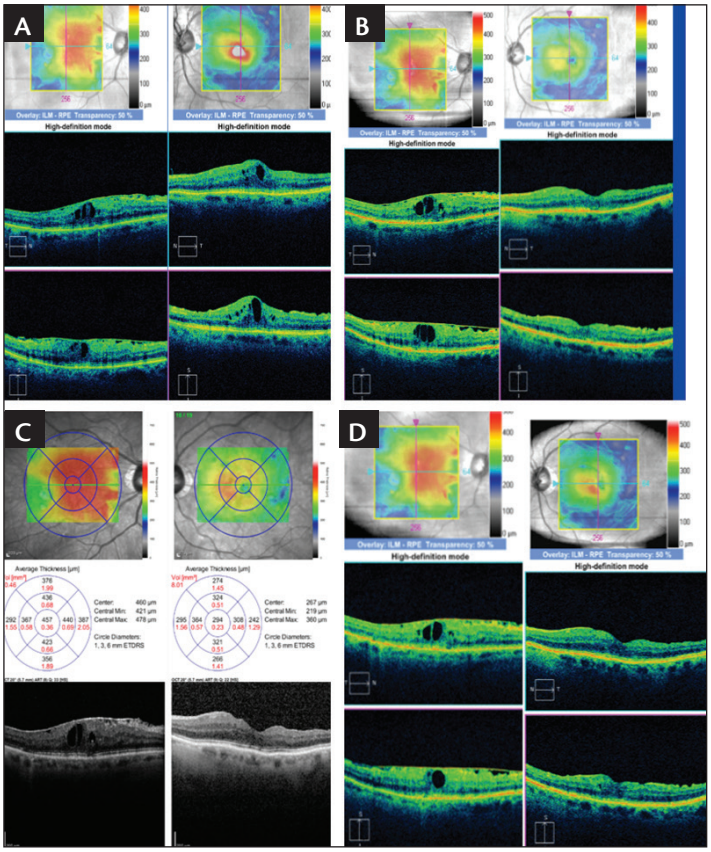

Figure 4. September 12: DME is present OU. OD was treated with aflibercept, OS with dexamethasone (A). October 24: DME is resolved OS but persistent OD, which is retreated with aflibercept (B). December 5: the presence of persistent DME OD again necessitates aflibercept treatment (C). January 29: OD again requires aflibercept treatment due to persistent DME, whereas OS remains fluid-free and does not require treatment (D).

(Continued from page 82)

80% less than aflibercept, yet it produced similar functional and anatomic effect in each eye. However, on the OCT, there was a fairly taut epiretinal membrane (ERM) in the right eye, which may have influenced the amount of retinal edema that recurred. In this particular case, there was clearly a cost benefit for the eye treated with the dexamethasone implant.

CASE NO. 3

A 67-year-old woman with a medical history of type 1 diabetes mellitus had been treated at my institution for many years. She was pseudophakic and had no history of glaucoma. Importantly, she was functionally monocular, with her visual acuity 20/400 OS due to long-term macular ischemia. The visual acuity in her right eye ranged from 20/30 to 20/40, thus, in this case, the cost of care was directly related to preserving vision in only her functional right eye. We did treat the patient's left eye as needed, based on the presence of recurrent DME.

Treatment Approach

The patient's right eye received consistent treatment with ranibizumab, but switching to dexamethasone allowed for a break in

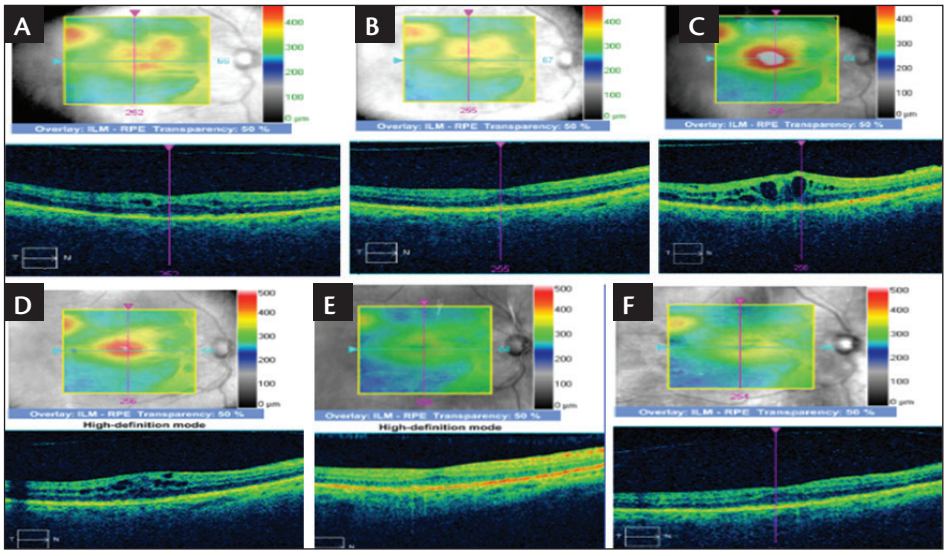

Figure 5. DME is present and initial anti-VEGF treatment showed improvement in retinal thickness (A and B), but despite several subsequent injections, on follow-up exam persistent DME was present (C), so dexamethasone was administered (D). The DME became quiescent and was absent for more than 3 months (E-F).

TABLE 4. CASE NO. 3: 12-MONTH TREATMENT SUMMARY

Date	VA OD	VA OS	Treatment (OD/OS)	Drug Cost (OD/OS)
Jan. 8, 2014	20/30	20/400	0.3 mg ranibizumab/none	$1150/$0
Feb. 19, 2014	20/30	20/400	0.3 mg ranibizumab/none	$1150/$0
April 7, 2014	20/40	20/400	0.3 mg ranibizumab/none	$1150/$0
May 12, 2014	20/25	20/400	0.3 mg ranibizumab/none	$1150/$0
June 30, 2014	20/25	20/400	bevacizumab/none	$40/$0
Aug. 11, 2014	20/50	20/400	bevacizumab OU	$40/$0
Sept. 29, 2014	20/25	20/400	0.7 mg dexamethasone OU	$1300/$1300
Nov. 10, 2014	20/30	20/400	none OU	$0/$0
Dec. 29, 2014	20/30	20/400	none OU	$0/$0
Jan. 12, 2015	20/50	20/400	0.7 mg dexamethasone OU	$1300/$1300

Abbreviations: OD, right eye; OS, left eye; OU, both eyes; VA, visual acuity

injection frequency. Visual and anatomic changes over 12 months of treatment are shown in Table 4 and Figure 5.

Cost to Maintain Vision

Again, the cost of saving this patient's vision was directly correlated with preserving visual function OD. The greatest proportion of such treatment is most certainly the cost of the drugs used. The cost of one dose of ranibizumab is $1150; for bevacizumab, it is $40; and for dexamethasone, it is $1300. The patient received four doses of ranibizumab between January 8, 2014, and June 30, 2014, which works out to $800 per month. She received two doses of bevacizumab between June 30, 2014, and September 29, 2014, for a total of $27 per month in cost. One dexamethasone implant provided effective treatment between September 29, 2014, and January 12, 2015, for a cost of $371 per month. Extrapolated to a yearly cost of treatment, the totals are: $324 for bevacizumab, $4452 for dexamethasone, and $9600 for ranibizumab.

In the end, bevacizumab was the least expensive treatment option (not taking into account direct physician fees, overhead, and the cost of patient time). However, as with other anti-VEGF drugs, treatment with bevacizumab requires monthly dosing and more frequent treatment. The cost of using dexamethasone was 55% less over the course of 1 year compared with that of ranibizumab. This patient essentially needed an injection at every visit when bevacizumab or ranibizumab was used, compared with needing an injection at every third visit when dexamethasone was used. Additionally, dexamethasone produced comparable visual acuity results. Extrapolating from these data, use of longer-lasting agents may allow clinicians to reduce the total number of visits, testing, and treatments—and consequently the cost—required to treat their DME population.

CONCLUSION

In patients with DME, anti-VEGF therapy is used successfully in many cases as an initial course of treatment. However, sustained-release corticosteroids such as the dexamethasone implant may provide equally efficacious visual benefits with a longer duration of action and at a relatively lower cost. Of course, side effects such as increased intraocular pressure and cataract formation could mitigate some of these savings, as more frequent visits, treatments, or surgery might be needed in some circumstances.

In eyes with chronic DME and DME that is poorly responsive to anti-VEGF treatment, corticosteroids should be strongly considered. In addition, in instances in which DME persists despite aggressive treatment, the clinician may want to carefully examine the patient for the presence of an ERM, which may be adding increased retinal thickness and may require surgical intervention.

At the end of the day, the goal is to treat patients as effectively and with as little cost and burden to them as possible. To this end, retina specialists should be familiar with the many options available to treat DME and have basic knowledge of the key clinical trials that help guide the selection of these treatments. ■

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A video of Dr. Kiernan presenting these and other cases can be found on *Retina Today's* DME Resource Center: bit.ly/0116RT_DME