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Case report

Candida parapsilosis keratitis treated successfully with topical and oral fluconazole

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ABSTRACT

A 73-year-old male patient presented with ocular pain, redness, and blurred vision in the left eye, which had been ongoing for more than 2 months. An oval-shaped paracentral corneal ulcer with stromal infiltration and a mild anterior chamber reaction were found. Despite treatment with empiric antibiotics, the lesion progressed and corneal thinning in the middle area was noted. The culture yielded *Candida parapsilosis*. We therefore prescribed topical 0.2% fluconazole (FCZ) in combination with oral FCZ as an antifungal treatment, following which the stromal infiltration gradually subsided. Complete epithelialization was noted on the 8th day after initiating FCZ therapy. There was no recurrent disease in the subsequent 2 years. Our case demonstrates that topical FCZ 0.2% in combination with oral FCZ can successfully treat *C. parapsilosis* keratitis and result in a good visual outcome.

1. Introduction

Cases of *Candida parapsilosis* keratitis have been reported in patients with topical or systemic corticosteroid usage, prior corneal surgery [e.g., corneal graft or laser-assisted *in situ* keratomileusis (LASIK) surgery], or chronic keratopathy.[1–5] Although *C. parapsilosis* is less virulent than *Candida albicans* in animal experiments, the clinical prognosis of *C. parapsilosis* keratitis is poor and indeed not better than that of keratitis caused by other *Candida* species.[5]

The first-line antifungal agent for yeast keratitis is usually topical amphotericin B (amp B).[6] However, previous studies have shown that most patients with *C. parapsilosis* keratitis treated with amp B have poor visual prognosis; furthermore, in these patients, corneal grafts or anterior chamber washing may be need to eradicate the pathogen.[5]

Topical azoles [e.g., fluconazole (FCZ) and voriconazole] are considered to be a good alternative to amp B for the treatment of *Candida* keratitis.[7–11] It has better ocular penetration and is less toxic to the corneal epithelium, compared with amp B. In this report, we present a case of *C. parapsilosis* keratitis treated successfully with topical 0.2% FCZ in combination with oral FCZ.

2. Case report

A 73-year-old male patient presented with ocular pain, redness, and blurred vision in the left eye, which had been ongoing for > 2 months. He had underlying diseases (Type 2 diabetes mellitus and hypertension) but no ocular trauma or surgery history. His blood sugar level was well controlled using oral antidiabetic drugs with hemoglobin A1c levels below 6.5%.

An oval-shaped paracentral corneal ulcer with stromal infiltration (Figure 1) and a mild anterior chamber reaction were found. The best-corrected visual acuity (BCVA) (oculus sinister) was 0.5 with the Snellen chart. The corneal sensitivity was intact. Despite treatment with empiric antibiotics, progressive corneal thinning in the middle area was noted. Initially, we treated him with one drop of 0.3% ciprofloxacin every 2 hours for 4 days but then shifted to 0.3% tobramycin four times daily because of the poor response to ciprofloxacin and concerns about the corneal toxicity of ciprofloxacin. The culture yielded *C. parapsilosis* on the 11th day. We therefore initiated antifungal therapy with topical 0.2% FCZ (Q2h)

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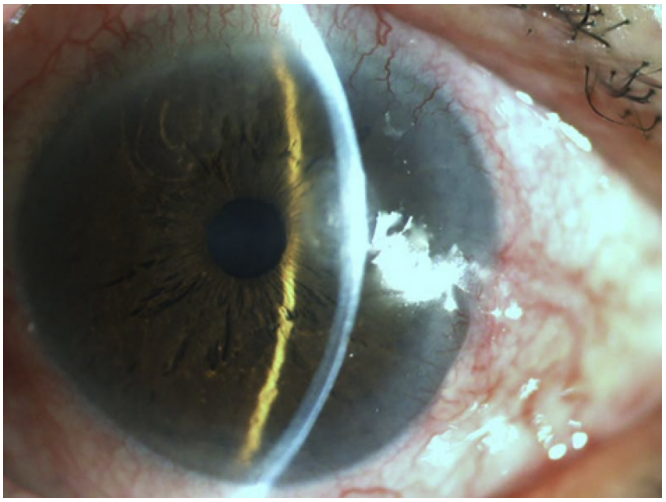

Figure 1. Photograph of the anterior segment showing an oval-shaped paracentral corneal ulcer with epithelial defect and stromal infiltration on the temporal side of the left eye in our patient with *Candida parapsilosis* keratitis. This photograph was taken when the patient initially presented to us.

prepared with an intravenous injectable solution (100 mg/50 mL) in combination with oral FCZ (100 mg 2 times daily). Of note, the 0.2% FCZ eye drops should be kept in the refrigerator (4°C). The storage life of the FCZ eye drops is 1 week. After 1 week, a new bottle of FCZ eye drops should be prepared at the time of use.[9]

After initiation of FCZ therapy, the stromal infiltration subsided gradually (Figure 2). Complete epithelialization was noted on the 8th day after initiating FCZ therapy. There was no recurrent disease in the following 2 years. Although a paracentral corneal opacity was found, the BCVA at the 3-month and 2-year follow-ups were 0.7 and 1.0, respectively (Figure 3).

3. Discussion

Infection due to *C. parapsilosis* is thought to be opportunistic. The incidence of *C. parapsilosis* infection (e.g., fungemia, endocarditis, and meningitis) has increased dramatically over the past decade, which may be due to the increasing use of corticosteroids and rising numbers of immunocompromised patients.[12,13] Previous studies have shown that *C. parapsilosis* is one of the most commonly cultured yeasts and are thus commonly detected on the hands of healthcare workers. Therefore, nosocomial infection is also a possible cause of the increasing prevalence of *C. parapsilosis* infection.[13]

Ocular diseases linked to *C. parapsilosis* include infectious keratitis and endophthalmitis. A large case series reported that *C. parapsilosis* accounted for ~10% of all causes of yeast keratitis in south Florida between 1982 and 1992.[14] According to a more recent study, *C. parapsilosis* constitutes about 31% of all *Candida* keratitis cases.[15] Because *C. parapsilosis* is an emerging fungal pathogen, we expect that there may be an increase in the number of cases of ocular infection in the future. Ophthalmologists should therefore pay attention to, and augment their knowledge of, *C. parapsilosis* keratitis.

The possible predisposing factors of *C. parapsilosis* keratitis are topical or systemic corticosteroid usage and prior ocular surgery, such as penetrating keratoplasty, LASIK surgery, or keratoprosthesis implantation.[1–5,16] In our case, the patient had not received any ocular surgery or systemic steroids. Nevertheless, his topical medical history was unclear; it is possible that he may have been exposed to topical corticosteroids due to poor compliance, although the exposure period would have been short (i.e., not longer than 1 week). He mentioned frequent visits to hospitals because of his wife's illness, and therefore, nosocomial infection due to *C. parapsilosis* was also a possibility.

The clinical presentation of *C. parapsilosis* keratitis has shown great diversity. Patients usually present with symptoms of redness, photophobia, pain, and decreased vision of variable severity. Some eyes have a yellow-white infiltrate with dry, raised slough, and feathery edges. Severe keratitis may cause wet, necrotic stromal inflammation to develop with features indistinguishable from those of other forms of microbial keratitis.[5] Infectious crystalline keratopathy has also been reported in some cases.[5,17] Anterior chamber reactions are variable[5] and may combine with endophthalmitis.[12,16]

To date, the Cochrane Reviews have reported no evidence that any particular drug, or combination of drugs, is more effective in the management of fungal keratitis.[18] Conventionally, amp B is the first-line antifungal agent for yeast keratitis; however, the ocular penetration of amp B is poor. Topical amp B prepared from powder is irritating for the cornea and toxic to the corneal epithelium.[19] Bourcier et al[5] reported four cases of *C. parapsilosis* keratitis treated with topical amp B with or without adjuvant oral azole antifungal agents; in their study, two patients needed therapeutic corneal grafts and one needed anterior chamber washing with diluted amp B to cure the infection. The other patient needed further keratoplasty due to persistent corneal opacity. The visual outcomes ranged from no light perception to 0.5. Chen et al[4] reported a case of *C. parapsilosis* interface keratitis after LASIK surgery; this patient was successfully treated with amp B after which visual acuity improved to 1.0.

It has also been reported that topical 0.2% FCZ is a safe and effective antifungal drug for the management of *Candida* keratitis.[8,9] The corneal penetration of topical 0.2% FCZ is good; the

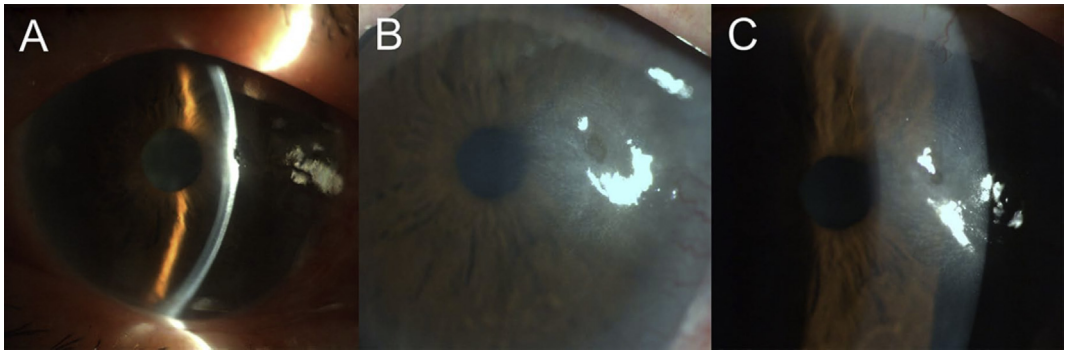

Figure 2. (A) Photograph showing progressive corneal thinning in the middle area of the lesion before starting antifungal therapy. Photograph taken (B) 2 days and (C) 7 days after FCZ therapy. It can be seen that the size of the epithelial defect, the stromal infiltration, and the depth of the lesion are gradually reduced.

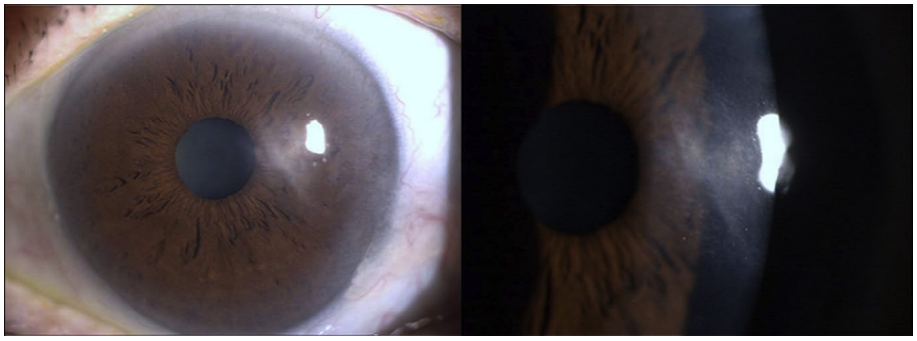

Figure 3. At the 3-month follow-up, complete healing of the corneal epithelium and resolution of the corneal infiltration were observed. Although the corneal opacity was evident, the best-corrected visual acuity at the 2-year follow-up is 1.0.

concentration in the aqueous humor satisfies the minimal inhibitory concentrations of most *Candida* strains, including *C. parapsilosis*. Therefore, topical 0.2% FCZ is thought to be a good alternative to topical amp B for the treatment of *Candida* keratitis.[11] Matsumoto et al[9] compared the efficacy of topical 0.1% micafungin and topical 0.2% FCZ in the treatment of *Candida* fungal keratitis and concluded that the efficacy of 0.1% micafungin eye drops appears to be comparable with that of 0.2% FCZ eye drops. In their study, six cases of *C. parapsilosis* keratitis were treated successfully with topical 0.2% FCZ as the first-line antifungal eye drops, and the mean healing period was 51 days. In the management of deep fungal keratitis, oral FCZ is usually considered as an adjuvant therapy because it is absorbed systemically with good levels in the anterior chamber and the cornea.[20] The recommend dosage of oral FCZ is 200–400 mg daily.[21]

Given the inconvenience and side effects of amp B, as well as the good penetration of FCZ, we prescribed topical 0.2% FCZ in combination with adjuvant oral FCZ for our patient once the culture yielded the growth of *C. parapsilosis*. We started from a relatively low dose (200 mg daily) of oral FCZ because we already prescribed topical FCZ and due to concerns of a possible drug interaction between FCZ and glimepiride, an antidiabetic medication that was used in this patient.[22,23] The stroma infiltration soon subsided and the epithelium healed in 8 days. The patient did not have any significant side effects to topical 0.2% FCZ.

Experimental studies have generally shown that *C. parapsilosis* is less virulent than *C. albicans* or *C. tropicalis*; however, poor prognoses due to *C. parapsilosis* keratitis have been reported. This pathogen may be associated with endophthalmitis and can lead to graft failure and poor visual outcomes.[5,12,16] Early diagnosis and appropriate antifungal treatment, which can result in good outcomes, are therefore important.[4] Our patient showed an excellent response to FCZ, and the healing period was much shorter than those reported previously.[9] The visual outcome of our patient was good and the BCVA was 1.0 at the 2-year follow-up. This may be attributable to the relatively healthy cornea of our patient and a successful strategy of antifungal treatment.

4. Conclusion

Cases of *C. parapsilosis* keratitis are rare. However, it is reported to occur in patients with compromised cornea or with long-term corticosteroid use. Although this pathogen is less virulent than *C. albicans*, relative poor prognosis and longer healing periods have been reported. Our case demonstrated that topical FCZ (0.2%) in combination with oral FCZ could successfully treat *C. parapsilosis* keratitis and result in good visual outcome.

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