Reduction of Diabetic Macular Edema in the Untreated Fellow Eye Following Intravitreal Injection of Aflibercept

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ABSTRACT: A 59-year-old patient with bilateral worsening diabetic macular edema received intravitreal injection of aflibercept (Eylea; Regeneron, Tarrytown, NY) to the left eye only. On 1-month follow-up, there was noted bilateral improvement of visual acuity and diabetic macular edema on spectral-domain optical coherence tomography imaging, reflecting bilateral effect of unilateral treatment with aflibercept.


INTRODUCTION

Aflibercept (Eylea; Regeneron, Tarrytown, NY) is an anti-vascular endothelial growth factor (VEGF) agent that has been approved for intravitreal injection for the treatment of diabetic macular edema (DME) in the United States, the European Union, Australia, and Japan. There are multiple reports of treatment effect, measured by reduction of central foveal thickness (CFT) and improvement in visual acuity, in the untreated fellow eye with intravitreal injection of other anti-VEGF agents, including bevacizumab (Avastin; Genentech, South San Francisco, CA) and ranibizumab (Lucentis; Genentech, South San Francisco, CA).1-3 Here we present the first reported case, to our knowledge, of improvement of DME in the untreated fellow eye with injection of intravitreal aflibercept.

CASE REPORT

A 59-year-old white woman with history of non-insulin dependent Type 2 diabetes returned for follow-up of moderate nonproliferative diabetic retinopathy and DME in both eyes. Visual acuity was 20/40 in the right eye and 20/50 in the left eye. During prior visits, mild DME was observed in the right eye. The left eye had received 11 intravitreal injections of ranibizumab 0.3 mg/0.05 mL in the past 13 months. Despite this treatment, spectral-domain optical coherence tomography (SD-OCT) showed macular edema had worsened in the right eye (CFT: 495 µm) and was persistent in the left eye (CFT: 641 µm) (Figures 1A and 1B). The patient received an injection of aflibercept 2 mg/0.05 mL in the left eye but declined treatment in the fellow eye. Four weeks later, vision had improved to 20/20-1 in both eyes, and macular edema improved in both eyes with CFTs of 385 µm and 372 µm, respectively, in the right and left eyes (Figures 1C and 1D).

DISCUSSION

Aflibercept is a 115-kDa recombinant fusion protein consisting of the VEGF binding domains of human VEGF receptors 1 and 2 joined to the Fc portion of human immunoglobulin G1 (IgG1).4 In contrast to bevacizumab and ranibizumab, this agent targets VEGF B and placental growth factor in addition to the VEGF A subtype. Aflibercept and bevacizumab both contain an Fc portion, which slows lysosomal degradation by binding to neonatal Fc receptor (FcRn). The serum half-life of aflibercept is 5 days to 6 days.

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in comparison to ranibizumab with a serum half-life of 2 hours. By design, ranibizumab is rapidly cleared from the bloodstream, and therefore has demonstrated little effect on the serum free VEGF concentrations. Compared to bevacizumab, aflibercept has shown a greater reduction in plasma-free VEGF levels despite having a lower initial serum concentration following injection. Serum-free VEGF concentrations have been measured to fall as soon as 3 hours following intravitreal injection of aflibercept and bevacizumab. Kim et al. demonstrated that retina-expressed FcRn is involved in transporting large IgG across the retina-blood barrier, which may be responsible for rapidly moving these large anti-VEGF agents into the systemic circulation.

Reduction of DME in the fellow, untreated eye after intravitreal injection of an anti-VEGF agent has been reported with bevacizumab and ranibizumab. This effect may be more common with bevacizumab; in a series of 35 patients treated in one eye with ranibizumab, no statistically significant reduction in CFT was found in the fellow eye, whereas in contrast,
a significant reduction in CFT was found with bevacizumab in the untreated eye of 55 patients.\textsuperscript{6}

There are reasonable clinical and pharmacokinetic data to support the reduction of DME with bevacizumab in the fellow, untreated eye. Given the similarities with bevacizumab in molecular structure and effect on serum VEGF concentration, aflibercept may potentially have similar effects in the untreated eye, as seen in this first report. Additional reports of aflibercept treatment effect in the fellow eye will be needed to further characterize and substantiate this phenomenon.

**REFERENCES**