Medical Mycology Case Reports 9 (2015) 1–6

Contents lists available at ScienceDirect

Medical Mycology Case Reports

journal homepage: www.elsevier.com/locate/mmcr

# *Colletotrichum truncatum* species complex: Treatment considerations and review of the literature for an unusual pathogen causing fungal keratitis and endophthalmitis

Victoria Squissato [a], Yeni H. Yucel [b,c], Susan E. Richardson [d], Alaa Alkhotani [b], David T. Wong [b], Navdeep Nijhawan [b], Clara C. Chan [b,*]

[a] Queen's University School of Medicine, 80 Barrie Street, Kingston, Canada K7L 3N6
[b] University of Toronto Department of Ophthalmology & Vision Sciences, St. Michael's Hospital, 30 Bond Street, Toronto, Canada M5B 1W8
[c] Ophthalmic Pathology Laboratory, Li Ka Shing Knowledge Institute, 30 Bond Street, Toronto, Canada M5B 1W8
[d] Public Health Laboratories, Public Health Ontario, University of Toronto Department of Laboratory Medicine and Pathobiology, The Hospital for Sick Children Division of Microbiology, 555 University Avenue, Toronto, Canada M5G 1 × 8

ARTICLE INFO

*Article history:*
Received 1 April 2015
Received in revised form
11 May 2015
Accepted 1 June 2015
Available online 6 June 2015

*Keywords:*
Colletotrichum
*Colletotrichum truncatum*
*Fungal keratitis*
*Fungal endophthalmitis*
Treatment
Infection

ABSTRACT

We present a case of *Colletotrichum truncatum* species complex fungal keratitis and endophthalmitis in an 87-year-old immunocompetent male in whom oral triazole antifungals were contraindicated. The patient had recently returned from 4 months in Jamaica with a one month history of progressively increasing pain and inflammation in his left eye. Corneal samples grew a filamentous fungus and internal transcribed spacer sequencing polymerase chain reaction confirmed the presence of *C. truncatum* species complex. Samples showed no microbial growth.



## 1. Introduction

Fungal endophthalmitis is a vision-threatening infection that is usually seen in immunocompromised individuals with fungemia, intravenous drug users, or immunocompetent individuals following direct inoculation from penetrating ocular trauma [1,2]. Fungal endophthalmitis is generally associated with poor visual outcomes and retinal detachment is a frequent occurrence [2]. However, fungi account for only 2–10% of all endophthalmitis cases making this serious condition quite rare [1].

Yeasts, especially *Candida albicans*, are the most common cause of culture-proven fungal endophthalmitis, followed by molds, usually *Aspergillus* species [2,3]. A limited number of species of *Colletotrichum* have been reported to cause infection in humans. The majority of these cases have been keratitis with a few endophthalmitis cases due to *Colletotrichum dematium* [4] and *Colletotrichum truncatum* [5].

The treatment of fungal endophthalmitis is a serious challenge for ophthalmologists as the outcome is unfavorable in a considerable number of cases. The treatment protocol in fungal endophthalmitis is still not optimized due to the low incidence of this disease at most centers. Various regimens combining oral and topical antifungals have been reported, including triazole and polyene antifungals. Unfortunately triazoles have been responsible for a number of clinically significant drug interactions. Triazoles are inhibitors of lanosterol 14 α-demethylase, which prevents lanosterol production and thereby cell membrane integrity. They also inhibit other cytochrome P450 enzymes, including CYP3A4 and CYP2C9. Therefore a number of CYP3A4 and CYP2C9 substrate drugs, such as alpha-adrenergic antagonists (ex. tamsulosin) are contraindicated, especially when administered in the high doses needed to treat fungal endophthalmitis [6,7].

This case report describes a patient on tamsulosin with *C. truncatum* fungal keratitis and endophthalmitis. Susceptibility data for this species is presented and we review the literature on the treatment and outcomes after ocular infections from *Colletotrichum* species.

* Corresponding author. Fax: +1 416 960 0333.

http://dx.doi.org/10.1016/j.mmcr.2015.06.001

### 1.1. Case

An 87 year-old man who recently returned to Canada after spending 4 months in Jamaica, presented (day 0) with a 1 month history of progressively increasing pain, redness, excessive tearing, decreased vision, and lid swelling in his left eye. He denied any history of ocular trauma or contact lens wear. The patient had decreased hearing but was otherwise healthy and was taking acetylsalicylic acid 81 mg daily. He reported that his doctor in Jamaica prescribed him an unknown topical ophthalmic solution. Once back in Canada he was seen by an optometrist who treated him with topical moxifloxacin and referred the patient 3 weeks later given the patient's worsening condition.

On examination of the patient's left eye, uncorrected visual acuity was light perception. The left pupil was fixed and mid-dilated. Intraocular pressure (IOP) was 22 mmHg. Slit lamp examination revealed limbal neovascularization; conjunctival injection; inferior keratic precipitates; a $4 \times 5$ mm$^2$, 90% thinned area of corneal stromal haze with no overlying epithelial defect; a dense cataract; and a shallow anterior chamber with temporal iridocorneal touch. Dilated fundoscopy was difficult but the retina appeared flat. A provisional diagnosis of herpes simplex immune stromal keratitis with uveitis was made. The patient was started on oral acyclovir 400 mg 5 times daily, as well as topical prednisolone acetate 1% four times daily, timolol maleate 0.5% twice daily, artificial tears four times daily, and Lacrilube ointment (Allergan, Irvine, CA) before bed.

Two weeks later (day 15), the patient's pain was improved with stable visual acuity, stable IOP, and diminished conjunctival injection. At the 3 week follow-up appointment (day 22), the cornea appeared hazier and had developed an ectatic bulge. A hypopyon measuring 1.6 mm was present and the cataract had become intumescent and white. Retinal consultation was sought and the prednisolone drops were increased to every 2 h, and dexamethasone 0.1% ointment before bed and home atropine 5% three times daily were added. One week later (day 28), the hypopyon had resolved but a $2 \times 2$ mm$^2$ epithelial defect at the 10 o'clock mid-peripheral cornea was noted. Topical moxifloxacin 4 times daily was restarted, prednisolone was decreased to 4 times daily, and the patient continued on oral acyclovir 400 mg 2 times daily as well as timolol/dorzolamide 2 times daily. The patient presented one week later (day 35) with increased redness and eye pain. A geographic ulcer covered the nasal half of the cornea and there was absent corneal sensation. Oral acyclovir was increased to 400 mg 5 times daily, prednisolone was decreased to 2 times daily and antibiotic prophylaxis was started. A week later (day 43), the patient presented with corneal perforation and uveal prolapse.

Urgent pars plana vitrectomy and lensectomy using a temporary keratoprosthesis, and penetrating keratoplasty was performed (day 51). The host cornea was divided into 2 and sent for pathological examination and bacterial and fungal culture. Direct microscopic examination of the specimen for fungi was not performed, as there was a very small amount of tissue received. Intravitreal injections of ceftazidime 2.25 mg/0.1 ml and vancomycin 0.1 mg/0.1 ml were given and post-operatively the patient was prescribed homatropine 5% three times daily, prednisolone 4 times daily, fortified vancomycin 31 mg/ml 4 times daily, fortified tobramycin 13.6 mg/ml 4 times daily, moxifloxacin 4 times daily, and oral acyclovir 400 mg 5 times daily.

On post-operative day (POD) 2 (day 53), the patient was admitted by the urology service for anuria secondary to benign prostatic hyperplasia (BPH). On slit lamp examination, the graft surface had epithelialized, peripheral anterior synechiae had formed 360 degrees, Descemet's membrane folds consistent with early post-operative stromal edema and pigmented precipitates on the endothelium were present. On POD 4 (day 55), the fungal culture became positive for a filamentous fungus, which grew on Sabouraud's agar with gentamicin, brain heart infusion agar with chloramphenicol, cycloheximide and gentamicin, and on Inhibitory Mold Agar. The initial colonial appearance was of a flat white colony with grey speckles and a beige periphery, with a grey reverse (Fig. 1). The culture was referred to the reference mycology laboratory, where it was found to be non-sporulating when examined microscopically. It was sent for ITS2 (internal transcribed spacer) sequencing PCR for identification. By POD 6 (day 57), the preliminary pathology report documented the presence of hyphae in the corneal tissue (Fig. 2). The molecular identification was reported as *Colletotrichum capsici*. After 7 days incubation, identifying features of sporulation were observed on microscopy of the colony, including dark brown, spherical and setose sclerotia, brown, rigid, smooth-walled setae, brown variably shaped appresoria, and one-celled falcate conidia (Fig. 3) with an acute apex. Further molecular testing, based on DNA sequencing using a combination of different primer sets and the MycoBank (CBS-KNAW) reference database indicated that the fungal identification was most consistent with *C. truncatum* species complex. Loci assessed included: D1/D2 (100% *C. truncatum,* accession No. DQ286159), ITS3/ITS4 (100% *C. truncatum*, accession No. AJ301944), beta-tubulin (*C. truncatum* 99.798%, accession No. HM575221.1), and translation elongation factor 1α (*C. truncatum* 96.538). Some entries indicated a high degree of homology with *C. capsici*, which is a synonym of *C. truncatum* and also of *Colletotrichum jasminigenum*, which is part of the *C. truncatum* species complex.

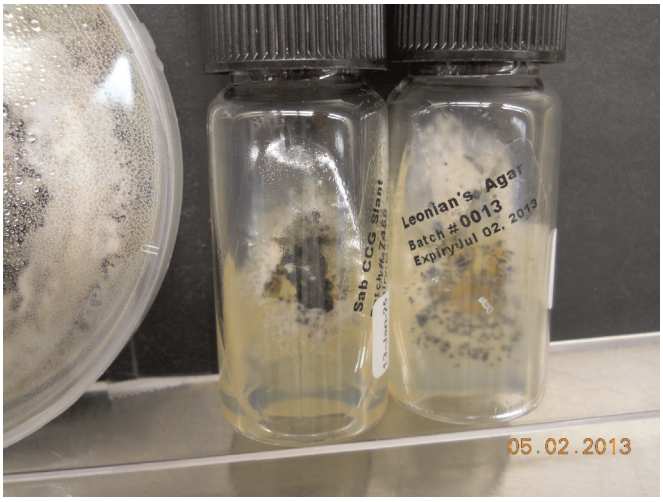


**Fig. 1.** Initial growth in Sabouraud's agar (left) and brain heart infusion agar (right).

Since the patient was receiving tamsulosin for his advanced BPH, an oral triazole was contraindicated. Infectious diseases was consulted and recommended that 0.15% amphotericin B could be used. Intravitreal injection of amphotericin B 0.01 mg/0.1 ml was attempted but the patient could not tolerate it. A subconjunctival depot was administered (day 78).

The patient once again was lost to follow-up and presented one month later (day 112) with a painful blind eye, mildly injected conjunctiva, clear PK graft with intact epithelium, a large fibrin plaque adherent to the endothelium, and dense vitritis on B-scan ultrasound, consistent with presumed fungal endophthalmitis. At this time, the patient requested and underwent left eye evisceration and reconstruction (day 129). GMS stained section from the evisceration specimen showed fungal elements in the corneal graft and in the anterior chamber (Fig. 4).