INTRAVITREAL BEVACIZUMAB FOLLOWED BY FOCAL LASER FOR DIFFUSE DIABETIC MACULAR EDEMA OF RECENT PROGRESSION. A CLINICAL CASE

BEVACIZUMAB INTRAVÍTREO SEGUIDO DE LÁSER FOCAL EN EL EDEMA MACULAR DIABÉTICO DIFUSO DE PROGRESIÓN RECENTE. CASO CLÍNICO

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ABSTRACT

**Case report:** We report the case of a 48-year-old man with diffuse diabetic macular edema of recent progression treated with two consecutive intravitreal injections of bevacizumab followed by focal laser therapy, with good anatomic and functional response.

**Discussion:** Diffuse diabetic macular edema is difficult to manage and frequently requires multiple therapies. We propose the use of bevacizumab as a strategy to reduce diffuse macular edema, facilitating the application of laser therapy (Arch Soc Esp Oftalmol 2009; 84: 209-212).

**Key words:** Diabetic macular edema, diffuse macular edema, antiangiogenic therapy, bevacizumab, combined treatment, antiangiogenic therapy plus laser.

RESUMEN

**Caso clínico:** Se presenta el caso de un varón de 48 años de edad con edema macular diabético (EMD) difuso en su ojo derecho (OD) de reciente progresión, que es tratado con dos inyecciones intravitreas consecutivas de bevacizumab seguido de láser focal, mostrando buena respuesta funcional y anatómica.

**Discusión:** El EMD difuso es de difícil manejo y con frecuencia precisa de multiterapias para su control. Proponemos el uso de bevacizumab intravítreo como coadyuvante para reducir el EMD difuso de progresión reciente, y facilitar la aplicación de fotoagulación con láser.

**Palabras claves:** Edema macular diabético, edema macular difuso, tratamiento antiangiogénico, bevacizumab, tratamiento combinado, terapia antiangiogénica más fotoagulación.
INTRODUCTION

Diabetic macular oedema (DME) consists of a retinal thickening of the macular area due to extracellular vacuolation of fluid and proteins. DME is secondary to structural changes of retinal vessels leading to their increased permeability, thus going through the blood-retinal barrier. The vascular endothelial growth factor (VEGF) has been mentioned as participating in the pathogenesis of several ocular diseases, including DME (1), due to its capacity to increase the permeability of the vascular endothelium. In addition, angiogenic and neuroprotective functions have been attributed to it.

DME is the most frequent cause of loss of vision in diabetes type II patients. Laser photocoagulation obtains good results in a focal macular edema but does not achieve significant visual acuity gains in diffuse macular edema (2), with the latter constituting a challenge for present day ophthalmology.

Recently, the results of the intravitreal application of different antiangiogenic agents have been published (3,4) in the management of DME refractory to other treatments such as laser photocoagulation, pars plana vitrectomy and intravitreal injections of triamcinolone.

This short communication presents the case of a male with unilateral diffuse DME with less than three months of evolution and involvement of the macular centre, treated with repeated bevacizumab injections followed by focal laser, which achieved a recovery of visual acuity (VA) to base levels.

CASE REPORT

A 48 year old male diagnosed with diabetes mellitus type II was referred to the retina practice of our hospital due to VA reduction in his right eye with less than three months of evolution. Upon exploration, the patient exhibited a best corrected visual acuity of 0.3 in the RE and 0.9 in the LE. Biomicroscopy of the anterior segment gave normal results. Intra-ocular pressure (IOP) was of 14 mm Hg in both eyes. The eye fundus exhibited microaneurisms with some hard exudate and dispersed intraretinal hemorrhages in both eyes as well as extended retinal thickening involving the centre of the macula in the RE. The image obtained by Optical Coherence Tomography (OCT) with Stratus OCT-3 (Carl Zeiss Meditec, Dublin, CA) of the RE showed an intraretinal edema with neurosensory detachment and foveal thickness of 577 µ. Fluorescein angiography (FAG) showed a diffusion of the dye which increased in late times and affected the entire macular area (fig. 1). The diagnosis was bilateral slight non-proliferative diabetic retinopathy with diffuse DME, severe in RE. Due to the consid-
erable retinal thickening with absence of macular traction shown by the OCT, it was proposed to treat with intravitreous bevacizumab (Avastin®, Genentech Inc, San Francisco, CA, USA) instead of triamcinolone acetate due to the reduced local side-effects exhibited by the former in what concerns IOP elevation and cataract progression.

After obtaining the patient’s informed consent and the authorization of the Health Ministry, the patient was treated with an intravitreous injection of 1.25 mg in 0.05 ml of Avastin®, revised 24 hours later, after one week and at 15 day intervals with complete ophthalmological exploration and OCT in each visit. Six weeks after the injection, the patient’s VA increased to 0.6 and the retinal thickening with foveal neurosensory detachment went down to a foveal thickness of 330 µ. Even so, the retinal thickening persisted and at eight weeks increased to 419 µ (fig. 2). Two months later, a second objection of 1.25 mg of Avastin® was administered. One month later, vision increased to 0.7 and 0.9 with stenopeic, while the OCT showed a minimum neurosensory detachment with resolution of the intraretinal edema and foveal thickness of 227 µ. In turn, the FAG revealed an important reduction of hyper-fluorescence with leaks in an area of 2 diameters of superior-temporal disc to fovea (fig. 3). Laser focal photocoagulation of the microaneurisms visible in the macular area was performed. One month later, uncorrected VA was up to 0.9 while the OCT showed a foveal thickness of 206 µ with physiological depression and without neurosensory detachment (fig. 4).

**DISCUSSION**

At present, the management of diffuse diabetic macular edema remains a challenge. In most cases, laser treatment of diffuse DME does not improve visual acuity (1). The proposed alternatives include vitrectomy with or without resection of the internal...
limiting membrane (ILM (5), which is particularly
indicated in the presence of macular traction either
due to posterior hyaloid or thickened ILM or to an
epiretinal membrane. Other strategies include
intravitreous injection of intra-ocular corticoids and
more recently of antiangiogenic agents (3,4).

Intravitreous injections involve risks inherent to
the surgical technique, to which we must add those
derived from local and systemic adverse reactions
to the drugs. The intravitreous injection of triamcin-
olone brings about well-known side-effects,
including increased intraocular pressure which
sometimes requires filtrating surgery, as well as
progression of cataracts and the risk of endoph-
thalmitis derived not only from the surgical tech-
nique but also from the immunosuppressant effect
of the drug. The result of the intravitreous triami-
cinolone injection a temporary, with the edema
relapsing at an early stage depending on the dosage
applied.

The use of VEGF inhibiting agents is supported by
numerous studies which involve this factor directly
in the pathogenesis DME (1). Bevacizumab is a com-
plete monoclonal anti-VEGF antibody and therefore
comprises two union sites for VEGF capable of
inhibiting all its active forms. According to its size, it
is allegedly incapable of penetrating retina layers,
which could be an advantage when treating diabetic
macular edema because in theory it reduces its elim-
ination due to vitreal cavity washing, thus increasing
the contact time with the internal retina and the reti-
nal vessels. To date, no serious local or systemic risks
derived from the intravitreous injection of 1.25 mg of
bevacizumab have been described. In comparison with
other antiangiogenic agents such as ranibizum-
ab and pegaptanib, bevacizumab has the advantage
of its lower cost and higher accessibility in the hos-
pital environment due to being a drug developed and
utilized in metastasic colon cancer treatment. How-
ever, it has the drawback of needing previous author-
ization by the Health Ministry for its application as a
medication for compassionate use.

This paper presents the case of a diffuse DME of
recent progression in a young adult, which
improved considerably after two intravitreal injec-
tions of Avastin®, thus facilitating the application of
laser on the microaneurisms. This is particularly
difficult in the presence of an extended macular
edema. No local or systemic adverse reactions have
been observed. This is a single case with a short fol-
low-up term but the rapid anatomic response with
significant visual improvements leads us to ponder
the convenience of an early use of this type of

drugs.

The use of bevacizumab in diffuse DME of
recent progression could be useful as a coadjuvant
for a laser to restore vision to the initial levels. Only
extended, progressive and comparative studies will
be able to demonstrate whether these new drugs are
beneficial in repeated injections or their optimum
use lies in being coadjuvants to other treatments.

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