American Journal of Ophthalmology Case Reports 10 (2018) 264–267

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.elsevier.com/locate/ajoc

Brief Report

Adrenocorticotropic hormone analogue as novel treatment regimen in ocular cicatricial pemphigoid

Yael Sharon[a,*], David S. Chu[a,b]

[a] Metropolitan Eye Research and Surgery Institute, Palisades Park, NJ, USA
[b] Institute of Ophthalmology and Visual Science, New Jersey Medical School, Rutgers University, Newark, NJ, USA

ARTICLE INFO

Keywords:
Adrenocorticotropic hormone
Ocular cicatricial pemphigoid
Clinical outcome

ABSTRACT

Purpose: To report the clinical outcome of a patient with ocular cicatricial pemphigoid, treated with adrenocorticotropic hormone gel.

Observations: A 75-year-old female with a biopsy proven ocular cicatricial pemphigoid (OCP) presented with bilateral conjunctival inflammation, fornix shortening, subepithelial fibrosis and corneal scarring. The patient was previously treated with topical steroids, topical cyclosporine and lubricating drops, and had undergone several amniotic membrane transplants due to recurrent corneal erosions. Once OCP diagnosis was established, the patient was started on oral corticosteroids (60 mg daily). In order to wean the patient off from systemic steroids, other immunomodulatory agents had been tried, including mycophenolate mofetil (1000 mg twice daily) and methotrexate (up to 25 mg weekly). However, none of these agents adequately controlled the ocular surface inflammation, and the patient experienced bilateral progressive cicatrization and corneal decompensation, as well as the development of side effects from the systemic corticosteroids, methotrexate and mycophenolate mofetil therapies. Treatment with twice weekly subcutaneous adrenocorticotropic hormone (ACTH) gel was initiated, along with tapering of systemic corticosteroids. During the 19 months treatment period, the patient demonstrated significant improvement in the ocular surface inflammation, visual acuity was stable and no significant adverse effects were observed. Systemic corticosteroids dosage was successfully reduced from 10 mg/day to none at last follow up.

Conclusions and importance: ACTH gel has shown to be an effective and safe treatment option for chronic, refractory and progressive ocular inflammatory disease. To the best of our knowledge, this is the first case report of a patient with OCP, treated successfully with ACTH gel. This case report may encourage ophthalmologists to employ ACTH gel in the management of OCP.

1. Introduction

Ocular cicatricial pemphigoid (OCP) is a specific entity in a group of chronic inflammatory mucocutaneous blistering conditions, called mucous membrane pemphigoid.[1] The disease is characterized by scarring and shrinkage of the conjunctiva as well as in extraocular mucous membranes, such as the oral mucosa, esophagus, larynx, and skin.[1,2] The disease commonly affects females with an average age of onset of 65 years.[3] OCP is diagnosed by linear antibody and complement deposition at the epithelial basement membrane of the involved mucosa. The earliest clinical finding is a chronic, recurrent, papillary conjunctivitis. Recurrent attacks of conjunctival inflammation can lead to destruction of goblet cells, lacrimal gland ductule obstruction, entropion, trichiasis and corneal abrasions, vascularization and ulceration. Progressive cicatrization is common, as well as remissions and exacerbations periods with therapy.

Treatment for the majority of OCP patients utilizes systemic immunomodulatory therapies in order to prevent cicatrization. Systemic treatments include corticosteroids, and steroid-sparing agents, such as cyclophosphamide, mycophenolate mofetil, azathioprine, methotrexate (MTX), and diaminodiphenylsulfone (dapsone).[4–7] Usually, monotherapy with corticosteroids, along with its adverse events, is not sufficient to produce long-term remission, nor able to achieve an adequate level of sustained immunosuppression in OCP patients. Furthermore, the later the stage of disease upon initiation of therapy, the more likely it will progress and not respond to therapy. However, the use of steroid-sparing medications also carries potential risks and side effects. Cyclophosphamide can cause leukopenia, anemia, bone marrow suppression, and bladder carcinoma.[2] Common side effects of mycophenolate mofetil are nausea, diarrhea, abdominal pain, fever and anemia. MTX

* Corresponding author.
E-mail address: yael@mersieye.com (Y. Sharon).

https://doi.org/10.1016/j.ajoc.2018.03.018
Received 29 September 2017; Received in revised form 12 March 2018; Accepted 19 March 2018
Available online 20 March 2018

may cause hepatotoxicity, pneumonitis, pulmonary fibrosis, pancytopenia, and malignancy. In some patients with reluctant disease, immunomodulatory treatments, such as intravenous immunoglobulin (IVIg) and rituximab, have shown some success.[8,9]

Adrenocorticotropic hormone (ACTH) is a member of a group of molecules called melanocortins (MCs), derived from the precursor proopiomelanocortin (POMC) and endogenously produced in the hypothalamic-pituitary pathway. ACTH acts primarily to stimulate and regulate steroids production. ACTH has recently been shown to have anti-inflammatory effects beyond endogenous steroid production.[10,11]

ACTH gel was approved by the United States Food and Drug Administration (FDA) in 1952 for a variety of autoimmune and inflammatory conditions. ACTH gel is indicated for severe acute and chronic allergic and inflammatory ocular processes including keratitis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis and anterior segment inflammation.[12] It also has shown efficacy in various systemic inflammatory diseases including systemic lupus erythematosus,[13] multiple sclerosis,[14] nephrotic syndrome,[15] infantile spams,[16] dermatomyositis, and polymyositis.[17]

To the best of our knowledge, treatment of ocular cicatricial pemphigoid with ACTH gel has never been reported. In this case report, we describe the clinical course and outcome of a patient with ocular cicatricial pemphigoid, treated with ACTH gel.

2. Case report

A 75-year-old woman was referred in April, 2015 due to chronic conjunctival redness, foreign body sensation, irritation and blurred vision in both eyes. She had previously been treated with topical steroids, topical cyclosporine (0.05%) and frequent use of lubricating eye drops. The patient had undergone amniotic membrane transplants in both eyes due to persistent corneal epithelial defects. She has a history of open-angle glaucoma, exudative age-related macular degeneration and cataract surgery in her right eye. The best corrected visual acuity (BCVA) was counting fingers (CF) in both eyes at the time of initial presentation. Slit-lamp examination revealed trichiasis, conjunctival injection, fornix shortening and subconjunctival fibrosis, as well as corneal scarring in both eyes. Serology testing was performed in order to exclude other infectious and autoimmune diseases and was negative. Ocular cicatricial pemphigoid (OCP) was confirmed using conjunctival biopsy with direct immunofluorescence testing of the conjunctiva. Based on the clinical findings, her disease was graded as stage 3.[18]

The patient was started on oral corticosteroids (prednisone 60 mg daily). Following initiation of oral corticosteroids, there was interval improvement in the ocular surface inflammation in both eyes. However, the patient developed multiple side effects attributed to systemic steroids including nervousness, moon facies, fatigue, ecchymoses, joint pain, swelling, and muscle weakness. In order to wean the patient off from systemic corticosteroids, initiation of immunomodulatory therapy was planned.

Mycophenolate mofetil was started (1000 mg twice daily), however, the patient had discontinued treatment after two months due to severe fatigue and persistent conjunctival inflammation after gradually tapering systemic corticosteroids dose. Methotrexate (MTX) was then initiated (15 mg weekly) and systemic corticosteroids were slowly tapered. After three months of MTX therapy, recurrence of bilateral conjunctival inflammation was observed and corneal ulcer had developed in the left eye. Methotrexate dose was increased to 30 mg weekly and the corneal ulcer was treated with topical antibiotics until resolved. However, the patient was still experiencing active conjunctival inflammation, recurrent corneal epithelial defects and systemic side effects from increasing MTX dose. These side effects included anemia, poor appetite, nausea, abdominal pain, skin rash, hair loss, recurrent urinary tract infections and was hospitalized due to pneumonia. Adalimumab and rituximab were suggested as alternative options, however, were not initiated because of denial for coverage for OCP by her insurance.

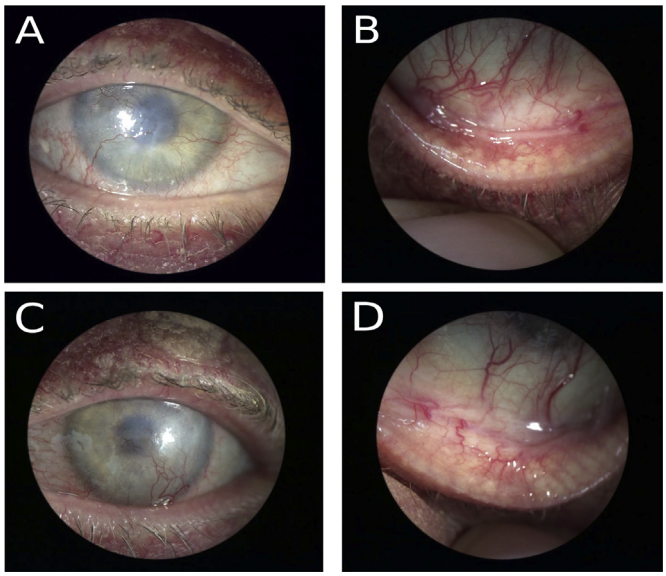

Fig. 1. Anterior segment photograph of both eyes under ACTH gel treatment. Right eye with corneal haze and vascularization (A), as well as inferior fornix shortening and subepithelial scarring, without active inflammation (B). Left eye with corneal scarring and vascularization (C), inferior fornix shortening and subepithelial scarring, without active inflammation (D).

The patient was started on twice weekly subcutaneous H.P. Acthar® Gel (repository corticotropin injection; Mallinckrodt Pharmaceuticals, St. Louis, MO), (80 units/ml), in June, 2016. On ocular examination, BCVA was CF in her right eye and hand motion (HM) in her left eye. Slit-lamp examination revealed active disease, characterized by conjunctival injection in both eyes. Following initiation of ACTH gel, MTX dose was gradually decreased, as well as the systemic corticosteroids. The patient remained under adequate control with ACTH gel and MTX. The conjunctiva remained scarred, but was no longer inflamed (Fig. 1). Following 6 months of treatment with ACTH gel, the patient had cataract surgery and penetrating keratoplasty (PKP) in her left eye, due to corneal scarring and vascularization that affected her vision.

On March, 2017, nine months after ACTH gel was started, the patient stopped treatment for 3 months (due to loss of coverage) and immediately flared up upon treatment cessation. Visual acuity in the left eye has decreased from 20/100 to CF and conjunctival inflammation was observed in both eyes. Corneal graft rejection and ulceration were noted in the left eye (as shown in Fig. 2), both of which subsided after resuming ACTH gel, but had left a scar in the corneal graft. PKP was later performed in the right eye as well, due to visually significant corneal scarring. On the last follow-up, after 19 months of treatment with ACTH gel, the BCVA was CF in the right eye and 20/200 in the left eye, no signs of inflammation were observed and corneal grafts were stable in both eyes. MTX was maintained on 25 mg weekly dose, and

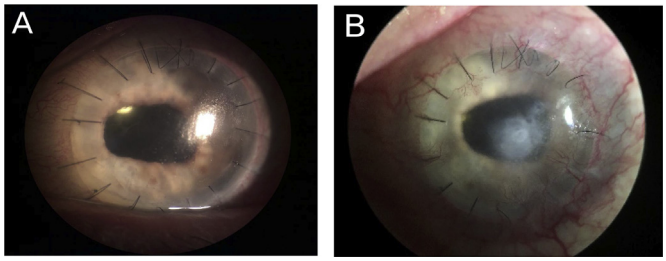

Fig. 2. Anterior segment photograph of the left eye, previously underwent penetrating keratoplasty with clear corneal graft, and on ACTH gel treatment (A). The patient stopped ACTH gel for 3 months and immediately flared up upon treatment cessation, with corneal graft rejection and ulceration (B).