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 intravitrea 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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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 photocagulation 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 0.651 ± 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 angiographs, 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>0.4313</td>
<td>0.24920</td>
<td>0.05</td>
<td>0.70</td>
<td>−2.379</td>
<td>0.017</td>
</tr>
<tr>
<td>VA pos</td>
<td>0.6313</td>
<td>0.31046</td>
<td>0.05</td>
<td>1.00</td>
<td></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>351.25</td>
<td>78.492</td>
<td>249</td>
<td>480</td>
<td>−2.521</td>
<td>0.012</td>
</tr>
<tr>
<td>POS</td>
<td>183.50</td>
<td>22.640</td>
<td>159</td>
<td>230</td>
<td></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.
pumping functions of the retina pigment epithelium. Indocya-
nine 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, dia-
abetic 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 ultra-
structural 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 postu-
lated 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 reduc-
tion 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 acu-
ity 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 estab-
lished at the onset. Frequently, there is a persistence of a slight
metamorphopsia, scotomas, 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 reduc-
tions 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 com-
paring 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 pig-
ment epithelium alterations would be smaller because the
duration of the episode is diminished with less visual reperc-
ussions 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 (beva-
cizumab) could be useful for treating relapsing and chronic
CSC in order to accelerate the resolution of the clinical con-
dition, 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 limi-
tations 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


