Original article

Recurrent and chronic central serous chorioretinopathy. Retina thickness evaluation one month after intravitreal bevacizumab injection

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ABSTRACT

Purpose: To evaluate the efficacy of intravitreal injection of bevacizumab in patients with chronic central serous chorioretinopathy.

Methods: A study of 8 patients with central serous chorioretinopathy who were treated with intravitreal injection of bevacizumab. We studied the visual acuity with Snellen’s method and the foveal thickness, before and after the injection.

Results: The mean age of the patients was 50.25 years. After one month of follow-up, visual acuity before the injection was 0.431 ± 0.249 vision lines and after was 0.631 ± 0.310 vision lines (P = .017). The foveal thickness was 351.25 ± 78.492 µm and after treatment was 183.50 ± 22.640 µm (P = .012).

Conclusions: Intravitreal bevacizumab can be an alternative treatment in patients with serous central chorioretinopathy as it leads to a better objective visual acuity and foveal thickness with optical coherence tomography.

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Resumen

Coriorretinopatía serosa central recidivante y crónica. Estudio del espesor retiniano al mes del tratamiento con una inyección de bevacizumab intravitreo

Propósito: Evaluar la eficacia de la inyección intravitre de bevacizumab en pacientes diagnosticados de coriorretinopatía serosa central crónica.

Método: Estudio de ocho pacientes con coriorretinopatía serosa central tratada con inyección intravitrea de bevacizumab. Se incluye la agudeza visual con la escala de Snellen y el grosor de la mácula, ambas pre- y post-inyección.

Palabras clave:
Bevacizumab
Coriorretinopatía serosa central

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Resultados: La edad media de los pacientes fue de 50,25 años. El estudio se evaluó al cabo de un mes de evolución. La agudeza visual previa media fue de 0,431 ± 0,249 líneas de visión y la posterior a la inyección fue de 0,631 ± 0,310 líneas de visión (P = 0,017). El grosor medio de la mácula fue de 351,25 ± 78,492 μm y post-tratamiento de 183,50 ± 22,640 μm (P = 0,012).

Conclusión: El bevacizumab intravitreal puede ser una alternativa en los pacientes con coriorretinopatía serosa central ya que existe una mejora objetiva tanto de la agudeza visual como del grosor macular objetivado con tomografía de coherencia óptica.

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Introduction

Central serous chorioretinopathy (CSC) is an idiopathic disease characterized by a serous detachment of the neurosensory retina (DNR). It generally affects healthy young males and courses with blurred vision, metamorphopsia and occasionally paracentral scotoma. Various factors have been associated with the appearance of CSC such as personality type A, some psychoactive drugs and mainly stress although conclusive studies are not yet available.\(^1\)

Several treatment options are available, including pharmacological treatment with acetazolamide, nonsteroid anti-inflammatories or carbonic anhydrase inhibitors, as well as other techniques such as argon laser photoacoagulation and photodynamic therapy.

The objective of this study is to assess the efficacy of intravitreal bevacizumab injections in CSC as a new treatment alternative.

Subjects, material and method

The study comprised 8 eyes of 8 patients who exhibited a DNR relapse. After 3 months of evolution, treated with oral carbonic anhydrase inhibitors during one month (acetazolamide) at a dose of 500 mg/day, the DNR had not resolved and the symptoms persisted. At this point it was decided to apply an intravitreal injection of bevacizumab (Avastin\(^{®}\)), which was made one week later.

The entire procedure was documented with optic coherence tomography (OCT), SOCT Copernicus model, OPTOFOL Technology (Germany), with software predetermined analysis for measuring thicknesses.

The main variables of the study were:
- visual acuity with Snellen scale, before and after treatment with the drug.
- macular thickness in μm, measuring the thickness at the foveal level with OCT, before and after treatment with the drug. All the measurements were made by the same examiner.

In addition, demographic data of patients were collected as well as the affected eye (left or right) (Table 1).

The study excluded patients with systemic diseases such as cardiopathies, cardiac insufficiency, previous thromboembolism and females in fertile age. The systemic and ophthalmological history included patient 1 with systemic arterial hypertension, patient 3 with refractive surgery 5 years back, patient 5 who was pseudophakic and patient 7 who was in treatment for obesity and anxiety. All these exhibited retina pigment epithelium (RPE) alterations, excepting patients 2 and 4 who had suffered a single CSC episode which had spontaneously resolved after 5 months but, due to their profession, preferred shorter symptomatic times. Patient 6 exhibited significant RPE atrophy due to 4 CSC episodes, but he was given the option to resolve the episode earlier. The rest of patients had exhibited one longer CSC episode at 6 months. In their previous episodes, all patients had been treated with oral carbonic anhydrase inhibitors during one month with a dose of 500 mg/day. The study was carried out with the approval of the ethical committee of our hospital and all the patients signed an informed consent authorizing treatment with intravitreal bevacizumab under the compassionate use protocol.

All the injections were applied in the surgery under aseptic conditions. The dose of bevacizumab was of 1.25 mg in 0.05 ml. Subsequently, the patients were treated with topical antibiotic (ciprofloxacin) during 10 days. The patients were assessed 10 and 30 days after the injection; during the assessments, data on the study variables were collected as well as the presence or absence of subjective symptom improvements (SPSS 15.0).

Results

The mean age was of 50.25 years, 50% were right eyes and a further 50% were left eyes. Seven patients were male and one female.

The mean prior visual acuity was of 0.431 ± 0.249 vision lines.

One month after the injection, visual acuity was measured again, verifying an increase in vision lines with a mean of 0.631 ± 0.310 vision lines (P = 0.017) (Wilcoxon test), a statistically significant result (Table 2). Seven of the 8 patients achieved a subjective improvement of symptoms and visual acuity. As mentioned above, the remaining patient exhibited large RPE atrophy due to several recurring DNR episodes.

The mean thickness of the macula prior to the injection was of 351.25 ± 78.492 μm. In fluorescein angiograms, 4 patients exhibited a leak point close to the fovea while the rest exhibited diffuse unclear leak points.

The mean thickness of the macula after the intravitreal injection of bevacizumab was of 183.50 ± 22.640 μm (P = 0.012) (Wilcoxon test) (Table 3). Figs. 1 and 2 illustrate examples of 2 patients.

All the patients exhibited subjective symptom improvements with the exception of patient 6, who previously had
Table 1 – Data of the patients in our series of cases.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>VA pre</th>
<th>VA post</th>
<th>OCT pre</th>
<th>OCT post</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54</td>
<td>Male</td>
<td>0.2</td>
<td>0.6</td>
<td>292</td>
<td>180</td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>Male</td>
<td>0.7</td>
<td>1</td>
<td>391</td>
<td>176</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>Male</td>
<td>0.5</td>
<td>0.6</td>
<td>263</td>
<td>195</td>
</tr>
<tr>
<td>4</td>
<td>46</td>
<td>Male</td>
<td>0.7</td>
<td>1</td>
<td>480</td>
<td>190</td>
</tr>
<tr>
<td>5</td>
<td>61</td>
<td>Male</td>
<td>0.2</td>
<td>0.4</td>
<td>249</td>
<td>160</td>
</tr>
<tr>
<td>6</td>
<td>45</td>
<td>Male</td>
<td>0.05</td>
<td>0.05</td>
<td>400</td>
<td>230</td>
</tr>
<tr>
<td>7</td>
<td>43</td>
<td>Male</td>
<td>0.6</td>
<td>0.7</td>
<td>355</td>
<td>159</td>
</tr>
<tr>
<td>8</td>
<td>49</td>
<td>Female</td>
<td>0.5</td>
<td>0.7</td>
<td>380</td>
<td>178</td>
</tr>
</tbody>
</table>


Table 2 – Visual equity comparison before and after the bevacizumab injection.

<table>
<thead>
<tr>
<th>No.</th>
<th>Mean</th>
<th>Typical deviation</th>
<th>Min.</th>
<th>Max.</th>
<th>Z</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA pre</td>
<td>8</td>
<td>0.4313</td>
<td>0.24920</td>
<td>0.05</td>
<td>0.70</td>
<td>-2.379</td>
</tr>
<tr>
<td>VA pos</td>
<td>8</td>
<td>0.6313</td>
<td>0.31046</td>
<td>0.05</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>

Wilcoxon test.

Table 3 – Retinal thickness comparison measured in μ before and after the bevacizumab injection.

<table>
<thead>
<tr>
<th>No.</th>
<th>Mean</th>
<th>Typical deviation</th>
<th>Min.</th>
<th>Max.</th>
<th>Z</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRE</td>
<td>8</td>
<td>351.25</td>
<td>78.492</td>
<td>249</td>
<td>480</td>
<td>-2.521</td>
</tr>
<tr>
<td>POS</td>
<td>8</td>
<td>183.50</td>
<td>22.640</td>
<td>159</td>
<td>230</td>
<td></td>
</tr>
</tbody>
</table>

Wilcoxon test.

exhibited low visual acuity and ophthalmological alterations at the level of the RPE.

In addition, all patients exhibited a significant subretinal liquid reduction after the bevacizumab injection. Even so, in some cases said reduction was partial with a minimum of DNR remaining which did not produce symptoms in the patients.

Discussion

CSC is a disease without a clear scheme for treatment. Typically, various medical treatments have been applied such as topical or systemic carbonic anhydrase inhibitors. However, these treatments are only beneficial in patients with first DNR episodes, when the detachment is small.

Other treatments include argon laser photocoagulation and photodynamic therapy. The former is carried out if the angiograph shows a clear leak point and provided this point is never close to the fovea. This is because the complications derived from the expansion of the scar and the severe alterations of the retina pigment epithelium could drastically reduce vision. Photodynamic therapy has been applied in patients with chronic CSC. However it has been suggested that said therapy can produce choroidal neovascularization in the long term.

The physiopathology of the disease is not yet known. It is believed that it is caused by small alterations in the barrier and

![Fig. 1 – Male, 46, exhibiting for one year LE central serous choroidopathy in follow-up. (Left) The previous VA is 0.7 and OCT shows neuroepithelium detachment associated to retina pigment epithelium detachment. (Right) It is decided to inject bevacizumab, observing one month later VA improvement of 1 while OCT showed significant reduction of liquid.](image-url)
pumping functions of the retina pigment epithelium. Indocyanine green angiography has allowed the observation of these hyper-permeable areas which later give rise to DNR.

Bevacizumab is a monoclonal antibody that selectively bonds with a protein, the vascular endothelial growth factor (VEGF). It has been utilized in ophthalmology to treat various conditions such as myopic choroidal neovascularization, diabetic retinopathy, central retinal vein occlusion, neovascular glaucoma, etc. The mechanism of action of bevacizumab in CSC is not known although it is believed it could be related with the involvement of vascular permeability. The ultrastructural findings encountered in experimental chronic CSC models demonstrate that the subretinal liquid leak is due to the disruption of the external blood-retina barrier caused by the degeneration of pigment epithelial cells associated with choriocapillary endothelial cell damages. It has been postulated that the certain degree of venous or capillary congestion subsequent to ischemia in one or several choroidal sectors could be the cause of the hyper permeability associated to chronic CSC as well as the stimulating for the over expression of VEGF in these patients.

In our series of cases, we have effectively verified a reduction of DNR in all patients, corresponding to a reduction in vascular permeability that would support said hypotheses on the action mechanism of bevacizumab in patients with chronic CSC.

Together with DNR reductions, our study has also verified a subjective as well as objective improvement of visual acuity in all patients except one who at baseline had a visual acuity under 0.1 lines of vision due to a considerably large RPE alteration. It is known that the visual acuity of patients with a first episode of CSC is generally able to recover, even though this occurs months after the DNR resolution and is spontaneously achieved in 80–90% of cases within 4 months. For this reason, in most occasions treatment is not established at the onset. Frequently, there is a persistence of a slight metamorphopsia, scotomae, contrast sensitivity alterations and slight defects in color vision, all these explained by the ultrastructural alterations in endured during the CSC episode. However, some eyes suffer permanent visual acuity reductions and up to 50% of patients exhibit recurring episodes. In the literature, the majority of authors apply bevacizumab to treat patients with chronic CSC. There are very few patients who were treated during the first episode although in all these the condition resolved after the treatment. Controversy arises because it is not known whether the resolution is due to the application of the drug or to the natural history of the disease. In the light of the results we have obtained and comparing these with the literature, it seems logical to think that treatment with bevacizumab would accelerate the resolution process and therefore the probability of suffering larger pigment epithelium alterations would be smaller because the duration of the episode is diminished with less visual repercussions in patients.

None of the cases exhibited relapses even though the follow-up period was very limited (one month) and this did not allow us to determine the mid-term evolution.

It can be concluded that antiangiogenic therapy (bevacizumab) could be useful for treating relapsing and chronic CSC in order to accelerate the resolution of the clinical condition, on the basis that in this series we have observed subretinal liquid reduction and objective as well as subjective improvements, provided that an extended period of evolution of the disease has not already caused irreversible damages in photoreceptors and other retinal structures. However, the limitations of this study must be taken into account, mainly the small number of patients and the absence of a control group. In order to verify that genuine benefits can be obtained with this therapeutic modality, it would be necessary to carry out randomized studies with higher number of patients.

Conflict of interests

The authors have no conflict of interests to declare.

References