

Diagnosis and Therapy in Ophthalmology

Candida albicans should be considered when managing keratitis in Atopic keratoconjunctivitis

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Acta Ophthalmol.

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doi: 10.1111/aos.12708

Case 1 A 44-year-old man with a history of atopic skin disease and atopic keratoconjunctivitis (AKC), treated with sodium cromoglycate drops only, was admitted complaining of ocular pain, redness and decreased vision in his left eye since 7 days. Examination of the left eye disclosed a corneal infiltrate measuring 2×2 mm in the upper temporal quadrant with a small perforation. Cultures revealed *C. albicans* and *S. aureus*, and cornea healed with a bandage lens and antibiotic drops only. However, six months later, symptoms recurred. Antiviral ointment as well as chloramphenicol drops and a low-dose steroid drops had been prescribed by a private practitioner but without improvement. A corneal abscess was found at the site of the former keratitis, and *C. albicans* and *Staphylococcus aureus* were found in cultures. Despite broad-spectrum antibiotics and topical as well as oral antifungals, the keratitis aggravated with final perforation of the cornea, Fig. 1. Keratoplasty combined with cataract extraction was performed, but the eye was lost to phthisis.

Case 2 A 40-year-old man with atopic dermatitis, AKC and glaucoma was referred to St. Erik's Eye Hospital for further treatment of a keratitis in the right eye. Following trabeculectomy 6 years earlier, he was free from glaucoma medication and used only antihistamine drops intermittently. Prior to referral, he had received treatment with a combination of steroid and antibiotic drops for five days with progressing symptoms. A 1×1 mm nasal corneal infiltrate and stromal oedema were seen, and there were precipitates on

the endothelium, no hypopyon was present. Samples were positive for *C. albicans*, and treatment was shifted to flucytosine tablets and topical amphotericin B. Despite adequate treatment, confirmed by resistance patterns and plasma concentrations, the ulcer showed increasing infiltration and descemetocoele formation, Fig. 2. A Gundersen conjunctival flap was performed and the infection and inflammation abated during the following weeks. Finally, the ulcer healed but with significant corneal vascularization.

Case 3 A 41-year-old man with severe AKC treated with mild steroid ointment for eyelid eczema and intermittent oral steroids presented with pain since 4 days in his right eye. On examination, a corneal erosion with a small infiltrate was seen; there was no reaction in the anterior chamber; BCVA was 6/60. *S. aureus* and *C. albicans* were found in cultures, and there was improvement with antibiotic treatment only. Over the following two years, the patient suffered relapsing epithelial defects corresponding to the initial erosion. After two years, the patient again presented with increased pain, and a small infiltrate was now seen in the area of the erosion, Fig. 3. *C. albicans* was found in cultures, and treatment was altered to amphotericin B and natamycin drops with improvement. After 3 months without antifungal treatment, the symptoms again worsened and examination revealed three small limbic infiltrates. This time amphotericin B drops were immediately prescribed without prior cultures and with a good response. After ten days, the cornea had surprisingly healed. One year later, following

cataract extraction, BCVA was 6/15. The eye, however, was lost a few years later due to perforating trauma.

Case 4 A 37-year-old man with AKC, bilateral glaucoma and recurrent herpesvirus infections was referred from a neighbour eye unit with a diagnosis of left eye *C. albicans* keratitis. Over the following months, the ulcer remained unchanged while being treated with a low dose of natamycin and steroid drops. After 5 months of treatment, an attempt to slowly taper treatment resulted in a worsening of the symptoms. The patient now presented with increasing pain, redness and decreasing vision for 4 days. Examination revealed a marked ciliary injection, corneal oedema with a deep nasal infiltrate and hypopyon. Cultures showed *C. albicans* only. Treatment was continued with high dose natamycin and amphotericin B drops with some improvement, Fig. 4. After three months, there was a small perforation managed with a Gundersen conjunctival flap. Treatment was discontinued after two years, but the cornea was severely scarred and vascularized.

Case 5 A 40-year-old woman with long-standing and severe AKC was followed for a persistent sterile epithelial defect in the right eye when symptoms got worse.

At this time, treatment was tacrolimus ointment 0.1% for the eyelids, cyclosporin eye drops 2% 5 times a day, quinolone ointment 5 times a day and in addition dexamethasone drops twice a day had been prescribed since 5 weeks. The erosion had increased, and a small infiltrate was seen in the centre.



Fig. 1. *Candida albicans* keratitis aggravated with perforation in a patient with atopic keratoconjunctivitis, case 1. This patient was treated with sodium cromoglycate drops only on first presentation, demonstrating the importance of bearing fungal infection in mind in this patient group also when stable and without steroid treatment. Mixed bacterial–fungal infection as found in this patient is not uncommon, and if *C. albicans* is present together with, for example, bacteria, the yeast also should be considered pathogenic and treatment must be given covering all identified organisms.

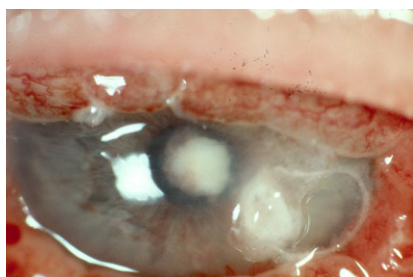


Fig. 2. Dense infiltration in *Candida albicans* keratitis in a patient with atopic keratoconjunctivitis, case 2. Antibiotic and steroid drops had been prescribed without samples for culture; this management probably aggravated the keratitis and delayed the diagnosis. Evaluating corneal ulcers in AKC patients is a challenge; an increased risk for *S aureus* and herpes simplex infections are well known, but also yeast fungi must be considered and cultures are essential for diagnosis.

Cultures revealed *Candida albicans*, and Natamycin was added 8 times per day while steroid drops were halted. The ulcer epithelialized, but after four months, a descemetocoele formed with pending perforation, Fig. 5. Repeated corneal lamellar patching were performed but failed to integrate. Due to side-effects and negative cultures, natamycin was stopped, but a few weeks later cultures again revealed *C. albicans* and treatment was shifted to amphotericin B drops. Cornea finally stabilized with severe vascularization, and the eye is now quiet.

In the Nordic countries, fungal keratitis is very rare. An annual incidence

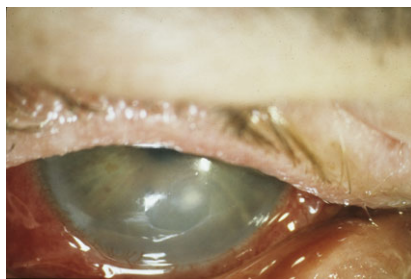


Fig. 3. Corneal infiltrate at second incident of *Candida albicans* keratitis in a patient with atopic keratoconjunctivitis, case 3. This patient had repeated incidents of *Candida* keratitis over several years and with this in mind prompt treatment at the third event probably promoted healing. Early suspicion and treatment might enhance the otherwise poor outcome in *Candida* keratitis and the antifungal therapy should further be continued well after epithelial recovery especially in this patient group with possible colonization in the eyelid margins and conjunctiva.



Fig. 4. Exacerbation of *Candida albicans* keratitis in a previously scarred cornea in a patient with atopic keratoconjunctivitis, case 4. This patient had recurrent herpes infections and scarring prior to the *Candida* infection. Distinguishing the cause of keratitis clinically is difficult especially during ongoing medication and especially in previously scarred and vascularized corneas.

of 0.6 per million individuals was recently reported from Denmark (Nielsen et al. 2015), and among these rare cases, yeast fungi dominate. It is well known that ocular surface disease (OSD) and host immunodeficiency are important predisposing factors for yeast keratitis (Bhartiya et al. 2007; Galarreta et al. 2007; Tuft & Tullo 2009). In addition to OSD and steroid use, a change in eyelid skin colonization could possibly contribute to the susceptibility to fungi in AKC patients (Huber-Spitzy et al. 1992). The risk for opportunistic keratitis in patients with atopy and atopic eczema might however be overlooked by the ophthalmologist if facial symptoms are stable.

These case presentations highlight the importance of bearing the risk for yeast

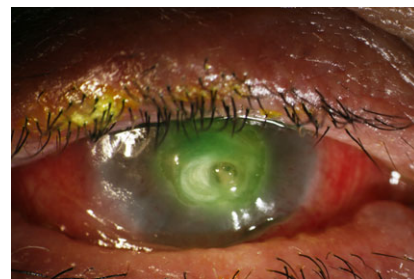


Fig. 5. Descemetocoele formation in the central part of cornea following a persistent epithelial defect and *Candida albicans* keratitis in a patient with atopic keratoconjunctivitis, case 5. In this patient, steroid drops had recently been added at the time of diagnosis. Steroid therapy prior to fungal keratitis is a well-known risk factor for opportunistic infections and might enhance virulence of the fungi but also mask signs of infection and thereby delay diagnosis.

keratitis in mind when managing AKC patients. The value of corneal sampling, the need to treat *Candida* when identified in cultures and a benefit from early clinical identification and long-term treatment is evident in these cases.

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Received on July 12th, 2014.

Accepted on February 6th, 2015.

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This work was supported by grants from S: t Eriks Forskningsstiftelse.