Corneal crosslinking in Pasteurella multocida–induced severe keratitis

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We report the case of a 37-year-old man who presented with redness and swelling in the left eye and visual acuity of light perception after a cat scratch. Slitlamp examination showed a total corneal opacity, inferior stromal thinning, and total corneal erosion. Cultures of the cornea swap revealed Pasteurella multocida, sensitive to the antibiotic regimen. Because of progressive thinning, corneal collagen crosslinking (CXL) was performed to stabilize the cornea. An amniotic membrane was later transplanted because of delayed wound healing. Currently the epithelium is closed and visual acuity is still poor (20/400) due to an extensive corneal scar. The patient is scheduled for keratoplasty. Corneal CXL even without riboflavin was effective in stabilizing the corneal integrity in severe keratitis. Pasteurella multocida can result in severe keratitis with permanent corneal scarring and visual impairment despite adequate therapy.

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A rare but potentially devastating agent of infectious keratitis is Pasteurella multocida, which is common in normal respiratory microbiota of domestic pets. The agent is known to cause zoonotic infections in humans, especially those in an immune-suppressed condition, after bites or scratches from domestic pets. Limited reports in the literature describe the occurrence of a severe keratitis caused by this pathogen, as ocular involvement is rare. Two cases of P multocida–induced keratitis as a complication of a corneal laceration following a cat scratch are described. Ho et al. report a case of corneal laceration with inflammatory reaction in the eye of a young woman after a cat scratch. In their case, with topical antibiotic therapy the infection resolved with excellent visual acuity. Robinson et al. report a P multocida-induced corneal ulcer. The patient suffered from a severe keratitis following an injury. After intensive topical and systemic antibiotics as well as steroids, the corneal ulcer healed but left the patient with reduced visual acuity.

While corneal collagen crosslinking (CXL) is a well-known method to induce stability of biomaterial, for example in bioprosthesis, it is a fairly new method for in vivo therapy of corneal pathologies. Corneal CXL using riboflavin and ultraviolet-A (UVA) light in combination increases the mechanical stability of corneal stromal tissue. The primary medical indications for CXL are corneal ectatic progressive pathologies such as keratoconus. Another current off-label indication for CXL is microbial keratitis; however, the clinical data on the efficacy of this indication are limited. The success against the bacteria itself seems to be restricted, but corneal stiffness and collagen stabilization can be achieved. To our knowledge, we describe the first case of a severe P multocida–induced keratitis treated with corneal CXL without the use of riboflavin (vitamin B2).

CASE REPORT

A 37-year-old man presented with acute redness, swelling, and pain in his left eye. The visual acuity in that eye was light perception. Slitlamp examination revealed conjunctival injection and chemosis, clouded cornea, and subtotal corneal erosion with inferior stromal thinning. The anterior chamber was formed, and no further details could be evaluated (Figure 1). Echographically, the vitreous body did not
present signs of an infection or retinal detachment. The right eye was irritation free and age appropriate.

Initial therapy consisted of topical neomycin sulfate–polymyxin B sulfate 8 times a day, moxifloxacin 0.5% 8 times a day, atropine 0.05% 2 times a day, and oral ciprofloxacin (500 mg) twice a day. Corneal scraping of the ulcer was performed immediately before starting the therapy and revealed *P. multocida* sensitive to the current antibiotic regimen. Clinically, the keratitis progressed despite the sensitive drug therapy. With progressive corneal thinning and impending infiltration into scleral tissue, CXL was performed in the left eye. Because of a shortage of riboflavin, the procedure was performed without it. Apart from this, the CXL procedure followed the Dresden protocol with additional pupillary constriction (pilocarpine 2.0%). Postoperatively, the therapy was reduced to neomycin sulfate–polymyxin B sulfate and bacitracin/gramicidin 4 times a day, moxifloxacin 4 times a day, atropine 0.05% twice a day; preservative-free steroidal eyedrops twice a day were added at this point. The cornea brightened and revealed a hypopyon of 2.3 mm (Figure 2). An anterior chamber irrigation was performed 2 days later because of lack of resorption. Visual acuity in the left eye was hand motion, and the patient was released from the hospital in stable condition.

At the ambulatory checkup 4 weeks later, the cornea showed beginning peripheral vascularization and persistent corneal erosion with no signs of infection. Visual acuity in the left eye was finger counting. Due to delayed epithelial wound healing, the patient was again hospitalized for therapy with autologous serum eyedrops (Figure 3). Amniotic membrane transplantation was successfully performed. The patient was released with a therapeutic contact lens. Topical therapy was preservative-free steroidal eyedrops 4 times a day and moxifloxacin 0.5% 4 times a day for 5 days.

At the latest ambulatory checkup another 4 weeks later, the epithelium was closed, the corneal limbus was strongly vascularized, the cornea was cloudy, and stromal thickness was reduced. The anterior chamber was formed with no sign of infection (Figure 4). Visual acuity remained 20/400 in the left eye. The patient is now listed for corneal transplantation, as the visual acuity is not expected to improve, and is in a stable state.

**DISCUSSION**

The patient was first examined 4 days after the cat scratch. At that time, the cornea in the left eye was fully...
clouded and the stromal thickness was significantly reduced inferiorly with the threat of perforation. Perforation would have led to an emergency keratoplasty. A keratoplasty à chaud has led an increased risk for transplant rejection and reinfection. Therefore, a more conservative approach with the goal of preventing the emergency keratoplasty was preferred. Initially the patient was treated according to the guidelines of the German Society of Ophthalmology with topical and systemic antibiotics.

In the past 10 years, CXL has become an essential part of treating keratoconus. Wollensak et al. show that corneal crosslinking increased the corneal rigidity and stopped keratctasia in eyes with progressive keratoconus. Recently, new indications for CXL were discovered. For example, in 2008 Iseli et al. proposed the efficiency of CXL for infectious keratitis. In 2010, Al-Sabai et al. reported a case in which CXL was effective in stopping corneal melting.

In light of these promising results and clinically progressive keratitis with impending corneal perforation and scleral infiltration, we decided to perform CXL in the patient’s left eye. Because of a shortage of riboflavin, the CXL was performed without it. It was proven in vitro that the antimicrobial effect of crosslinking was only mediated by the UVA light and not enhanced through riboflavin. We are aware that the safety of crosslinking is related to the use of riboflavin, as it absorbs UVA light and protects the inner parts of the eye such as the endothelium, lens, and retina. Without riboflavin, the cornea absorbs around 30% of the UVA light and the lens approximately 50%, with the risk for endothelial cell loss and inducing cataracts. With most of the UVA light resorbed in the anterior part of the eye, only a small portion may penetrate into the retina with the risk of oxidative stress to the retinal pigmented epithelium. This is known to be a risk for age-related macular degeneration, primarily because of continuous exposure to light. Riboflavin also protects the cornea from dehydration and thereby reduces the possibility of stromal scarring. The decrease in corneal thickness can be as much as 25%. Most studies of riboflavin–UVA–induced CXL report that riboflavin is a crucial factor in the safety of the procedure, but specific clinical risks are hardly defined. Furthermore, these studies are based on clear corneas. In our case with a fully clouded cornea, the UVA permeability was expected to be significantly less or even completely blocked. Weighing the pros and cons of the benefits CXL brings to corneal stability with possible damage through the UVA light, we decided to perform CXL without riboflavin. The lens has remained clear.

Several studies have shown the efficiency and epithelium-promoting properties of autologous serum eyedrops. The main indication is persistent corneal epithelium defects. A known therapeutic alternative for this indication is amniotic membrane transplantation. Amniotic grafts serve as a temporary bandage to prevent corneal exposure and contain growth factors to accelerate epithelial proliferation. Amniotic membrane transplantation induces reepithelialization and can decrease inflammatory reactions. As an additional effect, amniotic membrane transplantation leads to a decreased rate of corneal neovascularization.

In our case, CXL was successful in stabilizing the cornea without the use of riboflavin. Because of the higher safety, CXL should be performed using riboflavin. This case shows that urgent cases it can be individually evaluated and corneal crosslinking performed without riboflavin if necessary. Autologous serum eyedrops in combination with amniotic membrane transplantation promote healing of persistent epithelium defects. In combination with different therapy approaches, an emergency keratoplasty à chaud can ideally be prevented.

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