



Corneal Infection in a Child with Congenital Insensitivity to Pain and Anhidrosis Treated with Accelerated Corneal Cross-Linking: Case Report

Yonit Krakauer[#], Boris Knyazer[#], Baker Elsana* and Erez Tsumi

Department of Ophthalmology, Soroka University Medical Center, Ben-Gurion University of the Negev, Beer-Sheva, Israel

[#]Both author contributed equally to this study

Abstract

Purpose: To report a case of a child with CIPA and a corneal infectious keratitis that did not respond to standard antibiotic treatment and was successfully treated with accelerated Photo Activated Chromophore for Keratitis (PACK-CXL).

Methods: This is a report of an 11-year-old girl with CIPA who presented to the outpatient eye clinic with an active corneal abscess, stromal thinning and hypopyon. Standard antibiotic treatment brought no improvement in her condition and the child was ultimately treated successfully with accelerated PACK-CXL. A literature review summarizes the use of PACK-CXL in the treatment of corneal abscess.

Results: An 11-year-old girl with CIPA presented with a 3 mm active corneal abscess, stromal thinning and hypopyon. She was admitted to hospital and a standard topical antibiotic treatment was started. When no improvement was achieved after 4 days of intensive antibiotic treatment, she underwent accelerated PACK-CXL (UVA light of 30 mW/cm for 3 min for a total dose of 5.4 J/cm²), with improvement of the corneal abscess and resolution of the hypopyon. The patient has been followed for ten years.

Conclusion: PACK-CXL can be a safe and effective adjunct therapy for corneal infectious keratitis in CIPA patients, and for other complicated corneal abscesses that do not respond to conventional, intensive topical treatment in CIPA patients.

Keywords: PACK-CXL; Corneal cross-linking; Neurotrophic keratitis; CIPA; Infectious keratitis

Introduction

Congenital insensitivity to pain with anhidrosis (CIPA), a rare autosomal-recessive disorder of the nervous system that inhibits pain and temperature sensation, is characterized by self-inflicted injuries and burns that often lead to surgical amputations of limbs. The ocular manifestations of this disorder, which include corneal neurotrophic keratopathy which can lead to keratitis and corneal abscess, constitute a significant therapeutic challenge due to inadequate healing ability and violent contaminants that are often resistant to treatment [1,2].

Studies have reported success in using corneal cross-linking (CXL) to treat patients with various conditions of corneal keratitis [3-5]. Schnitzler was successful in preventing perforation in three out of four patients with noninfectious corneal melting treated with CXL. Iseli and co-workers [5-7] successfully treated 5 eyes using the standard CXL settings of 3 mW/cm for 30 min (Dresden protocol) for infectious keratitis. Knyazer et al. [8] described 20 cases with infectious keratitis successfully treated with accelerated PACK-CXL, 30 mW/cm for 3 min, as additional treatment to standard antimicrobial therapy. They reported the therapeutic effect of PACK-CXL to be safe and effective in patients with moderate therapy-resistant infectious keratitis. The anti-infectious activity of CXL, or by its correct name, Photo activated Chromophore for Keratitis (PACK-CXL), is based on the use of riboflavin as a photo sensitizer, which generates reactive oxygen species when activated by UV-A light at 365 nm. Both, UV-A light itself and photo activated riboflavin, fragment the RNA and DNA of microorganisms by direct damage and by oxidation processes [6,7].

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*Correspondence:

Baker Elsana, Department of Ophthalmology, Soroka University Medical Center, Ben-Gurion University of the Negev, Beer-Sheva, Israel, Tel: +972-54-2350063;

E-mail: bakerelsana1@gmail.com

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Figure 1: A: Absence of lower teeth, which were surgically removed following diagnosis of Congenital Insensitivity to pain with Anhidrosis (CIPA). B: Bone deformity; note the unequal lengths of the left and right arms. Loss of fingertips, minimal in this case, due to biting of fingers.

We report here a CIPA child who had a corneal keratitis that did not respond to standard antibiotic treatment and was treated successfully with accelerated PACK-CXL. To the best of our knowledge this is the first reported case of treating a CIPA child with PACK-CXL.

Case Presentation

An 11-year-old girl with CIPA presented to the outpatient eye clinic with redness in the right eye that began 3 days earlier. The child of consanguineous parents with a cousin with CIPA, physical examination revealed mental retardation, severe self-mutilation, finger deformities, and right above-knee amputation. Informed consent was gathered from the parents of the patient Figure 1. She had a history of repeated corneal erosions in the left cornea, and 3 years earlier was treated successfully with topical fortified antibiotics for a corneal abscess in the same eye.

Slit lamp examination showed a 3 mm active corneal abscess with stromal thinning (up to mid-stroma), and a 1mm hypopyon in the anterior chamber. She was admitted to hospital, cultures and smears were taken, and hourly treatment was begun with topical fortified vancomycin eye drops (50 mg/ml) and fortified ceftazidime eye drops (50 mg/ml). After 4 days of no improvement of the corneal infection, she underwent accelerated PACK-CXL treatment under sterile conditions in an operating room setting. Following topical anesthesia with 0.4% benoxinate hydrochloride drops, the epithelium was removed 1 mm around the borders of the ulcer and hypo-osmolar 0.1% riboflavin solution (Medio-Cross 0.1%, Peschke Meditrade GmbH, Huenenberg, Switzerland) was instilled topically on the entire cornea every 2 min for 20 min. The eye was then irradiated with a UVA device (LightLink-CXL, Light Med, San Clemente, CA, USA) for 3 min with an irradiance of 30 mW/cm² (total dose 5.4 J/cm²). The corneal abscess gradually improved over the next few days and on the fourth day of hospitalization she was discharged with a 1.5 mm corneal staining, resolution of the hypopyon, and decreasing stromal infiltrate. After release, she was treated with topical antibiotics only. Bacterial and fungal cultures of the cornea were negative.

Three weeks later, when re-epithelization of the cornea was not complete despite treatment, she underwent a second accelerated PACK CXL procedure combined with a lateral tarsorrhaphy and amniotic membrane graft. Re-epithelization was recorded after absorption of the amniotic membrane. On the last follow-up visit, the child had no complaints about her left eye. On slit lamp examination, the conjunctiva was quiet bilaterally, and corneal opacities without infiltration in were seen in the eye (Figure 2). The rest of the ocular examination was normal.

Discussion

We have described the treatment and follow-up of a corneal



Figure 2: Right eye two years after Corneal Cross-Linking (CXL), showing a residual corneal scar that remained after the procedure and topical antibiotics.

abscess with corneal melting secondary to neuropathic keratopathy in an 11-year-old CIPA patient whose infection, after failing to respond to standard antibiotic therapy, was controlled by treatments with accelerated PACK-CXL. Our patient presented with a corneal abscess that was probably a result of NK that caused an epithelium defect, in addition to repeated self-mutilation, both part of the clinical characteristics of CIPA. Taking these causes into account, treating this CIPA patients with CXL was a logical choice. The safety and efficacy of the treatment were demonstrated in earlier studies [3,5,8], in addition to which cross-linked corneas were reported in an in vitro study to have increased resistance to enzymatic digestion with pepsin and collagenase [4].

These findings and our experience provide strong evidence that PACK-CXL can be a safe and effective adjunct therapy in CIPA patients as soon as melting appears in infected corneal ulcers not responding to conventional, intensive topical treatment. Since CIPA patients are prone to recurrent self-induced corneal injuries, neuropathic ulcers and severe abscess, routine ophthalmic examinations in addition to parental education on ocular manifestations of the disease are highly recommended.

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