Short communication

Cystoid macular oedema after fingolimod treatment in multiple sclerosis∗

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ABSTRACT

Case report: A woman, treated with immunomodulatory and immunosuppressive drugs for multiple sclerosis, developed macular edema 4 months after oral fingolimod administration. The patient was previously seen by an ophthalmologist, with a normal anterior segment and funduscopic examination. Four months after the treatment she referred to decreased visual acuity in both eyes. The funduscopic and OCT examination now revealed cystoid macular edema (CME).

Discussion: Attention to visual changes and periodic funduscopic examinations are an important part of monitoring while using fingolimod. In our patient early recognition and discontinuation of fingolimod did not result in resolution of the CME.

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Edema macular quístico por fingolimod en esclerosis múltiple

RESUMEN

Caso clínico: Mujer, tratada con inmunomoduladores e inmunosupresores por esclerosis múltiple, desarrolló edema macular 4 meses después de iniciar terapia oral con fingolimod. Previamente la paciente fue explorada por un oftalmólogo: el segmento anterior y el fondo de ojo fueron normales. Cuatro meses después del tratamiento refirió disminución de la agudeza visual en ambos ojos; el estudio fundoscópico y la OCT muestra edema macular quístico (EMQ).

Discusión: Atención a los cambios en la visión y estudios periódicos del fondo de ojo son importantes en la monitorización del paciente tratado con fingolimod. En nuestro paciente la identificación precoz y la retirada del esfingolimod no resolvió el EMQ.

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Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system which predominantly affects young women. It is the first cause of neurological disability in young people.\(^1\) In the past 20 years significant developments occurred in MS breakouts therapy. Fingolimod is a modulator of the sphingosine-1-phosphate receptor (RE-1-F) recently approved at a dose of 0.5 mg/day orally administered.\(^2,3\) This drug has brought about a revolution in the treatment of MS (breakouts, administration groups) although it exhibits significant side effects such as bradycardia in the first few hours and macular edema in the first few months of administration. A patient is described with severe vision loss and cystoid macular edema with fingolimod which was not resolved with drug withdrawal.

Clinic case

Female patient who in 2002, at the time aged 31, exhibited peripheral vertigo. In 2004, she visited the emergency service due to acute pain in the left abdomen. In 2005, she exhibited bilateral pars planitis. In 2006, dyesthesia appeared in the lower limbs. In 2009, dyesthesia also expressed in the upper limbs together with voiding urgency. Resonance was performed with gadolinium, evoked potential and cerebrospinal fluid study which gave a diagnostic of MS. Treatment was established with immunosuppressants and symptomatic treatment, despite which the patient exhibited arthokinetic symptomatology and disabling motor alteration in the left lower limb with outbreaks. In 2011, she visited with cerebellum dysfunction and cognitive involvement. In May 2011, with previous ophthalmological study, she began treatment with Gilenya\(^\text{®}\) (Gilenya\(^\text{®}\) 0.5 mg, Novartis Pharma Stein AG, Stein, Switzerland). The patient did not refer ophthalmological symptoms and visual acuity was of one in both eyes. Anterior biomicroscopy study was normal, as well as ocular fundus without evidence of macular edema. After 4 months treatment with Gilenya\(^\text{®}\) visual acuity was of 0.2 in the right eye (RE) and 0.4 in the left eye (LE). The anterior segments did not exhibit alterations but through funduscopy and optic coherence tomography (Topcon OCT; 3D OCT-2000) bilateral cystic macular edema was observed (Fig. 1 left and Fig. 2 left). The drug was withdrawn but the macular edema did not improve after 2 months, with a visual acuity remaining unchanged (Fig. 1 right and Fig. 2 right). The macular edema was not treated due to the patient refusal upon severe worsening of systemic pathology.

Discussion

In 1993, standard therapy for MS was introduced, i.e., interferon beta-1a injections.\(^4\) Since then other drugs (Avonex, Copaxone, Rebif and Tysabri) have been developed with varied results, all being injectable. Clinical trials have demonstrated that 2 oral immunosuppressants (fingolimod and cladribine) are efficient and superior to interferon and reduce outbreaks between 50% and 60%. Fingolimod (Gilenya\(^\text{®}\)) has been recently authorized by the Spanish medication and health products agency (registration number 11677005). This drug is a selective immunosuppressant that modulates the sphingosine receptor (RE-1-F) and redistributes lymphocytes, preventing infiltration into the central nervous system.\(^2,3\) It is indicated in patients with highly active remitting-recurring MS which does not respond to interferon or those in which sclerosis evolves very quickly.\(^2,3\) RE-1-F is distributed throughout the body and for this reason fingolimod has the potential of exhibiting a broad range of side effects. In clinical studies, macular edema expressed in 0.4% of cases, against 0.1% of controls, particularly in the first 4 months of treatment. If the patient had a history of diabetes or uveitis, the risk of macular edema was 20%.\(^2,3\) Saab et al.\(^5\) described one case of reversible macular edema in a kidney transplant patient treated with fingolimod. This drug can produce loss of vision secondary to macular edema which is dose-dependent and typically resolves when treatment is withdrawn.\(^3\) Infrequently, vision loss is permanent after drug withdrawal, as in the described case, where macular edema persisted 2 months after withdrawing the drug. Accordingly, an ophthalmological study is recommended before establishing treatment and after 4 months. At present there is no conclusion for issues such as course (irreversibility) and best treatment of macular edema caused by fingolimod. Patients with a history of diabetes melitus and/or uveitis are at greater risk of macular edema and possibly a more torpid course, although both processes do not constitute contraindications for treatment.\(^3\)

Fig. 1 – Left: Right eye spectral domain optic coherence tomography (SD-OCT) at month 4 of treatment with fingolimod: scan passing through the fovea. Cystic macular edema with intraretinal and subretinal liquid without hyaloid traction. Right: right eye SD-OCT two months after treatment withdrawal: scan passing through the fovea in the same direction as the previous figure. Very little changes are evidenced.
Fig. 2 – Left: left eye spectral domain optic coherence tomography (SD-OCT) at month 4 of treatment with fingolimod: scan passing through the fovea. Central macular thickening with intraretinal cysts and focal detachment of pigment epithelium. Right: left eye SD-OCT two months after withdrawing treatment; scan passing through the fovea in the same direction as the previous figure. The irreversible nature of the process is evidenced.

Conflict of interests
No conflict of interests has been declared by the authors.

REFERENCES


