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Case Report

CASE REPORT

# Early treatment of bilateral fungal keratitis with corneal cross-linking as adjuvant therapy

Juan Cruz González Castellanos[1,2,*], Matías Osaba[1,2], Virginia Reviglio[2], Marcela Tatiana Canchi[1,2], Maitén Cuyén Arrigone[1,2] and Víctor Eduardo Reviglio[1,2]

[1]Instituto de la Visión Cerro de las Rosas, Sanatorio Allende – Sede Cerro, Córdoba X5009CGE, Argentina, [2]Facultad de Ciencias de la Salud, Universidad Católica de Córdoba, Córdoba X5004FXT, Argentina

*Correspondence address. Instituto de la Visión Cerro de las Rosas. Av. Rafael Núñez 5019, Córdoba X5009CGE, Argentina. Tel: 03514811955; E-mail: juancgonzalezcastellanos@gmail.com

## Abstract

Fungal keratitis is an ocular infection that has no standardized treatment. The etiological agents most frequently reported in the literature are *Fusarium* spp., *Aspergillus* spp., *Alternaria* spp. and *Curvularia* spp., related to injuries and *Candida albicans* related to contact lens wear. Here we present a case of bilateral fungal keratitis of a few days of evolution with insufficient response to antifungal pharmacological treatment and with early application of cross-linking in both eyes as an adjuvant therapy. A review of the current status of cross-linking for the treatment of corneal infections is presented.

## INTRODUCTION

Fungal keratitis is a threat to visual function and may even lead to blindness. Corneal injuries with contaminated elements and vegetable matter are the main cause of fungal keratitis. The main etiological agents of these infections are directly related to the geographical area, time of the year and patient's socioeconomic level. The fungi most frequently reported in the literature are *Fusarium* spp. and *Aspergillus* spp. that are related to injuries and *Candida albicans*, related to the use of contact lens [1].

The loss of integrity of the corneal epithelium is one of the most important factors in the development of infectious keratitis. Once this first barrier has been damaged innate and cell immunity plays a critical role in growth inhibition of the infective agent. Currently, there are new treatment options due to advances in the pharmacological field and new surgical techniques.

Corneal cross-linking (CXL) is a technique that improves mechanical and biochemical stability of the corneal stroma. The procedure consists of the administration of a photosensitizer, such as riboflavin, which produces reactive oxygen species (ROS) when irradiated with ultraviolet-A (UVA) light [2].

We present a case report showing the successful outcome of early intervention with CXL in *Fusarium solani* superficial bilateral keratitis unresponsive to conventional treatments, as well as a review of the relevant literature.

## CASE REPORT

A 45-year-old female presented with bilateral eye pain over the past few days, reporting inappropriate handling of contact lenses and risky behavior. On first examination, visual acuity was 20/100 in the right eye and 20/80 in the left eye. Biomicroscopy showed conjunctival hyperemia, purulent conjunctivitis, corneal abscess in both eyes and hypopyon in the right eye. The presumptive diagnosis was bilateral infectious keratitis. Multiple samples were taken from the lesions.

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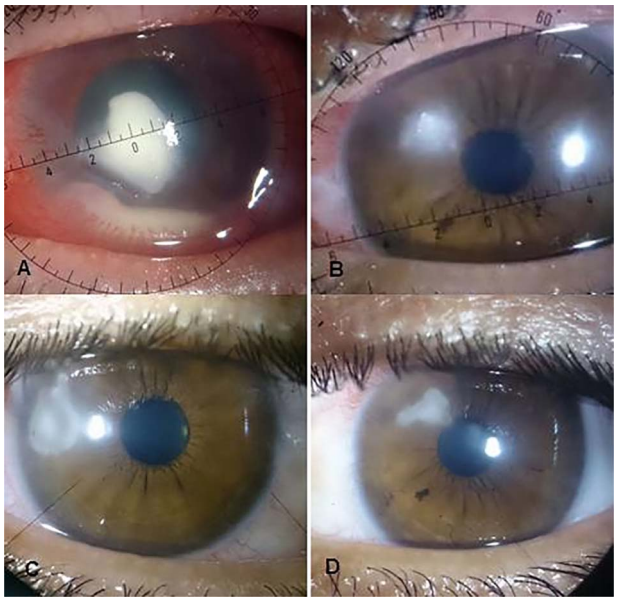


**Figure 1: A**. Corneal abscess, conjunctival injection and RE hypopyion before CXL. **B**. Corneal abscess and conjunctival injection of the LE, before CXL. **C**. Corneal leucoma caused by fungal keratitis in the right eye 15 days after CXL. **D**. Corneal leucoma caused by fungal keratitis in the left eye 15 days after CXL.

Treatment was initiated with cyclopentolate vancomycin 50 mg/ml, ceftazidime 50 mg/ml, amphotericin B 5 mg/ml and oral fluconazole 150 mg. At the 7-day follow-up examination, size of lesions remains unchanged (Fig. 1); therefore, topical voriconazole 0.5 mg/ml was initiated.

Although the maximum antifungal treatment was initiated, corneal lesions began to increase in size and depth. Conjunctival autograft was performed but with unsuccessful results.

With the patient's consent, CXL was performed in both eyes using Dresden Protocol with riboflavin instillation (vitamin B2, 402.7 Osm/L) for 30 minutes, followed by UVA irradiation (3 mW/cm$^2$, 5.4Joules/cm$^2$, and 370 nm) for additional 30 minutes while riboflavin instillation continued.

After 48 hours of CXL treatment, corneal abscesses were more defined, with a minor stromal inflammatory reaction and with no pain.

After 17 days, the result of the microbiological culture showed the presence of *F. solani* in both eyes.

The abscesses developed into inactive corneal scars and 6 months after treatment, corneal scar lesions remained, with a consequent best corrected visual acuity of 20/40 in the right eye and 20/30 in the left eye.

## DISCUSSION

In the past years, promising results have been obtained with CXL in the treatment of the severe forms of infectious keratitis; in those cases, the treatment is termed PACK-CXL (photo activated chromophore for infectious keratitis corneal collagen cross-linking).

During the course of the PACK-CXL application, a photochemical reaction occurs and ROS (singlet oxygen, triplet oxygen and oxygen-free radicals) are generated [1]. Several studies have demonstrated that the combination of riboflavin and UV light would have direct effects on DNA strands and indirect effects caused by ROS. This phenomenon would trigger a suppression of pathogen replication effective for the treatment of viral, bacterial and fungal infections.

The effects of PACK-CXL are not similar in the entire corneal thickness due to the diffusion gradient of riboflavin and the high UV absorption coefficient. Hence, the effects observed are limited to the anterior stroma. Price *et al*. estimated this reduction in the percentage of the incident UVA irradiance as it passes through a cornea soaked with riboflavin 0.1% [3].

The use of PACK-CXL in bacterial keratitis has been found to be effective, especially when the superficial anterior stroma is involved. The results obtained in fungi and viruses vary with the characteristics of the etiological agent and the clinical characteristics of the infection process [4]. This technique has not been found to give satisfactory results in the treatment of Acanthamoebas keratitis [5].

Galperin states that the use of CXL combined with riboflavin reduces severity and intensity of *F. solani* infectious keratitis [6]. Wei *et al*. conclude that CXL appears to be promising in the treatment of infectious keratitis [7].

However, Uddaraju *et al*. claimed that in those patients with deep corneal abscesses and who do not respond to treatment, photodynamic therapy is not enough, and may even lead to ocular perforation [8].

Although the consulted literature describes ambiguous results, CXL appears to be promising for the early management of infectious keratitis with certain characteristics and the ophthalmologist should be able to determine the cases in which the use of CXL can be beneficial as adjuvant therapy.

This is an interesting case because the patient presented with a bilateral infection, limited to the anterior stroma and did not respond to the usual treatments, with the infection resolving after CXL was performed. This result supports the use of this technique for the initial management of corneal infections and especially those that remain on the tissue surface [9–10].

To establish CXL as an adjuvant therapy for infectious keratitis, additional research evaluating the depth of corneal infiltration and identifying the fungal species involved is needed to draw further conclusions.

## CONFLICT OF INTERESTS

No conflicts declared.

## FUNDING

This research did not receive any specific grant from funding agencies.

## ETHICAL APPROVAL

Since no experimental process was involved in the diagnosis and treatment of the patient, a local ethics committee approval was not necessary.

## CONSENT

Before the initiation of the diagnostic and treatment processes, the patient filled out an institution informed consent form. A consent form was also filled out, process and anonymous publication of the case data.

## GUARANTOR

The author JUAN CRUZ GONZALEZ CASTELLANOS (juancgonzalezcastellanos@gmail.com) is the guarantor of the present study.

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