MODULE 9.6
Anti VEGF Challenges and Side Effects

The ophthalmologist faces considerable challenges when treating patients with diabetic macular edema (DME) with anti - vascular endothelial growth factor (anti-VEGF) agents. According to a review by Blumenkranze and colleagues,[1] the correlation between baseline best-corrected visual acuity (BCVA) and macular thickness in patients with persistent macular edema is only modest. Numerous factors can influence visual function in eyes with DME, including the morphologic pattern of edema (focal or diffuse), duration of retinal edema, retinal perfusion, total retinal volume, and vitreomacular interface abnormalities (posterior hyaloidal traction, epiretinal membrane, and serous or tractional retinal detachment). Newer imaging technologies, such as swept-source optical coherence tomography (SS-OCT) and ultra-widefield angiography)[2-4] are being developed to improve the clinician's ability to observe morphologic changes in the retina and assess treatment efficacy and safety.

Although a considerable body of research has been conducted to evaluate anti-VEGF treatment protocols and retreatment criteria, the number of injections required for long-term improvement as well as the general long-term efficacy and safety of these agents (eg, beyond 5 years) is still unknown.[5] One review reported that ocular adverse events (AEs) occurred in up to 50% of eyes treated with bevacizumab, up to 80% of those treated with ranibizumab, up to 53% of those treated with lasers, and up to 70% of those treated with sham injections.[5] However, most of these events were not serious (eg, red eyes, eye pain, transient increases in intraocular pressure). The most frequent serious ocular AEs in the studies evaluated were:

- Significant increases in intraocular pressure
- Vitreous hemorrhage
- Endophthalmitis

In the VIVID and VISTA trials, the most common ocular AEs with aflibercept were conjunctival hemorrhage, eye pain, cataract, and intraocular pressure increases.[6] Ocular AEs were observed in approximately 59% of all patients who received aflibercept treatment. The most frequent serious ocular AEs in the VIVID and VISTA studies were vitreous hemorrhage and cataract.

Cardiovascular events have also been reported in studies of anti-VEGF agents with DME.[5,6] However, it is difficult to discern the effect of intravitreal treatment in a patient population that is already at elevated risk for cardiovascular disease, particularly if these events occur with similar frequency in the laser treatment groups.[6]

Another caveat with anti-VEGF therapies, as with other types of treatment, is the phenomenon of the nonresponder. Even though anti-VEGF treatment has demonstrated better outcomes than those achieved with alternative treatments, clinicians should be aware that in every study that analyzed the proportion of patients who gained a clinically relevant number of letters/lines of visual acuity, most patients (60%-85%) did not achieve this level of improvement.[5] Yet, this needs to be considered against the fact that alternative therapies (eg, laser therapy) have thus far predominantly been able to achieve vision stabilization only, not visual improvement. VEGF acts to promote the progression of diabetic retinopathy (DR) steps and the conversion to proliferative DR. Therefore, anti-VEGF agents act to block these effects, thus ameliorating the disease process itself.

References

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