Vitrectomy in the Management of Diabetic Macular Edema

A valid option in selected cases.

BY ANSELM KAMPIK, MD

Diabetic macular edema (DME) is a major source of vision loss in people with diabetes mellitus. DME affects up to 25% of people after 10 years of diagnosis of diabetes and will develop in more than 40% of patients with type 1 diabetes over the course of their lifetimes.[1,2] Compounding the problem is the fact that the incidence of diabetes is growing worldwide with the aging of the population and the increase in overweight and obesity in certain populations.

The role of laser focal/grid photocoagulation as a treatment option for DME is well established.[3] Evidence is also beginning to emerge supporting the use of vascular endothelial growth factor (VEGF) inhibiting agents, either alone or in combination with laser, as beneficial treatments for DME.[4] However, we also know that not every patient with DME responds well to intravitreal anti-VEGF therapy and/or laser.

Evidence-based medicine to date supports treatment of DME with laser and with anti-VEGF drugs. Clinical experience suggests that DME not involving the foveola usually responds well to laser treatment. However, if the edema is more diffuse and involves the foveola, laser has more variable results, and today anti-VEGF treatment is preferred in these cases.

VITRECTOMY FOR DME

With the documented efficacy of the pharmacologic and laser treatments currently available to us, is there a rationale for the use of vitrectomy in the management of DME? Despite 20 years' worth of publications, it must be said that the effect of vitrectomy in DME is not fully understood. We are just beginning to understand the physiologic effects of vitrectomy in DME beyond the mechanical removal of the vitreous.

The initial rationale for use of vitrectomy was gleaned from epidemiologic studies. Nasrallah et al[5] observed that the incidence of posterior vitreous detachment (PVD) was lower in patients with DME than in diabetics without macular edema. This finding suggested that attached vitreous is a risk factor for DME. Further, Hikichi and colleagues[6] noted that, after PVD, spontaneous resolution of DME was observed in 55% of diabetic patients, while in patients without PVD, resolution of DME occurred in only 25%. Again, this suggested that the vitreous plays a role in DME.

In a seminal paper in 1992, Lewis et al[7] observed that vitrectomy can improve visual prognosis in some eyes with DME and macular traction, and he coined the term "taut posterior hyaloid" to denote the clinically observed alteration of the vitreoretinal interface in patients deriving benefit from vitrectomy. This led to a string of papers reporting experience with this approach to DME.[8-13] Our group added internal limiting membrane (ILM) peeling to this type of vitrectomy.[14]

All of these studies and many more in recent years have demonstrated that vitrectomy can improve visual acuity in DME. However, as noted above, we still have only begun to understand what we are doing, beyond the physical removal of the vitreous gel, when we perform vitrectomy in DME. To understand more clearly, it may be helpful to review the terminology used to describe and classify DME. DME can include focal or diffuse edema, and when we consider the vitreoretinal interface we may also describe another form as tractional edema. In addition, ischemic maculopathy may be associated with edema. The problem is that there is only very indirect correlation between these morphologic descriptions and the functional reality in DME. The interdependence of morphology and function is not well understood.

Perhaps it would be more appropriate to use the term "diabetic maculopathy" instead of DME. This term would encompass the intraretinal changes, which include not only edema but also ischemic and neuronal changes (neuropathy). It would also take in the epiretinal changes that occur

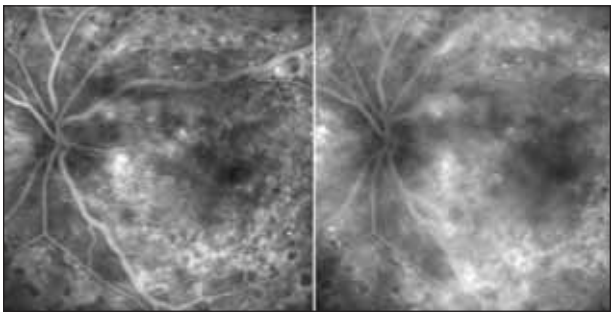

Figure 1. Preoperative fluorescein angiography of a 46-year-old patient with type 2 diabetes demonstrating proliferative diabetic retinopathy and diffuse DME, clinically without tractional forces but with glistening appearance of the retinal surface.

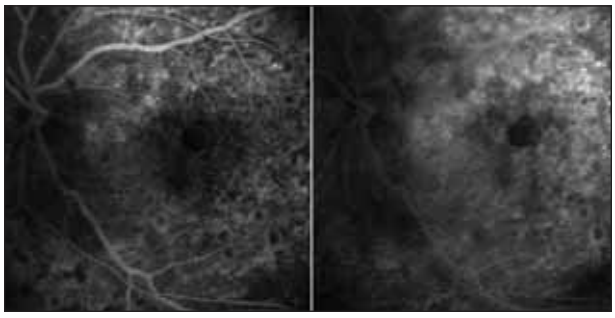

Figure 2. After vitrectomy and ILM peeling, visual acuity improved from 0.1 to 0.4 with disappearance of metamorphopsia. Result has remained stable over 23 months of observation without further treatment.

in DME in some instances, including in the vitreous and in the form of fibrovascular and fibrocellular proliferations.

INDICATIONS FOR VITRECTOMY

How can we use our understanding of the pathology of DME to determine when vitrectomy is indicated? Fluorescein angiography and high resolution optical coherence tomography are helpful to differentiate whether the pathology is due to traction, to the edema itself, or to ischemia. This information can help us to determine the major cause or causes of damage. Is the decreased visual acuity in a particular patient associated with edema involving the center of the macula, or is it mainly foveolar ischemia? Is it perhaps traction, or some other cause so far unrecognized, such as neuronal degeneration, which would be more difficult to diagnose?

This approach helps us to form a rationale for performing vitrectomy in a given case. Are we principally trying only to relieve tractional forces at the retinal surface? This was the original indication, but since vitrectomy for DME was introduced we have established other reasons to remove the vitreous, such as reducing the oxygen consumption of the vitreous, reducing hypoxia at the retina by increasing the oxygen level in the posterior segment, and removing the vitreous collagen from the retinal surface, where its potentially high concentration of VEGF is probably not well reached by anti-VEGF agents.

This understanding also helps us to select the proper operative strategy and assess the potential benefits of surgical adjuncts such as intravitreal injection or laser. Vitrectomy can be done with or without peeling of the ILM. In phakic eyes with cataractous lenses it can be combined with cataract surgery and posterior chamber IOL implantation. It may be combined with intravitreal drug application or with laser treatment at the time of surgery or later. Pharmacologic agents to assist with surgical management can include one of the anti-VEGF drugs to reduce

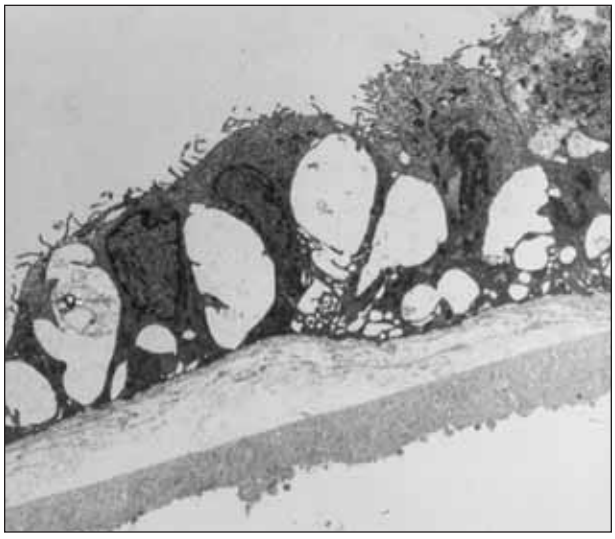

Figure 3. Transmission electron microscopy of epiretinal membrane removed from a patient with tractional DME.

edema, steroids to reduce edema and improve visualization of the vitreous at the time of surgery, or staining agents to facilitate visualization of the vitreoretinal interface and ILM.

As noted above, numerous reports in the literature indicate that vitrectomy can improve visual acuity in DME. In almost all cases the thickness of the retina is reduced after surgery, although visual improvement is reported in only about 40% of patients, regardless of the presence of tractional membranes. However, in patients who experience a visual benefit from vitrectomy, the surgery provides a long-lasting treatment effect, unlike what is seen with anti-VEGF therapy alone.

CASE REPORT

A case presentation from our series illustrates the potential beneficial effects of vitrectomy in DME. A 46-year-old female patient with type 2 diabetes presented with proliferative diabetic retinopathy, diffuse DME,

and visual acuity of 0.1 (Snellen decimal). Clinically, no tractional forces were detected, but there was a glistening appearance on the retinal surface (Figure 1). After vitrectomy and ILM peeling, visual acuity improved to 0.4 with disappearance of the metamorphopsia (Figure 2). This result has remained stable over 23 months of observation without any additional treatment.

HOW MUCH SURGERY?

How much surgery is really necessary in vitrectomy for DME? Is vitrectomy with peeling of epiretinal tissue enough, or should we peel the ILM as well? What about staining for visualization?

Histopathology was performed on specimens harvested from eyes undergoing standard pars plana vitrectomy with induction of posterior vitreous detachment, epiretinal tissue removal, and ILM peeling.[15] A multilayered appearance of epiretinal tissue was seen on histopathology, with cellular proliferations overlying a layer of native vitreous collagen (Figure 3).

The findings of this investigation indicate that complete mechanical removal of all epiretinal tissue is almost impossible without removal of the ILM. Epiretinal vitreous should be removed together with the cortical vitreous, and it seems to be important to peel the ILM to ensure removal of all epiretinal tissue and avoid recurrences of epiretinal membranes.

The evidence for the efficacy of ILM peeling, however, is limited to case series.[16,17] There are no prospective randomized studies of the use of ILM peeling for treatment of nontractional DME. The role of ILM peeling therefore to a degree remains undetermined in DME.

In our experience,[18] however, complete removal of epiretinal membranes with ILM peeling leads to a high rate of anatomic and visual improvement. Resolution of macular thickening after vitrectomy is often independent of the presence of contractile epiretinal membranes. Also, in eyes without epiretinal tangential traction on the retina, complete removal of cortical vitreous leads to fluid reabsorption.

This suggests, therefore, that vitrectomy can be considered in cases of DME with traction maculopathy (the presence of epiretinal membranes), with taut posterior hyaloid, with vitreoschisis, or with a glistening appearance of the retinal surface. It is an open question, so far not supported by clinical studies, whether vitrectomy also works well in other cases of DME without these signs.

CONCLUSIONS

In eyes with diffuse DME involving the center of the macula, anti-VEGF therapy is currently the treatment of choice to reduce DME and potentially convert the diffuse edema into DME not involving the foveal center and thus more amenable to laser. Vitrectomy is a valid option in patients with a tractional component of their DME or with complete vitreous attachment who have not responded to intravitreal medical therapy. The vitreoretinal interface should, however, be properly evaluated before making therapeutic decisions.

The rationale for vitrectomy in DME is to remove tractional forces at the retinal surface, to reduce oxygen consumption of the vitreous by removal of vitreous, to reduce hypoxia at the retina, and to remove the vitreous collagen on the retina, which has a potentially high concentration of VEGF. We still have much to learn about the effects of vitrectomy in DME beyond the mechanical removal of the vitreous. ■

Anselm Kampik, MD, is Professor and Chairman of the Department of Ophthalmology at Ludwig Maximillian University, Munich, Germany. Prof. Kampik states that he has no financial interests relevant to the products or companies discussed in this article. He may be reached at +49 8951603800; fax: +49 8951604778; or via e-mail at akampik@med.uni-muechen.de or akampik@lmu.de.

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