

Penicillium chrysogenum endophthalmitis

First reported case

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Abstract

Infections caused by *Penicillium chrysogenum* are rare. The first case of posttraumatic endophthalmitis caused by this saprophytic fungus is reported. Therapy with amphotericin B and topical natamycin eradicated the organism.

Introduction

Ocular mycoses have become more common during the past thirty years (4, 5). They are frequently a sequela of corneal trauma (4, 5) often caused by vegetative foreign bodies (4). Speciation of the fungus is not always performed. Endophthalmitis caused by *Penicillium chrysogenum* is reported here for the first time.

Case report

A 32 year old man was admitted in October, 1978 for right eye pain. Twenty hours earlier, he struck a steel bit with a hammer and experienced immediate pain in the right eye. Findings were limited to the painful eye, which the patient could not open. A corneal ulcer was present and was associated with thick, frothy mucus which covered the conjunctival sac. Slit lamp examination revealed a foreign body in the posterior lens with hypopyon formation. Corneal opacification prevented fundal examination, and the patient retained only light perception.

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As emergency surgery was being performed, intravenous antimicrobial therapy was initiated with carbenicillin (5 grams every 4 hours), gentamicin (50 mg every 6 hours), and cephalothin (2 grams every 6 hours). Surgery was unsuccessful in removing the metal sliver. During surgery a swab which had been inserted into the anterior chamber was immediately streaked onto chocolate and blood agar plates.

Mycology

Aerobic growth within the inoculation sites was observed at three days on both primary culture plates at 35 °C. The apparent fungus was the only organism isolated.

Colonies were visible on sub-culture on Sabouraud dextrose agar after three days at room temperature. Mature colonies were covered with a greenish-gray aerial mycelium and were light yellow on the reverse. Microscopic features of the isolate were one-celled globose conidia borne in chains from the tips of phialides which, in turn, arose from metulae oriented in a brush-like arrangement or penicillus. The metulae branched from the ends of septate conidiophores which showed little or no enlargement at the tips. No

distinctive foot cells were observed at the bases of the conidiophores. The conidia were not enclosed in mucus and did not have a basal ring and pore. The vegetative hyphae were septate. These characteristics placed the fungus in the genus *Penicillium*. The speciation was kindly done by Dr. K. J. Kwon-Chung and confirmed by Professor Kenneth B. Raper.

Hospital Course

After surgery, intravenous antibiotics were continued and chloramphenicol eye drops (2 drops every 2 hours), subconjunctival gentamicin (5 mg daily), and oral prednisone (50 mg daily) were begun. Three days postoperatively the patient complained of unrelenting pain in the involved eye and examination revealed extension of the hypopyon. A culture of the conjunctival sac was obtained but showed no growth. Prednisone and all antibiotics were discontinued. Intravenous nafcillin (3 grams every 4 hours) and 10% topical sulfacetamide (2 drops every 2 hours) were instituted empirically, and while awaiting identification of the isolated fungus, amphotericin B therapy was begun subconjunctivally with 5 mg, intravenously with 50 mg per day, and topically with 1% drops (3 hourly). Intravenous nafcillin was discontinued on the ninth hospital day and 5% topical natamycin (3 drops every 4 hours) was added. Thereafter, natamycin eye drops were alternated hourly with amphotericin B eye drops until discharge. On hospital day 20, the patient experienced less eye pain, examination revealed less inflammation, and intravenous amphotericin B was discontinued after a cumulative dose of 625 mg. Four weeks after the accident the patient was discharged and maintained on topical natamycin for two more months.

Follow-up examination of this patient has revealed extensive persistent corneal clouding with resolution of the hypopyon. The patient retains light perception and is pain-free one year after the original injury.

Discussion

Fungal endophthalmitis can result from an invasive superficial infection such as keratomycosis,

hematogenous infection, or either surgical or inadvertent penetrating injury. Exogenous intraocular mycoses have been reviewed and divided into posttraumatic and postoperative intraocular mycoses (4). Of 20 reports of the posttraumatic type reviewed, none was caused by *Penicillium* (4). In only one of over 50 reports of postoperative intraocular mycoses reviewed (4) was *Penicillium* described; in that report *Cephalosporium* or *Penicillium* was identified from anterior chamber fluid in 13 cases, but no further information was given (1).

The most common ocular mycosis is keratomycosis. *Penicillium* species have only rarely been implicated as the cause of keratomycosis (3, 5, 6, 8). In the single reported case of *P. notatum* keratomycosis, the infection had a prolonged but benign course following therapy with fungistatic agents (6). We found no prior reports of ocular infection caused by *P. chrysogenum*.

Medicine was revolutionized by Fleming's discovery of penicillin produced by *P. notatum* (7). Clinical advances were hindered by the minute amounts produced by *P. notatum*. In the search for a high-yielding organism, *P. chrysogenum* was identified and continues to be used for penicillin's commercial production (11). Prior to this report *P. chrysogenum* had been reported only once as a cause of human disease; it was a patient with nosocomial endocarditis of a prosthetic aortic valve (10). Consequent to its rare recovery from clinical specimens, it has been generally regarded a non-pathogen.

Initial cultures of our patient's anterior chamber fluid grew *P. chrysogenum* in pure culture. Since anterior chamber penetration by intravenous antibiotics is slow, it is unlikely that significant levels of antibacterial agents had been achieved in the aqueous humor at the time of culture. Therefore, it is doubtful that other organisms were responsible for the keratoconjunctivitis and endophthalmitis in this case. A conjunctival culture obtained three days postoperatively before antifungal therapy showed no growth, an observation consistent with negative cultures of conjunctival exudates reported during active fungal infection with an intraocular mycosis (4). Steroids, frequently used in the therapy of keratoconjunctivitis, potentiate fungal invasion and destruction of the cornea in cases of keratomycosis (4). Although our patient received a cor-

ticosteroid postoperatively, the drug was promptly discontinued after a *Penicillium* species was isolated. Antibacterial therapy ameliorated neither the corneal inflammation nor the eye pain.

Natamycin, a polyene antibiotic, is considered to be the drug of choice for treating keratomycosis (2). This recently released antifungal agent is closely related to nystatin and amphotericin B but produces less local pain and is more efficacious in ocular mycosis than earlier polyene compounds. Our patient's clinical improvement correlated with the addition of natamycin. Although precise determination of the role of each antifungal agent in this case is not possible, one week of intravenous and topical amphotericin B did not decrease pain or corneal inflammation. Clinical improvement occurred within a week of the addition of topical natamycin to continuing topical amphotericin B therapy. Although the benefits of amphotericin B might have accrued slowly, there was no improvement until after topical natamycin was begun.

There is only one case report of natamycin therapy of keratitis caused by an unspiciated member of the genus *Penicillium* (3). In that case a therapeutic penetrating keratoplasty was used to enhance penetration of the drug. There is only one *in vitro* study documenting the sensitivity of an unspiciated *Penicillium* to natamycin (9), and there are no prior reports of natamycin treatment of intraocular mycosis caused by *Penicillium*.

Infections caused by the genus *Penicillium* are rare and when they occur speciation of the organism is usually not attempted. The current case is notable in that a fungal species of low pathogenicity caused posttraumatic endophthalmitis in a normal adult. Since all *P. chrysogenum* species studied produce penicillin in varying amounts (7), it is interesting to speculate on the role of penicillin produced by the infecting fungus in preventing the growth of bacterial pathogens in this case.

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