Short communication

**Methotrexate as a treatment in ocular cicatricial moderate pemphigoid**

**A. Hervás Ontiveros** a,*, **D. Salom** a, **E. España Gregori** a, b, **E. Jiménez Herrero** c, **M. Díaz-Llopis** a, b

a Servicio de Oftalmología, Hospital Universitario la Fe, Valencia, Spain
b Departamento de Cirugía, Unidad Docente de Oftalmología, Universidad de Valencia, Hospital Universitario La Fe, Valencia, Spain
c Departamento de Anatomía Patológica, Universidad de Valencia, Hospital Universitario la Fe, Valencia, Spain

**ABSTRACT**

**Clinical case:** A 73-year-old woman presented with a history of non-specific symptoms and photophobia in both eyes of 1 year progression. The examination revealed a bilateral symblepharon and fornix shortening. Immunohistochemical analysis confirmed the presence of linear deposits of IgG, IgM and C3 along the conjunctival basement membrane. With the diagnosis of ocular cicatricial pemphigoid, systemic treatment with subcutaneous methotrexate was prescribed.

**Discussion:** We consider such treatment a very effective initial immunosuppressive alternative in patients with moderate conjunctival inflammation and in cases of rapid progression.

© 2013 Sociedad Española de Oftalmología. Published by Elsevier España, S.L.U. All rights reserved.

**Metotrexato como tratamiento en el penfigoide ocular cicatricial moderado**

**RESUMEN**

**Caso clínico:** Una mujer de 73 años se presenta con historia de molestias inespecíficas y fotofobia en ambos ojos (AO) de un año de evolución. A la exploración se observa un simblefaron bilateral y acortamiento de fondos de saco. El análisis inmunohistoquímico (IHQ) confirma la presencia de un depósito lineal de IgG, IgM y C3 a lo largo de la membrana basal conjuntival. Ante el diagnóstico de penfigoide ocular cicatricial (POC) se pauta tratamiento sistémico mediante metotrexato (MTX) subcutáneo.


* Corresponding author.
E-mail address: anheront@gmail.com (A. Hervás Ontiveros).

2173-5794/$ – see front matter © 2013 Sociedad Española de Oftalmología. Published by Elsevier España, S.L.U. All rights reserved.
Introduction

Ocular cicatricial pemphigoid (OCP) is a recurrent, chronic, autoimmune inflammatory disease affecting the mucous membranes. It is characterized by bilateral, asymmetrical conjunctival cicatrisation with fibrosis and the formation of symblepharon.\(^1\) Its diagnosis is based on its clinical manifestations and progression, although the definitive diagnosis is established by immunohistochemistry (IHC) of the conjunctival biopsy. A linear deposit of IgG, IgA, IgM or C3 along the epithelial basal membrane should be demonstrated by direct immunofluorescence (DIF).\(^2\) In this paper, we present the case of a patient with moderate OCP where treatment with methotrexate enabled a complete remission and disease control.

Clinical case

A 73-year-old woman with a history of hypertension and diabetes was referred due to non-specific discomfort in both eyes and photophobia for one year, which failed to improve with lubricating treatment. Visual acuity (VA) was 0.8 in her right eye and 0.7 in her left eye. There was bilateral conjunctival hyperaemia with lower superficial punctate keratitis (SPK) (Fig. 1A). The patient had bilateral symblepharon with shortened fornices and subconjunctival fibrosis, in addition to mild lower trichiasis (Fig. 1B). Since ocular involvement due to OCP was suspected, the patient was treated temporarily with topical steroids (FML®) and artificial tears (Artific®, single dose) and a decision was made to perform a conjunctival biopsy with an IHC test. At first, the DIF showed poorly defined deposits of Ig and complement on the basal membrane, and, therefore, the result was inconclusive. The histological exam showed the appearance of subepithelial microvesicles tending to epithelial dehiscence, fibrosis of the substantia propria, squamous metaplasia and stromal inflammatory changes with plenty of lymphocytes (Fig. 2).

Due to the presence of histological signs consistent with OCP, a second IHC test was conducted. After the second staining, the presence of a linear deposit of IgG, IgM and C3 was confirmed along the basal membrane (Fig. 3) with a linear immunoperoxidase staining positive for IgG and IgM.

Due to the moderate nature and active phase of the disease, immunosuppressive treatment was initiated with methotrexate 15 mg weekly by subcutaneous route for two years. An outstanding improvement was observed after six months of treatment with complete remission of the discomfort. The VA increased to 0.9 in both eyes. An important reduction of the conjunctival hyperaemia was observed and the SPK disappeared. A stable shortening of the fornices was also seen (Fig. 4). No adverse effects of any kind were experienced.

At present, and after two years of treatment, the patient remains stable with no relapses or new disease outbreaks.

Discussion

An early diagnosis of the ocular involvement is required in OCP due to its progressive nature and the seriousness of its sequelae. The differential diagnosis should include burns, trauma, infectious conjunctivitis and sarcoidosis, among others. The pathology is non-specific and, even though the clinical course may help us in the diagnosis, a definitive exam is required. The confirmation is provided by DIF, with a 60–80% certainty. The most sensitive test is the amplified biotin-streptavidin immunoperoxidase test, which was positive in our case, thus confirming with certainty the suspected diagnosis; based on that result we initiated the
immunosuppressive therapy. Inflammation control is paramount for treatment. Local therapy consists of lubricants, anti-inflammatory drugs, topical steroids and therapeutic contact lenses, in addition to the surgical treatment of complications. However, the overall approach should address the systemic immune process, including the use of steroids, dapsone, sulfonamides, azathioprine, methotrexate, mycophenolate and cyclophosphamide. Additionally, the use of rituximab and intravenous immunoglobulin has been described in serious cases refractory to conventional treatment. Despite this, the disease progresses with serious consequences in 10% of cases. The main function of immunosuppressive agents is to work as long-term substitutes of steroids. As in our case, that drug may be first used when the initial conjunctival inflammation is significant and the progression is fast. The drugs used for OCP have many side effects, although no complications were recorded in our case. Additionally, blood tests every 4–6 weeks, liver function tests every 12 weeks and renal function monitoring are required.

We consider that early diagnosis and timely treatment are important steps for an adequate control. In our patient, initiating treatment with methotrexate was effective to stop the inflammatory activity and for healing progression. We consider such treatment a very effective initial immunosuppressive alternative in patients with moderate conjunctival inflammation and in cases of rapid progression.

Conflicts of interest

The authors declare that they do not have any conflicts of interests.

References