CASE REPORTS

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Case report

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EFFECTS OF INTRAVITREAL AFLIBERCEPT (EYLEA) IN THE TREATMENT OF BILATERAL CYSTOID MACULAR EDEMA IN RETINITIS PIGMENTOSA – A CASE REPORT

EFEKTI INTRAVITREALNOG AFLIBERCEPTA (EYLEA) U LEČENJU BILATERALNOG CISTOIDNOG EDEMA KOD RETINITIS PIGMENTOSAE – PRIKAZ SLUČAJA

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Summary

Introduction. The aim of the study was to evaluate the effects of intravitreal injections of aflibercept (Eylea) on bilateral cystoid macular edema in a patient with retinitis pigmentosa. Material and Methods. A 17-year-old man presented with a moderate bilateral decrease of visual acuity (0.3) and ocular examination was performed. Optical coherence tomography imaging was performed and cystoid macular edema was detected in both eyes. Due to disease progression in a short period of time, intravitreal repeated injections of aflibercept (Eylea) were initiated according to recent clinical reports. Results. The initial values of cystoid macular edema before intravitreal therapy were 248 μm in the right and 237 μm in the left eye; they increased slowly in next several weeks. Four bilateral repeated doses of intravitreal aflibercept injections at 6-week intervals were given in local anesthesia. The patient reported a subjective improvement, and his visual acuity was 4/10 in both eyes. Objectively, the macular edema decreased at week 24, reaching 173 μm in the right and 188 μm in the left eye. Conclusion. There are few literature reports on the possible effects of intravitreal aflibercept injections in the treatment of retinitis pigmentosa-related cystoid macular edema. In our study, bilateral macular edema in a patient with retinitis pigmentosa has improved significantly after four consecutive treatments. Further studies are necessary with a larger sample size and longer follow-up period to obtain information on the role and safety of intravitreal drugs for cystoid macular edema in retinitis pigmentosa.

Key words: Macular Edema; Retinitis Pigmentosa; Intravitreal Injections; Recombinant Fusion Proteins; Treatment Outcome

Introduction

The term retinitis pigmentosa (RP) refers to a group of hereditary conditions [1] also known as retinal dystrophy. It is caused by the loss of photoreceptors, and is clinically characterized by retinal pigment deposits visible on fundus examination [2]. The disease can be inherited as an autosomal-dom-
from all the other anti-vascular endothelial growth factor (VEGF) medications, because it acts as a decoy receptor [4]. Aflibercept is a fusion protein (Fc) with constant region of human immunoglobulin G (IgG) and consists of extracellular domains of human VEGF 1 and 2, with improved binding affinity and superior pharmacokinetics. In case report of Mustafa et al., a single unilateral intravitreal injection of aflibercept was given to a patient with RP-associated CMO. Improvement in both visual acuity and macular thickness was seen at 1 month post-injection as well as maintenance of this improvement documented at 6 months [19].

None of the existing therapies has been confirmed so far to have absolute supremacy when it comes to the therapy of RP-related CMO. Despite the fact that pathogenic mechanisms of CMO development in RP have not yet been fully clarified, it is known that VEGF plays a significant role in its development, and can be a potential target of therapy. Aflibercept, as a newer drug, can have a leading role in RP associated CMO therapy, due to all its pharmacological characteristics, as well as the safety profile shown during long-term treatment [20]. More extensive studies, with larger samples of patients and longer-lasting application of intravitreal drugs are needed to confirm improvement of symptoms and clinical aspect, with caution due to potential adverse effects of intravitreal therapy.

**Case Report**

In 2017, a 17-year-old young man visited the private Eye Center in Novi Sad, Serbia, with his parents. He was previously diagnosed with myopic and astigmatic correction of -3.0 D sph/-1.0 D cylax 0 in both eyes, with best corrected visual acuity (BCVA) of 6/10 ever achieved, suggesting mild bilateral amblyopia. Fundoscopy revealed bilateral dense bone spicules, bilateral CMO, attenuated retinal vessels, and pale optic discs (Figure 1). Spectral domain optical coherence tomography (SD-OCT, Zeiss) showed marked bilateral CMO with central macular thickness (CMT) of 248 and 237 μm in the right and left eye, respectively (Figure 2). Intraocular pressure was 17/18 mmHg, and computerized visual field (VF) was performed by Zeiss Humphrey perimeter revealing constricted fields of 10 – 20 degrees in both eyes. He had no history of any previous CMO in earlier 3-year regular ophthalmologic follow-ups, with last CMT of 190 μm in his right, and 182 μm in his left eye. His mother and his brother also have RP, with a mildly clinical form, and BCVA of 20/20.

Initially, he received topical dorzolamide (20 mg/ml) eye drops bilaterally twice a day for 3 months, with no significant improvement in the degree or extent of CMO. On further examination, BCVA got worse in a short period of time due to CMO and it was 3/10 in both eyes. Therefore, this young man and his parents were given the information about new clinical study reports and a possible intravitreal treatment of CMO with aflibercept (Eylea).
The anti-VEGF medication selected for this patient was aflibercept (EYLEA; Regeneron Pharmaceuticals, Inc., Tarrytown, New York, USA, and Bayer Healthcare Pharmaceuticals, Berlin, Germany). Risks and benefits of the treatment were discussed with the patient. It was also highlighted that there was a limited evidence base for its usage in RP-associated CMO.

An informed consent was taken and the patient received bilateral intravitreal injections of 0.05 ml aflibercept (40 mg/ml) via standard aseptic technique in the operating theatre. There were no peri- or post-operative complications. A post-operative steroid anti-inflammatory antibiotic and non-steroidal anti-inflammatory drug eye drops were prescribed. Other oral and local medications were immediately discontinued with the start of aflibercept course.

Six weeks after the first treatment, BCVA improved to 4/10 in both eyes and the patient noticed subjective improvement. Optical coherence tomography revealed a marked CMO in both eyes, with CMT of 263 and 243 μm in the right and left eye, respectively. Second uncomplicated bilateral intravitreal injection of aflibercept was undertaken.

After 12 weeks from the beginning, his CMT in the right eye was reduced to 53 μm and to 46 μm in the left eye. After 18 weeks, the patient was treated with the third intravitreal aflibercept injection in both eyes, due to persistent CMO and re-accumulation of fluid (increase in CMO was noticed, 20 μm in the right and 35 μm in the left eye compared to CMT right before the third injection). After the third dose, only a minimal reduction of CMO was observed, and there was no major change in BCVA bilaterally. After the fourth injection of aflibercept in both eyes, and after 6 weeks of follow-up, CME decreased by 57 μm in the right and 44 μm in the left eye, compared to values measured before the fourth injection (Table 1). At week 24, the patient’s BCVA remained stable, at 4/10 in both eyes, but he had subjective impression of brighter vision, while his CMT returned to 173 μm in the right, and 188 μm in the left eye.

Regular follow-ups were scheduled for this patient and his CMO varied over time. It worsened seriously after the discontinuation of intravitreal aflibercept therapy after a year to almost double in regard to the baseline.
Table 1. Central macular thickness in cystoid macular edema in a patient with retinitis pigmentosa during four consecutive intravitreal injections of aflibercept in both eyes

<table>
<thead>
<tr>
<th>Central macular thickness (μm)</th>
<th>Aflibercept intravitreal injection</th>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central debljina makule (μm)</td>
<td>Aflibercept intravitrealna injekcija</td>
<td>Desno oko</td>
<td>Levo oko</td>
</tr>
<tr>
<td>3 months before aflibercept therapy/3 meseca pre početka intravitrealne terapije afliberceptom</td>
<td>1st dose/1. doza</td>
<td>190</td>
<td>182</td>
</tr>
<tr>
<td>0 week/0. nedelja</td>
<td>2nd dose/2. doza</td>
<td>248</td>
<td>237</td>
</tr>
<tr>
<td>6th week/6. nedelja</td>
<td>3rd dose/3. doza</td>
<td>263</td>
<td>243</td>
</tr>
<tr>
<td>12th week/12. nedelja</td>
<td>4th dose/4. doza</td>
<td>210</td>
<td>197</td>
</tr>
<tr>
<td>18th week/18. nedelja</td>
<td>–</td>
<td>230</td>
<td>232</td>
</tr>
<tr>
<td>24th week/24. nedelja</td>
<td>–</td>
<td>173</td>
<td>188</td>
</tr>
</tbody>
</table>

Conclusion

There are only few literature reports on the possible role of intravitreal aflibercept therapy for the treatment of retinitis pigmentosa-related cystoids macular edema. In our patient with retinitis pigmentosa, bilateral macular edema has improved significantly after four consecutive intravitreal treatments with aflibercept. Further studies are necessary with a larger sample size and longer follow-up period, to obtain information on the role and safety of intravitreal drugs for cystoids macular edema in retinitis pigmentosa.

References