Retinal vein and artery occlusions (RVOs and RAOs) are usually related to systemic disease, most commonly hypertension and atherosclerosis. The obesity epidemic, which drives the development of the metabolic syndrome, as well as the alarming continued prevalence of smoking are the most significant behavioral risk factors. Highly effective new treatments are now available for RVO; therapy for RAO remains problematic.

RETINAL ARTERY OCCLUSION
Risk Factors
Arterial embolism, not retinal arteriolar disease, causes both central retinal artery occlusion (CRAO) and branch retinal artery occlusion (BRAO). Aortic valvular disease and cardiac arrhythmias are common causes of cholesterol plaque’s or platelet emboli’s entering the retinal arterial circulation. Carotid atherosclerotic plaque can also often result in cholesterol plaque or platelet embolization to the retina. Coronary artery bypass grafting and carotid endarterectomy can also produce RAO.

Significantly reduced carotid blood flow is an indication for carotid endarterectomy. Therefore, patients with small carotid plaques and CRAO or BRAO with near-minimal obstruction to flow noted on Doppler ultrasonic imaging are often incorrectly informed that the carotid ultrasound examination is negative when, in fact, they should begin anticoagulant therapy.

“Although a fluorescein angiogram is diagnostic in RAO, it is not needed, and obtaining this test may delay therapy.”

Diagnosis
The diagnosis of CRAO is straightforward when patients are seen soon after its onset. Findings include a so-called cherry red spot appearance caused by widespread axoplasmic stasis, an interruption in the blood column in the retinal vessels, and a marked loss of vision. Although a fluorescein angiogram is diagnostic in RAO, it is not needed, and obtaining this test may delay therapy. The retinal whitening will disappear after several weeks, making the diagnosis more difficult. Still, profound visual loss, an afferent pupillary defect, an absent electroretinogram B-wave, a marked loss of retinal architecture, and retinal thinning on optical coherence tomography will confirm the diagnosis.

Treatment
Many local therapies have been attempted for the treatment of CRAO and BRAO, including ocular massage, paracentesis, a retrobulbar block, and the retrobulbar injection of antivascular agents. Retrobulbar injec-

Anti-VEGF therapy is poised to be the treatment of choice.

BY STEVE CHARLES, MD
tions are no longer used. There are anecdotal reports of success with ocular massage and paracentesis but no sound evidence of efficacy. If the patient is placed in a hyperbaric oxygen chamber within 6 to 12 hours of CRAO, vision can be preserved while he or she is in the chamber, but there is no evidence of long-term efficacy.

Prompt intra-arterial thrombolysis with a tissue plasminogen activator can improve visual outcomes. Patients seldom present to a retinal specialist in the appropriate 6- to-12-hour time interval, however, and there is a significant risk of systemic bleeding. Although there is no clinical trial evidence of its efficacy, I have the patient take 325 mg of aspirin immediately when RAO is suspected without waiting for any workup.

RETINAL VEIN OCCLUSION

Risk Factors

Hypertension is the most significant systemic risk factor for RVO; glaucoma is the only ocular risk factor. The occurrence of CRVO in young individuals without glaucoma or hypertension requires a medical workup, especially if the condition is bilateral. Although many ophthalmologists habitually order a wide variety of tests in CRVO patients, a large meta-analysis demonstrated a relationship with only two laboratory findings in CRVO: anticardiolipin antibodies and homocysteine.

Diagnosis

The diagnosis of CRVO, hemi-RVO, and BRVO can usually be made with a 90.00 or 78.00 D lens at the slit lamp. Optical coherence tomography will show macular edema in BRVO and CRVO, sector edema in hemi-RVO, and BRVO and widespread edema in CRVO. Although fluorescein angiography can further validate the diagnosis and help to determine the extent of ischemia, it rarely changes the diagnosis or therapeutic strategy.

Treatment

Until recently, grid or sector laser treatment for macular edema and the use of panretinal photocoagulation for neovascular glaucoma secondary to CRVO were the only treatment strategies. A branch vein decompression technique that I developed unfortunately does not restore capillary circulation. Radial optic neurotomy, developed by Opremcak et al, is ineffective as well. Holekamp and colleagues have shown that vitrectomy permanently increases the partial pressure of oxygen in the vitreous cavity. This probably explains the positive effect of vitrectomy on diabetic macular edema as well as macular edema secondary to RVO. It is also likely that the levels of vascular endothelial growth factor (VEGF) and other cytokines are reduced on a dilutional basis as postulated by Stefánsson.

Most retinal specialists have used intravitreal steroids to treat macular edema secondary to RVO: triamcinolone (generic, off label), later Triesence (Alcon Laboratories, Inc.), fluocinolone implant (Retisert; Bausch + Lomb), and more recently dexamethasone (Ozurdex; Allergan, Inc.). Because it is impossible to separate steroidal agents’ glaucoma and cataract effects from their anti-inflammatory effects, I have chosen to use only anti-VEGF intravitreal injections to treat macular edema secondary to RVO. For years, it was taught that approximately 6% of the population were steroid responders, but this statistic was based on the use of topical 1% prednisolone acetate. In fact, approximately 90% of patients develop glaucoma—often irreversible—when a Retisert implant is used and 30% with intravitreal triamcinolone (personal communication, Glen Jaffe, MD).

Approximately 15% of patients develop glaucoma with Ozurdex, and 1% require a filtering procedure. Neither cataract nor glaucoma occurs with anti-VEGF therapy. It was also thought that steroid-induced glaucoma was reversible when the drug was discontinued, but it can be permanent after the use of intravitreal steroids or implants.

I have used bevacizumab (Avastin; Genentech) off label since July 2005 to treat macular edema secondary to RVO as well as neovascular glaucoma secondary to CRVO. Ferrara et al emphasized initiating anti-VEGF therapy as soon as the diagnosis is made instead of waiting for a period of observation or using it as so-called rescue therapy. In my mind, there is no rationale for a period of observation prior to the use of anti-VEGF therapy, nor is there an alternative therapy that should be used first. The best results can be obtained by starting with monthly injection intervals and adjusting the interval depending upon the patient’s response.

In June 2010, the FDA approved ranibizumab (Lucentis; Genentech) for the treatment of macular edema. Although a head-to-head comparison of ranibizumab and bevacizumab for RVO has not been published, ranibizumab is far more effective than bevacizumab, because it has a 25 times greater molecular affinity for VEGF. VEGF levels in CRVO and diabetic macular edema are at least 1,000 times higher than in age-related macu-
lar degeneration (AMD). The Comparison of Anti-VEGF Treatments Trial (CATT) is a National Eye Institute-funded, head-to-head, randomized, multicenter trial that compared Avastin to Lucentis in patients with wet AMD. CATT demonstrated near equivalence of the two compounds in AMD. These data do not apply to RVO or diabetic macular edema, because the VEGF levels in these conditions are much higher. VEGF trap (VEGF Trap-Eye; Regeneron Pharmaceuticals, Inc.) is an anti-VEGF compound developed for AMD, diabetic macular edema, and RVO; it has shown superb results for all three conditions, but it has not yet been approved by the FDA. VEGF trap has greater durability than Lucentis and an even greater molecular affinity for VEGF, making the rationale for the use of intravitreal steroids in patients with RVO even less attractive.

CONCLUSION

Unfortunately, most patients with CRAO and BRAO are not treated because of a delay in therapy and the bleeding risk associated with tissue plasminogen activator. On a more positive note, anti-VEGF therapy, especially Lucentis and probably VEGF Trap-Eye when approved, have produced excellent results in RVO patients. This is especially true when therapy is initiated immediately, and these strategies should supplant steroid therapy with its inherent risk of associated glaucoma and cataract development.

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