Intravitreal Anti-VEGF Drugs for the Treatment of IJRT

This method of treatment remains controversial but shows promise.

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idiopathic juxtapfoveal retinal telangiectasis (IJRT), refers to a heterogeneous group of well-recognized clinical entities characterized by telangiectatic alterations of the juxtapfoveal capillary network of 1 or both eyes. Classically, 3 groups of IJRT are identified. These groups differ in appearance, presumed pathogenesis, and management strategies. Group 1 is unilaterally easily visible telangiectasis occurring predominantly in men and causes visual loss as a result of macular edema. Group 2, the most common, is bilateral occurring in both middle-aged men and women, and presents with telangiectasis that is more difficult to detect on biomicroscopy in early stages, but that has characteristic and diagnostic angiographic and optical coherence tomography (OCT) features. Group 2 is divided into 2A, acquired, and 2B, congenital. Yannuzzi et al subdivided type 2A into nonproliferative (telangiectasis, exudation, intraretinal pigments, and foveal atrophy) and proliferative disease (subretinal neovascularization [SRNV] or fibrosis). Vision loss in group 2 is due to retinal atrophy, not exudation, and subretinal neovascularization. Group 3 is very rare and characterized predominantly by bilateral progressive obliteration of the perifoveal capillary network without exudation, and usually occurs in association with a medical or neurologic disease.

**TYPE 2A IJRT**

IJRT type 2A is the most common type of IJRT in our clinic. The precise pathogenesis of IJRT type 2A is controversial. Primary degeneration or dysfunction of the parafoveal Mueller cells leads to retinal thinning, particularly photoreceptor atrophy and retinal endo-

thelial cell dysfunction. Photoreceptor atrophy leads to invasion of proliferating capillaries into subretinal space, causing SRNV and later anastomosis with the choroidal vessels. A recent report from Kurihara et al reported blocking VEGF-A in adult mouse retinal pigment epithelial (RPE) cells rapidly led to vision loss and ablation of the choriocapillaris.

Fluorescein angiography in IJRT type 2A will typically reveal parafoveal ectatic capillaries and late-stage diffuse leakage, mainly temporal to the fovea. Both atrophy and secondary choroidal neovascularization have been reported to occur with disease progression. Imaging with OCT typically shows intraretinal hyporeflective spaces in the foveal region, thinning and disruption of the photoreceptor layer, and intraretinal hyperreflective lesions causing posterior shadowing corresponding to hyperpigmented RPE plaques. In the presence of SRNV, highly reflective dots in the inner and outer nuclear layers with intraretinal/subretinal fluid with or without localized increase in retinal thickness are noted. Change in autofluorescence can be helpful in early diagnosis and to follow the progression of disease. Disruption of foveal autofluorescence, hypautofluorescence corresponding to pigments, and hypo- or hyperautofluorescence in parafoveal areas are common changes in fundus autofluorescence.

In their histological analysis, Green et al described thickening of the wall of retinal capillaries resulting from proliferation of basement membrane and narrowing of the capillary lumen in an eye with type 2 IJRT. They also observed degeneration of pericytes and occasional areas of degenerated endothelial cells.
Intravitreal inhibition of VEGF has been shown to be effective for a variety of ocular diseases with destabilized blood-retina barrier or pathologic growth of new vessels. Recently, it has been hypothesized that VEGF may play an essential role in the pathogenesis of macular telangiectasia as well. Charbel Issa et al showed a reduction in the ectatic capillaries in early stage on fluorescein angiography as well as marked reduction in size and intensity of late stage hyperfluorescence at 4 and 8 weeks after injection of anti-VEGF agents in eyes with IJRT. This reduction in leakage suggests the role of VEGF in extravasation of fluorescein through altered endothelium. OCT imaging revealed decrease in intraretinal thickness as well. However, this effect was temporary, and rebound increase in parafoveal leakage and central retinal thickness was noted. Similarly, several studies reported decrease in leakage in nonproliferative IJRT with intravitreal bevacizumab.

Charbel Issa et al hypothesized that these structural capillary changes could lead to a disturbed exchange of oxygen and substrates between the vascular lumen and neurosensory retina. This may lead to a hypoxia-induced increased VEGF release by retinal cells. The loss of pericytes may render the capillaries more susceptible to effects mediated by VEGF.

In previous studies, however, there were no short-term visual acuity or anatomic improvements in nonproliferative IMT eyes after intravitreal anti-VEGF treatment, which suggests that there may be no short-term benefit in treating before the development of SRNV. Takayama et al also showed no effect of intravitreal bevacizumab on retinal thickness or intraretinal cysts in type 1 IJRT. VEGF is thought to play a role in vitro photoreceptor survival. Anti-VEGF agents may cause photoreceptor degeneration. Therefore, use of anti-VEGF drugs in the nonproliferative stage is still controversial.

**OTHER THERAPIES FOR SRNV IN TYPE 2A IJRT**

SRNV in type 2A IJRT is unique in its origin. Yannuzzi et al termed this intraretinal SRNV as type 3 neovascularization, similar to early retinal angiomatous proliferation, and different from type 1 (under the retinal pigment epithelium or occult) and type 2 (above pig-
ment epithelium or classic) neovascularizations, which originate from the choroid in age-related macular degeneration.

SRNV is the only treatable cause of vision loss in eyes with type 2A IJRT. The SRNV lesions are not usually large; they begin in the retina and then progress into the subretinal space. Numerous treatments have been tried, including focal/grid laser,25 surgical removal of the subretinal neovascular membrane,26 transpupillary thermotheraphy,27 photodynamic therapy (PDT),28,29 and intravitreal triamcinolone acetonide.30 These treatment modalities failed to maintain or improve visual acuity,25,26,31 PDT may lead to RPE atrophy after treatment with no visual improvement and associated with higher incidence of recurrence and excessive scarring.31 Surgical removal of the SRNV is difficult because of strong adhesion with the overlying neurosensory retina.26 Intravitreal triamcinolone is generally associated with cataract progression and glaucoma.

Although the etiology of type 2A IJRT is not clearly understood, VEGF seems to have a role in the pathogenesis of SRNV. Several case reports and our case series reported the resolution of subretinal and intraretinal fluid on OCT and the regression of SRNV leakage along with significant improvement in visual acuity in eyes treated with intravitreal anti-VEGF monotherapy (Figure 1).19,32,33 Mean number of injections in our study was 1.9 (range, 1-3). Improvement in visual acuity and control of SRNV with anti-VEGF drugs makes this the preferred treatment. In our series, we found that ranibizumab and bevacizumab were both equally effective, although there were insufficient data in the study to conclusively prove this.

**SUMMARY**

The role of anti-VEGF drugs in visual acuity or structural improvement in nonproliferative type 2A IJRT is still controversial. Anti-VEGF drugs definitely help to prevent disease progression and maintain or improve visual acuity in eyes with SRNV associated with type 2A IJRT. Larger series with long-term follow-up, however, are needed to address the long-term outcomes, the needed frequency of anti-VEGF administration, and its side effects.

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