

Diagnosis and Management of Neovascular Glaucoma

Neovascular glaucoma (NVG), a secondary glaucoma that has significant potential to cause visual loss, is characterized by neovascularization of the iris (NVI) and of the angle (NVA) as well as elevated intraocular pressure (IOP). George Coats first described the condition in 1906, identifying the presence of NVI in eyes with prior central retinal vein occlusion (CRVO). In 1963, the name *neovascular glaucoma* was proposed by Daniel Weiss et al., replacing older terms such as thrombotic, congestive, rubeotic, and hemorrhagic glaucoma.¹

NVG presents most commonly in elderly patients and, in more than 95% of cases, is secondary to conditions that cause retinal ischemia, including proliferative diabetic retinopathy (PDR), CRVO, and carotid artery occlusive disease (CAOD).² Early identification and treatment of NVG is critical in order to avoid irreversible vision loss.

Pathophysiology

Retinal ischemia acts as a stimulus for proangiogenic growth factors (including vascular endothelial growth factor, or VEGF). The subsequent neovascularization begins at the pupillary border and eventually invades the iridocorneal angle, disrupting drainage of aqueous fluid through the trabecular meshwork and leading to elevated IOP.

Several ocular and systemic disorders, discussed below, are associated

with ischemia that may drive neovascularization and, potentially, NVG.

Underlying Conditions

Proliferative diabetic retinopathy.

Poor glycemic control in patients with diabetes may lead to PDR, which may be associated with neovascularization of the anterior segment. Notably, PDR is the most common cause of bilateral NVG.³

The time interval between the onset of PDR and the development of NVG is difficult to predict, ranging from 1 month to several years. Patients with elevated HbA_{1c} should have frequent ophthalmologic examinations to monitor for progression of diabetic eye disease.

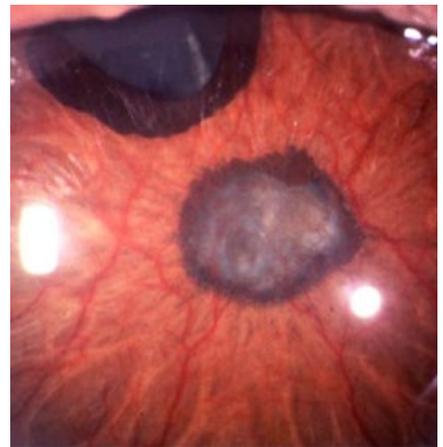
Central retinal vein occlusion.

Ischemic CRVO is the second leading cause of NVG. This type of NVG is sometimes called “90-day glaucoma” because it commonly presents around 3 months after the initial ischemic event. Although NVG can take from 2 weeks to several years to develop after CRVO, the majority of cases develop within the first 6 months.³

Carotid artery occlusive disease.

CAOD can lead to ocular ischemic syndrome caused by ocular arterial hypoperfusion, with symptoms including amaurosis fugax and reduced vision.⁴

Because the resulting ciliary body hypoperfusion leads to decreased aqueous humor production, these patients



ADVANCED NVI. This eye of a patient with NVG shows vessels traversing most of the iris. Also note the iridotomy at the top.

may, paradoxically, have either normal or low IOP, confounding the diagnosis of NVG. Thus, it is important to look for other features that suggest CAOD-induced NVG, including absence of any apparent ocular cause of NVI or stark asymmetry of retinopathy.³

Central retinal artery occlusion.

CRAO, an uncommon cause of NVG, can occasionally lead to neovascularization. In such cases, new vessels are typically seen early; thus, post-CRAO NVG was historically referred to as “30-day glaucoma.”¹¹

Other uncommon causes. Other potential causes include retinal detachment, intraocular tumors, and uveitis.⁵

Diagnosis

To make an accurate diagnosis of NVG, the physician should consider the patient’s symptoms and clinical signs in

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conjunction with common risk factors. A high index of suspicion should be maintained in patients with a history of systemic or ocular disease that may result in retinal ischemia, including poorly controlled diabetes, hypertension, or arteriosclerosis, as well as PDR, CRVO, CAOD, and CRAO.

Symptoms. Patients may be asymptomatic early on. When symptoms develop, the most common are ocular pain and decreased vision.⁴

Clinical signs. When evaluating a patient with possible NVG, a complete ophthalmologic examination of both eyes should be performed. The condition of the fellow eye can provide useful information, especially in cases of proliferative disease due to diabetes.

The clinician should examine the cornea for microcystic edema, the anterior chamber for hyphema, and the iris and anterior chamber angle for NVI/NVA. In the vast majority of cases, NVI and NVA occur before IOP increases; thus, early recognition and prompt treatment of neovascularization may prevent progression to NVG.^{3,4}

Abnormal blood vessels. Early on, tufted vessels can be visualized at the pupillary margin. Unlike normal iris vessels, which are distributed radially, these pathologic vessels grow in a meandering pattern. NVA will first appear as vessels crossing the scleral spur and trabecular meshwork.¹

As the disease progresses, NVA becomes more prominent, and the fibrovascular membrane that develops will disrupt the functioning of the trabecular meshwork, leading to increased IOP. If left untreated, the membrane contracts, causing synechial angle closure and permanently compromising the outflow pathway.^{1,4}

Corneal edema. If corneal edema is present in the affected eye, it can limit visualization of the anterior chamber structures. In these cases, B-scan echography can be performed to look for vitreous opacities, tractional retinal detachment, or intraocular tumor.

Management Options

Panretinal photocoagulation. PRP is considered the mainstay of treatment for NVG. Ablation of ischemic areas

of the retina reduces the angiogenic stimulus. PRP has been shown to cause lasting regression of NVI and NVA and is used in cases of neovascularization both with and without further signs of progression to NVG.⁶

PRP can be performed only if there is an adequate view of the retina.

Anti-VEGF agents may be valuable in improving visibility in patients with vitreous hemorrhage, significant media opacities, or poor pupillary dilation.

Anti-VEGF agents. Intravitreal injection of anti-VEGF agents, such as bevacizumab, ranibizumab, and aflibercept, has been shown to decrease angiogenesis. These agents may be used for neovascularization alone or for NVG and have been successful both as monotherapy and as an adjunct to procedures such as PRP.⁵

However, if the angle is completely closed with 360 degrees of synechiae, anti-VEGF therapy may reduce the neovascularization without lowering the IOP.

Cautions. Anti-VEGF agents should be used with caution in eyes with concurrent and significant neovascularization elsewhere (NVE), as rapid involution of NVE may lead to tractional retinal detachment.

Moreover, the long-term effects of anti-VEGF treatment in NVG have yet to be studied, and definitive treatment with laser photocoagulation is still necessary for most patients with NVG.⁵

Medical therapy. When IOP is elevated, various topical agents are used to lower the pressure, including beta-blockers, carbonic anhydrase inhibitors, alpha-agonists, and prostaglandin analogues. Topical atropine and topical corticosteroids are useful for managing inflammation and pain.⁴

Medical therapy often functions as a bridge to surgical therapy for patients who present with significant synechial angle closure.

Surgical Procedures

Trabeculectomy. Although commonly used for open-angle glaucoma, trabeculectomy is less effective for NVG. Patients with NVG often present with a “hot eye,” and significant inflammation reduces the likelihood of a successful

outcome with filtering surgery.

In addition, patients with NVG often require subsequent surgeries for problems such as vitreous hemorrhage and tractional retinal detachment. These later procedures can jeopardize the functioning of the bleb.

Finally, because of the intensive postoperative follow-up required after trabeculectomy, compliance is often an issue for patients who have undergone this procedure.^{5,6}

However, trabeculectomy combined with anti-VEGF pretreatment and use of adjunctive antimetabolites such as mitomycin C has shown moderate success rates. This approach may be useful for patients with NVG refractory to PRP and medical management.⁵

Drainage implants. Glaucoma drainage implants have gained increasing popularity in recent years as a surgical management option for glaucoma.⁷

Types of shunts. Two basic drainage implant designs—valved (e.g., Ahmed) and nonvalved (e.g., Baerveldt)—are available in a range of sizes. Smaller valved implants may yield better results in NVG patients, allowing early IOP control while minimizing the risk of hypotony (common in eyes with significant ischemia).

A valved shunt is functional upon implantation. Cohesive viscoelastic can be left in the anterior chamber at the end of the case to help tamponade bleeding that occurs during the procedure; it also prevents delayed hemorrhage that may result from a sudden drop in IOP.

In contrast, nonvalved shunts are not functional for 4 to 6 weeks, until the implant has become encapsulated. During this time, the shunt must either be tied off with a suture or have the tube lumen occluded. Various methods to control the IOP during the early postoperative phase have been employed (fenestrations, orphan trabeculectomy, etc.), but most are inconsistent and unpredictable.

Our choice. Therefore, the authors prefer placement of valved implants initially for all cases of active NVG. If this does not achieve adequate long-term IOP control, a nonvalved implant can be placed in a different quadrant,

or cyclophotocoagulation (CPC) can be performed.

Cyclodestruction. If the eye has limited visual potential, cyclodestructive laser therapies such as CPC provide another option for IOP management. Either continuous wave or micropulse CPC can be offered; the advantage of micropulse is that the tissue is allowed to cool between the pulses of laser delivery, preventing damage from thermal build-up. Complications of laser cyclodestruction include hypotony and phthisis as well as inflammation caused by the procedure.⁶

Addressing the Causes

Because NVG is a secondary glaucoma, it is essential for the patient to receive treatment for the underlying cause of ischemia. This may involve multidisciplinary management with a cardiologist, vascular surgeon, or primary care physician, depending on the specific etiology.

Complications

NVG typically results in severe vision loss and carries a poor prognosis, underscoring the importance of early recognition and prevention. A blind, painful eye can be a common, but unfortunate, outcome of refractory NVG. When this occurs, retrobulbar alcohol injection can be administered for pain management, but enucleation may be necessary to relieve intractable pain.³

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3 Havens SJ, Gulati V. *Dev Ophthalmol.* 2016;55: 196-204.

4 Rodrigues GB et al. *Int J Retina Vitreous.* 2016; 2:26.

5 SooHoo JR et al. *Semin Ophthalmol.* 2013;28(3): 165-172.

6 Olmos LC, Lee RK. *Int Ophthalmol Clin.* 2011; 51(3):27-36.

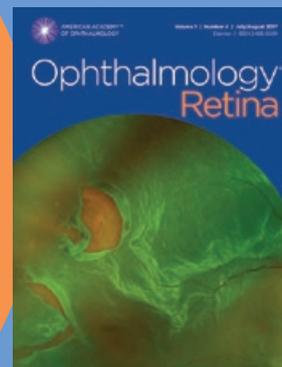
7 Vinod K et al. *J Glaucoma.* 2017;26(8):687-693.

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