

# Successful Medical Treatment of a Case of *Paecilomyces lilacinus* Keratitis

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**Purpose:** To report a successful medical treatment of a case of keratitis caused by *Paecilomyces lilacinus*.

**Methods:** A 68-year-old woman developed an infection of the left cornea after minor trauma. The causative organism was found to be a particularly virulent organism, *P. lilacinus*. The patient was initially treated with natamycin topically and itraconazole orally, but the organism was resistant and failed to respond. She was then switched to topical voriconazole and oral terbinafine.

**Results:** The patient was successfully treated with these medications without surgical intervention, an unusual outcome for this organism.

**Conclusions:** If one encounters a case of fungal keratitis that fails to respond to the more commonly used agents, one should suspect a resistant organism such as *Paecilomyces* and should switch to voriconazole and/or terbinafine both topically and orally.

**Key Words:** *Paecilomyces lilacinus*, keratitis, voriconazole, terbinafine (*Cornea* 2008;27:1077–1079)

**P**aeilomyces is a rare cause of corneal infection.<sup>1–3</sup> Most cases of ocular infection with this type of fungus result in poor outcomes.<sup>1</sup> We report a successful medical treatment of *Paecilomyces lilacinus* keratitis using topical voriconazole and oral terbinafine (Lamisil).

## CASE REPORT

A healthy, 68-year-old white woman presented in early June of 2006 to S.T.G. after a week of worsening pain, increasing redness, and decreasing vision in her left eye. One week before presentation, she had a foreign body removed by an optometrist who placed her on a tobramycin–dexamethasone combination drop 4 times a day. She was found to have a feathery infiltrate of the left cornea that looked consistent with a filamentary fungal infection (Fig. 1). The infiltrate was scraped and cultured at this point. Gatifloxacin, tobramycin, and natamycin 5% were given hourly topically, and the tobramycin–dexamethasone drop was stopped. Two days later, growth was seen on several culture plates (Sabarouds, blood, and chocolate agar) that

appeared to be fungal. Gatifloxacin and tobramycin were discontinued, the natamycin 5% was continued every hour, and oral itraconazole 200 mg twice daily was added. The patient was observed daily. Over the next week, the keratitis seemed to stay the same without signs of obvious improvement. The cornea was quite edematous, and there was some thinning in the bed of the ulcer. Because of the lack of significant response, oral terbinafine was initiated (250 mg a day). A day later, the keratitis seemed to worsen with increase in corneal edema and infiltrate. A small hypopyon developed. All cultures were found to be a species of *P. lilacinus* (Fig. 2).

The patient was referred to a corneal specialist (J.G.F.). The patient's visual acuity was 20/200 with spectacle correction. A central, superficial corneal infiltrate was present and appeared chalky white with feathery margins. It measured less than 1 mm both vertically and horizontally. The anterior chamber was found to have 2+ cell and flare, and a small hypopyon was present. The iris vessels were engorged. A posterior chamber intraocular lens was present with an intact clear capsule. Topical voriconazole 1% hourly while awake was substituted for natamycin. With the combination of topical voriconazole 1% hourly, oral itraconazole 200 mg twice a day, and terbinafine 250 mg once a day, the keratitis slowly improved, the hypopyon cleared, and the infiltrate diminished with healing of the epithelium over a period of approximately 15 days. Oral itraconazole was eventually stopped after sensitivities returned 6 weeks after cultures were performed, showing that this organism was resistant to it (Table 1). The organism was found to be sensitive to only terbinafine and moderately sensitive to voriconazole. The patient was continued on topical voriconazole 1% (hourly for 2 weeks, then 6 times a day for 2 weeks, then 4 times a day for 2 weeks, etc.) and oral terbinafine 250 mg a day for a total of approximately 10 weeks since their initiation. No evidence of recurrence was detected, and a central scar was present in the location of the infection.

The patient was last examined 1 year after discharge. The patient's visual acuity was 20/30 with spectacle correction. She did notice glare and starburst, but she was able to tolerate these symptoms. The central scar had faded, and there was no obvious thinning of the cornea in the area of the scar.

## DISCUSSION

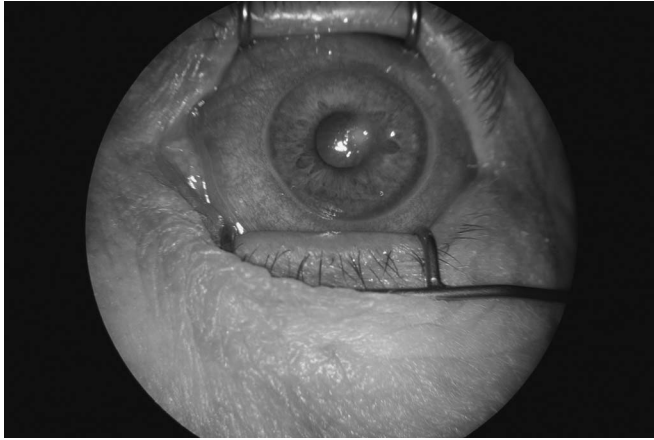
*Paecilomyces* ocular infections are uncommon despite being one of the more abundant saprophytic soil fungi.<sup>1–11</sup> It is a septated filamentous fungus that usually demonstrates rapid growth with fast-growing colonies that have a velvety texture. *Paecilomyces lilacinus* produces a violet or lilac color.<sup>2</sup> A very thorough review of *Paecilomyces* can be found in a report by Anderson et al.<sup>2</sup> When causing an infection of the eye, this organism seems to have aggressive behavior, with most cases having very poor visual outcomes.<sup>1–11</sup> This observation may be explained in part by the resistance of this organism to most antifungal agents.<sup>1–3</sup>

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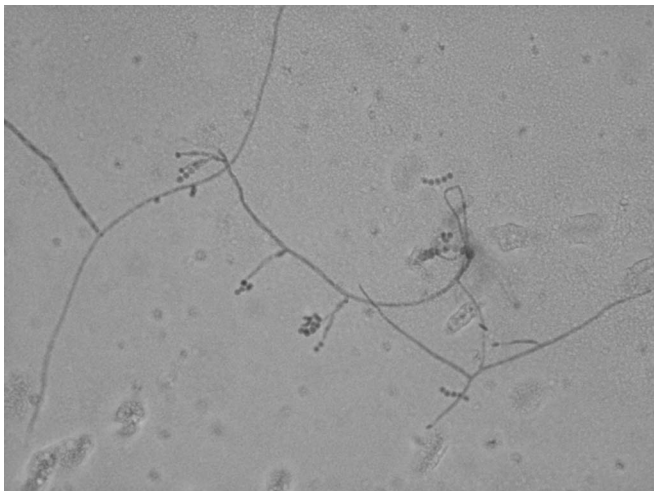
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**FIGURE 1.** Photograph of patient's inflamed left eye on presentation demonstrating central corneal ulceration with an infiltrate with feathery margins caused by *Paecilomyces lilacinus*. (Photograph by Janet McMullen, Certified Ophthalmic Technician).

The reported cases of *P. lilacinus* keratitis that were medical failures had complicated treatment courses in most cases.<sup>2-5,7,8,10,11</sup> Variable combinations of topical, oral, and intravenous antifungal agents including azoles, polyenes, and antimetabolites were given and often were interchanged in each case in an attempt to gain control over a progressive infection. Most cases had to undergo therapeutic penetrating keratoplasties combined with other surgical interventions such as vitrectomy and repeated intracameral injections of antifungals. Most cases ended with very poor outcomes.<sup>1</sup>

Only 2 cases of successful medical treatment of *P. lilacinus* keratitis exist in the literature.<sup>8,9</sup> It is not clear why the above-mentioned successful medically treated cases came out so well compared with the failure cases. The same topical medications were used in most of the failure cases as the successful ones. The superficial location of the 2 successful



**FIGURE 2.** Photomicrograph of *Paecilomyces lilacinus* from this case demonstrating the single sterigmata arising along hyphae with characteristic, long, tapering conidia-bearing tubes.

**TABLE 1.** Sensitivity of *Paecilomyces lilacinus* to Various Antifungals

Drug Tested	MIC at 48 h (µg/mL)	Laboratory Interpretation
Terbinafine	0.06	Sensitive
Miconazole	4.0	Resistant
Ketoconazole	2.0	Resistant
Voriconazole	0.5	Moderately sensitive
Itraconazole	8.0	Resistant

MIC, minimum inhibitory concentration.

cases may be an important factor. Our successful case shares this factor as well. Also, it may be that in the 2 successful cases, the particular strains of *P. lilacinus* may have had different sensitivities to the antifungals compared with the failure cases.

Based on the experience gained in our case and the information gathered from reviewing the literature, we recommend that one should use voriconazole and terbinafine in the treatment of *P. keratitis*.<sup>1-5,12-15</sup> Both can be used topically and orally. Voriconazole, an “-azole” antifungal interfering with the synthesis of ergosterol in fungal cell membranes, has been demonstrated to be effective in treating experimental *Paecilomyces* keratitis.<sup>5</sup> In the same study, it penetrated very well into the cornea and anterior chamber. However, in a study, a large number of ocular fungal isolates were tested against voriconazole and it was found that the 1 isolate of *P. lilacinus* in the study was resistant to voriconazole.<sup>16</sup> In our case, this organism was found to be moderately sensitive to voriconazole. Our clinical experience with voriconazole 1% used hourly is that it is well tolerated by the patient in terms of comfort and by the corneal epithelium. No reports are in the literature concerning voriconazole and its effect on the corneal epithelium.

Less is known about terbinafine, an allylamine antifungal that interferes with ergosterol synthesis but at a different step than the “-azole” antifungals. One study using topical terbinafine 0.2% in corn oil solution demonstrated adequate penetration of this drug into the cornea and anterior chamber of rabbits.<sup>13</sup> Another study tested a large number of filamentous fungal isolates from different body locations to terbinafine.<sup>14</sup> Most of the isolates were sensitive to terbinafine including the 6 isolates of *P. lilacinus*. Interestingly, the *Fusarium* species isolates and the *Aspergillus fumigatus* isolates were resistant. There are no reports in the literature concerning the clinical use of topical terbinafine in the treatment of corneal ulcers.

Only 1 report exists in the literature in which voriconazole and terbinafine were used in combination to treat a case of *P. lilacinus* keratitis.<sup>2</sup> In this case, these drugs were used orally. Voriconazole was given 200 mg twice daily, and terbinafine was given 250 mg once daily. However, they were initiated 17 days after a therapeutic graft at a point in time in which there was no obvious evidence of residual fungal infection. They were continued for 3 months, and no signs of hepatic toxicity developed.

The oral dosage of these medications is as described above. Both of these medications are metabolized by the liver,

and monitoring of the liver function should be performed if either one or both of these medications are used. There are no reports in the literature that would indicate an increased risk of hepatic toxicity if both the medications are used simultaneously.

The management of fungal keratitis can be very challenging especially if *Paecilomyces* is involved. Determining the identity and obtaining sensitivities of this organism usually occur after many days to weeks into the course of the infection. If one identifies a fungal keratitis, either by clinical suspicion or by fungal smear or culture after corneal scraping, and it seems that the infection does not respond properly to the most commonly used topical antifungal, natamycin, one should suspect a rare organism such as *P. lilacinus*. When these types of cases occur, we recommend the use of voriconazole and/or terbinafine both topically and orally.

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