MAJOR ARTICLE

Invasive Infections Due to *Trichoderma* Species: Report of 2 Cases, Findings of In Vitro Susceptibility Testing, and Review of the Literature

T. Chouaki,[1] V. Lavarde,[2] L. Lachaud,[3] C. P. Raccurt,[1] and C. Hennequin[1]

[1]Service de Parasitologie-Mycologie, Centre Hospitalier Universitaire Amiens, Amiens, [2]Service de Microbiologie Hôpital Européen G. Pompidou, Paris, and [3]Service de Parasitologie-Mycologie, Centre Hospitalier Universitaire Montpellier, Montpellier, France

Trichoderma **species are filamentous fungi that were previously considered to be culture contaminants. We report 2 well-documented cases of invasive *Trichoderma* infections, and we comprehensively review the literature on this topic. *Trichoderma* species are mainly responsible for continuous ambulatory peritoneal dialysis–associated peritonitis (7 cases) and invasive infections in immunocompromised patients (9 cases) with a hematologic malignancy or solid-organ transplant. Definitive diagnosis is difficult to achieve because of the lack of specific diagnosis tools. Species identification can benefit from a molecular approach. *Trichoderma longibrachiatum* is the most common species involved in these infections. Regardless of the type of infection, the prognosis was poor, with 8 deaths among 18 cases. This may be partially because of the resistance of these organisms to the majority of available antifungal agents, including amphotericin B. *Trichoderma* species now should be added to the growing list of emerging filamentous fungal pathogens.**

Trichoderma species are common plant saprophytes and wood-decaying fungi. Allergic manifestations associated with *Trichoderma* exposure have been reported elsewhere [1]. However, *Trichoderma* species also appear to belong to the growing list of emergent pathogens, with an increasing number of reports of invasive infections [2, 3]. These infections are characterized by the presence of fine septate hyphae in tissue sections, the so-called "hyalohyphomycosis pathological entity," for which differential diagnosis with invasive aspergillosis is critical. On the basis of 2 well-documented cases and a review of the literature, we describe the main clinical and therapeutic features of these infections. Differential characteristics with invasive aspergillosis and other hyalohyphomycosis are also emphasized.

CASE REPORTS AND METHODS

Case 1. A 63-year-old woman underwent liver transplantation in August 1997 because she had hepatitis C virus–induced cirrhosis. Immunosuppressive therapy included oral tacrolimus (6 mg q.d.) and prednisolone (20 mg q.d.). The postoperative course was on the whole satisfactory except for persistent pancytopenia of unclear origin. Nine months later, when her WBC count was 1700×10^6 cells/L (45% polymorphonuclear cells), the patient presented with abdominal pain in the right-upper quadrant. She had a temperature of 38.5°C. Otherwise, the findings of a clinical examination were normal. Biological measurements, including determination of hepatic enzyme levels, did not reveal any abnormality. Abdominal ultrasonography revealed a subcapsular collection (3.5×1.5 cm) related to suture

Received 29 March 2002; accepted 8 August 2002; electronically published 7 November 2002.

Reprints or correspondence: Dr. C. Hennequin, Unité de Génétique Moléculaire des Levures, Institut Pasteur, 25 rue du Dr Roux, 75724 Paris cedex 15, France (christophe.hennequin@laposte.net).

Clinical Infectious Diseases 2002; 35:1360–7

1058-4838/2002/3511-0009$15.00

threads. Examination of the abscess aspirate obtained through a fine needle–transparietal puncture demonstrated numerous fine septate hyphae with regular dichotomy division. Testing for *Aspergillus* antigenemia by ELISA (Sanofi Diagnostic Pasteur) yielded negative results. Culture of a sample of the pus yielded pure cultures of *Trichoderma* species (i.e., no microorganism other than *Trichoderma* species was detected), identified as *Trichoderma pseudokoningii* on macro- and microscopic examination of the colonies. Similar findings were obtained during a 3-month period from 2 other samples obtained from a scar swabbing and from biopsy specimens of perilesional tissues. The latter revealed a granulomatous hypodermitis containing numerous hyphae noted on periodic acid–Schiff stains, with septa and heterogeneous diameter (figure 1). During this time, the patient became intermittently febrile without any other clinical symptoms. Her WBC count oscillated from 1500 to 3700 cells/mm^3, of which 728–1100 cells/mm^3 were polymorphonuclear cells. No antifungal drugs were administered. Concomitant surgical debridement and local administration of povidone iodine resulted in total recovery. No relapse was noted after 4 years of follow-up.

Case 2. An 11-year-old boy with cystic fibrosis underwent a pulmonary transplantation in October 1998 because of terminal respiratory failure. He had previously received multiple courses of antibiotics for recurrent bronchitis exacerbations complicating *Staphylococcus aureus* and *Pseudomonas aeruginosa* colonizations. The antibiotics included mainly ceftazidime, tobramycin, and ciprofloxacin. The patient was also chronically colonized with *Aspergillus fumigatus*. Postoperative immunosuppressive therapy consisted of corticosteroid therapy (prednisone, 1 mg/kg q.d., progressively decreased to 0.2 mg/kg q.d.), azathioprine (3 mg/kg q.d.), and cyclosporine (dosage adapted to achieve a seric assay at 250 mg/mL). Preventive antifungal therapy with oral itraconazole (400 mg q.d.) was also initiated. The patient's postoperative course was immediately complicated by septic shock, which was treated with antibiotics (vancomycin, ceftazidime, tobramycin, and ciprofloxacin) plus amphotericin B lipid complex (3 mg/kg q.d.). Moreover, because of cytomegalovirus antigenemia, the patient received ganciclovir (3 g q.d. iv). Unfortunately, the clinical course did not improve, and the child developed bilateral pulmonary edema. Amphotericin B lipid complex was then replaced by oral itraconazole solution (500 mg b.i.d.). Thoracic tomodensitometry revealed bilateral pneumothorax, pneumopericardium, and a dense lesion of the right apex. On day 14 after transplantation, a sample obtained from the transcutaneous tracheal puncture and a bronchoalveolar lavage fluid sample obtained on the same day tested negative on direct examination, but both samples yielded *Trichoderma* species on pure culture. Conventional methods (culture plus morphomicroscopic evaluation) identified the isolate as *Trichoderma konigii*. A new episode of respiratory distress was attributed to acute graft rejection and treated with 3 bolus injections of methylprednisolone (125 mg each) on days 18–20 after transplantation. Two days later, pleural drainage samples became positive for a multidrug-resistant strain of *P. aeruginosa* and *Trichoderma* species. Treatment with

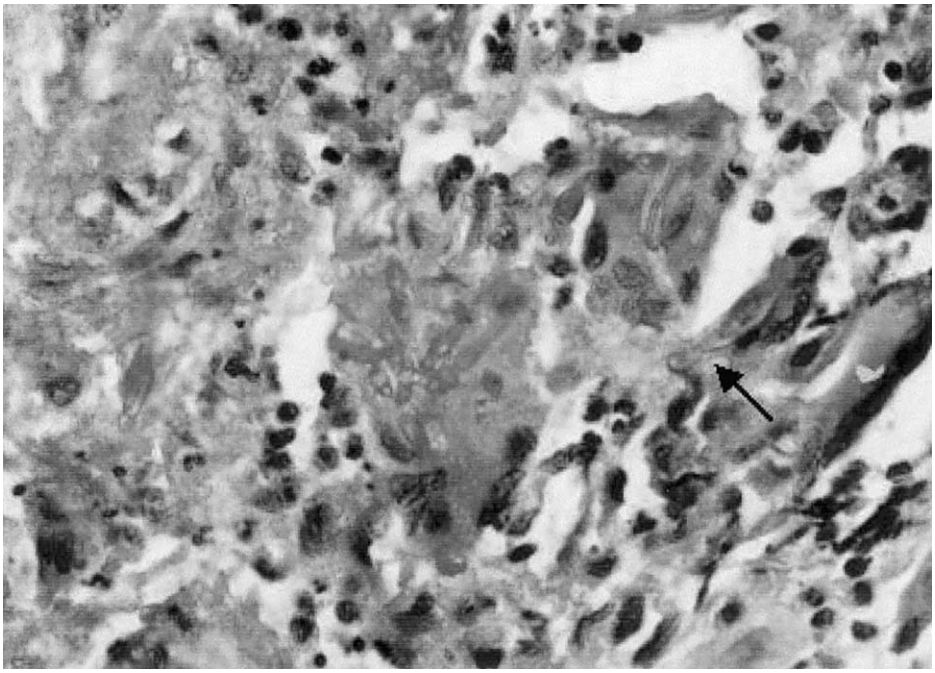

Figure 1. Histopathologic findings of needle biopsy of a subcapular hepatic abscess due to *Trichoderma longibrachiatum* (case 1): thin (3–4-mm) septate branched hyphae with a feature suggestive of conidiogenesis *(arrow)*. (Periodic acid–Schiff stain; original magnification, ×10,000).

Table 1. Clinical characteristics of systemic and disseminated infections due to *Trichoderma* species.

Manifestation, case	Reference	Year	Age in years, sex	Underlying disease or risk factor	Site of infection	Fungal species	Treatment	Outcome
Exogenous peritonitis								
1	[20]	2000	33, M	IgA nephropathy, CAPD	Peritoneal fluid	*Trichoderma pseudokoningii*	Removal of catheter	Cure
2	[7]	1998	60, M	Diabetic nephropathy, CAPD	Peritoneal fluid	*Trichoderma* species	Ketoconazole; removal of catheter	Cure
3	[13]	1996	82, M	Non–insulin-dependent diabetes, CAPD	Peritoneal fluid	*Trichoderma harzianum*	Ketoconazole; ip flucytosine	Death
4	[17]	1984	63, F	Renal failure of unknown origin, CAPD	Peritoneal fluid	*Trichoderma koningii*	Removal of catheter; miconazole	Cure
5	[9]	1996	40, M	Diabetic nephropathy, CAPD	Peritoneal fluid[a]	*T. koningii*	Removal of catheter; fluconazole, flucytosine, and amphotericin B	Death
6	[15]	1983	47, M	Amyloidosis, renal failure, CAPD	Peritoneal fluid[a]	*Trichoderma viride*	Amphotericin B; removal of catheter	Death
7	[22]	1995	48, M	Renal transplantation, CAPD	Peritoneal fluid	*Trichoderma longibrachiatum*	Amphotericin B	Death
OI in immunocompromised patients								
After solid-organ transplantation								
8	[12]	1999	68, M	Renal transplantation	Brain abscess,[b] lungs[b]	*Trichoderma harzianum*	None	Death
9	[10]	1998	29, F	Small bowel and liver transplantation	Invasive sinusitis	*T. longibrachiatum*	Amphotericin B; itraconazole; surgical debridement	Cure
10	[14]	1992	44, M	Liver transplantation	Perihepatic hematoma	*T. viride*	Amphotericin B; fluconazole; surgical debridement	Death
11	PR, case 1	1998	63, F	Liver transplantation	Subcapsular hepatic collection	*T. longibrachiatum*[c]	Surgical debridement; povidone iodine	Cure
12	PR, case 2	1998	11, M	Lung transplantation	Bronchoalveolar lavage, pleural drains	*T. longibrachiatum*[c]	Lipid-associated amphotericin B	Death

With hematologic malignancies								
13	[18]	1999	29, M	Acute lymphoblastic leukemia, bone marrow transplantation	Stool, perianal ulcer, liver,[b] lungs,[b] sigmoid colon,[b] ileocecal valve,[b] brain[b]	*T. longibrachiatum*	Amphotericin B; itraconazole	Death
14	[16]	1997	11, M	Aplastic anemia	Skin (catheter)	*T. longibrachiatum*	Amphotericin B lipid complex	Cure
15	[21]	1995	17, F	Leukemia with prolonged neutropenia	Ethmoidal, brain abscess	*T. longibrachiatum*	Amphotericin B; itraconazole; surgical resection	Cure[d]
16	[11]	1995	45, F	Acute erythroleukemia, bone marrow transplantation	Bronchoalveolar lavage, skin (catheter), lung,[b] brain,[b] heart,[b] stomach[b]	*T. longibrachiatum*[c,e]	Amphotericin B; flucytosine	Death
Miscellaneous infection								
17	[19]	1969	26, F	IV infusion contaminated with *Trichoderma* species	Blood	*Trichoderma* species	Amphotericin B	Cure
18	[8]	2000	66, M	Aorta replacement	Endocarditis	*Trichoderma* species	Graft replaced; antifungal NS	Cure
19	[23]	1989	NS, NS	NS	Keratitis	*Trichoderma* species	NS	NS
20	PC[f]	1992	NS, M	None	Keratitis	*T. viride*	No antifungal	NK

NOTE. CAPD, continuous ambulatory peritoneal dialysis; NK, not known; NS, not specified; OI, opportunistic infection; PC, personal communication; PR, present report.

[a] Including postmortem positive culture results.
[b] Postmortem finding.
[c] Identification confirmed by intergenic transcribed spacers sequencing.
[d] Died 11 months later free of infection.
[e] First identified as *T. pseudokoningii*.
[f] A. M. Le Flohic, personal communication.

liposomal amphotericin B was then initiated (5 mg/kg q.d.) in combination with itraconazole at the same dosage. However, the child died of respiratory distress and cerebral complications 26 days after transplantation. A postmortem examination was not performed.

Mycological study. To confirm the species identification, 1 isolate from each patient was directly sequenced according to a published protocol [4], which gives a 650-bp fragment coding for the intergenic transcribed spacers region (including ITS1, ITS2, and the 5.8S rDNA).

These 2 isolates were also tested in vitro against amphotericin B, itraconazole, and voriconazole by a colorimetric microdilution method adapted from the M38-P method proposed by the National Committee for Clinical Laboratory Standards [5, 6]. In brief, antifungal agents were serially diluted 2-fold in $2 \times$ RPMI 1640 medium supplemented with l-glutamine and buffered with 0.165 *M* of morpholinesulfonic propane acid buffer to achieve final concentrations of 0.125–64 mg/L. Each dilution was dispensed in sterile U-bottom 96-well plates. Inocula were prepared by adjusting spore suspensions to 2×10^4 cells/mL in sterile distilled water and then dispensing into each well. The colorimetric reagent Alamar blue (BioScience International) was added to each well. Sterility controls (no inoculum), growth controls (no drug), and a quality control (*Candida krusei* American Type Culture Collection [ATCC] 6258) were included for each plate. Incubation was done at 35°C for 48 h. For determination of MICs, we considered the lowest drug concentration that showed a slight color change from blue to purple for itraconazole and voriconazole and the lowest drug concentration that showed no color change or the first well that remained blue for amphotericin B. This method has been demonstrated to be highly correlated with the M38-P protocol [6].

Literature search. An electronic search was done with use of the key words "*Trichoderma*" and "human infection" in the PubMed database (http://www.ncbi.nlm.nih.gov) and the Current Contents Clinical Medicine database (http://www.isinet.com/isi/products/cc/editions/cccm/).

RESULTS

Literature review. In a comprehensive search, we found 16 well-documented published cases of invasive *Trichoderma* infection [7–22]. Also, there were 2 cases of keratitis (A. M. Le Flohic, personal communication) [23]. The clinical characteristics are shown in table 1. Moreover, Kulhs et al. [24] and Walsh et al. [25] cite 8 and 1 additional cases, respectively, but because of their lack of clinical details, these cases were not included in the present review. One case of superficial infection (otitis externa) [26] and a case of pulmonary fungus ball [27], which corresponded to a saprophitism state of the fungus, were also excluded from the present review.

Clinical manifestations. The first case was described in 1969 [19], but 17 of the 20 reviewed cases were reported during the 1990s. There were 7 cases of peritonitis, all complicating continuous ambulatory peritoneal dialysis (CAPD) (table 1). A previous history of bacterial peritonitis was noted for 5 of 7 patients, but *Trichoderma* species were always isolated on pure culture. The clinical impact ranged from mild (abdominal discomfort) to more severe (bowel obstruction). Fever was noted in 2 of 5 documented patients. No clinical symptoms could suggest a fungal origin rather than a bacterial origin. Treatment included removal of the dialysis catheter in 5 cases, and antifungal therapy was also provided in 4 of these cases. In 2 cases, antifungal drugs were prescribed without withdrawal of the catheter, but this did not result in recovery [13, 22]. Despite these treatments, 4 patients died, $\geq$2 of whom still had progressive fungal infection, as documented by positive culture results after death [9, 15].

Opportunistic infections complicated the course of hematologic malignancy in 4 patients and solid-organ transplantation in 5 patients (table 1). Infection occurred in 3 patients while they were receiving treatment with antifungal drug(s). In 6 cases, the upper (sinusitis, in 2 patients) or lower airways (pulmonary infections, in 4) were involved without clinical specificity. In 3 cases, the infection was disseminated ($\geq$2 noncontiguous organs involved), as documented by postmortem examination. In these cases, there was brain involvement, which presented as a mass-expanding syndrome in 1 case [12]. In another case, the brain abscess corresponded to a contiguous infection from an ethmoidal invasive sinusitis [21]. Skin lesions (ulceronecrotic) were seen in 3 patients; in 2 of these patients, the lesions were at the site of insertion of an intravenous catheter [11, 18]. Five of these patients died, despite administration of antifungal therapy.

Among the miscellaneous cases (table 1), there were 2 cases of keratitis in subtropical countries (India and Mali) (A. M. Le Flohic, personal communication) [23] and 1 case of postsurgical endocarditis [8]. The original case described by Robertson [19] corresponded to an accidental intravenous infusion of contaminated fluid.

Causative species and in vitro susceptibility testing. Molecular analysis of the 2 isolates recovered from our patients revealed a 100% identity with *Trichoderma longibrachiatum* (GenBank accession number Z48935) for both isolates. In the aforementioned cases, species identification relied on morphology, sometimes completed by molecular identification. *T. longibrachiatum* was the most common species, being identified in 8 cases. Seven of the 8 cases cited by Kulhs et al. [24] were also due to *T. longibrachiatum*. In 4 cases, the identification to the species level was not performed.

Our isolates had MICs of amphotericin of 1 and 2 mg/L, an MIC of itraconazole of 16 mg/L, and an MIC of voriconazole of 2 mg/L. Although the methods used for in vitro susceptibility testing differed widely from one report to another, tested clinical isolates clearly exhibited resistance to fluconazole and flucytosine, frequently exhibited resistance to itraconazole, and exhibited slight susceptibility to amphotericin B (MIC, $\geqslant$1 mg/L).

DISCUSSION

On the basis of a review of the literature, *Trichoderma* infections in humans appear to be rare, including cases of CAPD-related peritonitis [28–30], but they are increasingly being reported, with 85% of the cases being reported the past 10 years. This increase probably reflects the opportunistic behavior of these fungi, favored by the increasing number of immunocompromised patients and the increasing attention of microbiologists to these fungi that were previously considered to be nonpathogenic.

It is important to understand the sources of contamination and routes of infection to adapt preventive measures. Considering the clinical forms (i.e., sinusitis, pneumonia, and abscess following surgery), ambient air is the likely source of infection for some opportunistic infections. This contamination may be enhanced from water-related sites, because *Trichoderma* species were found to be the most prevalent fungus, after *A. fumigatus,* among filamentous fungi cultured from samples from outlets, waste pipes, and shower heads in a bone marrow transplantation ward [31]. *Trichoderma* species have also been isolated from food [32], and contaminated food may explain the digestive involvement described in a patient who had a positive stool culture result [16]. As demonstrated for *Fusarium* infections [33], the catheter may be a portal of entry for invasive *Trichoderma* infections [11, 16] and CAPD-related infections. Finally, contaminated infusion product can lead to disseminated infection when infused intravenously [19]. This can also be hypothesized as a source of infection for some CAPD-related cases, as has already been mentioned for infections due to yeasts and other filamentous fungi, such as *Aspergillus* species [34, 35].

Definitive diagnosis of *Trichoderma* infection may be difficult to make, because, as is the case for the diagnosis of other hyalohyphomycosis, it requires the demonstration of hyphae in tissue sections. Culture of blood samples does not appear to be a valuable diagnostic tool, because, despite documented dissemination, there is only 1 report of positive blood culture results for *Trichoderma* species cited by Kuhls et al. [24], in addition to the accidental case described by Robertson [19]. This is similar to invasive aspergillosis but contrasts with disseminated *Fusarium* infections, for which blood culture results are positive in ~50% of cases [36, 37]. Thus, diagnosis frequently relies on the demonstration of hyphae associated with positive culture results in nonbiopsy specimens obtained from accessible sites (e.g., skin and upper and lower airways) and, more rarely, from urine. The repeated isolation of the same fungus—if possible, from different sites—reinforces this highly probable diagnosis for immunocompromised patients. On direct examination, *Trichoderma* infection can be misdiagnosed as aspergillosis and other hyalohyphomycosis, because the hyphae are morphologically quite similar. Recently, Guarro et al. [12] emphasized the complexity of the branching pattern of *Trichoderma* hyphae in tissue. Figure 1 also demonstrates a feature suggestive of an adventitious conidiogenesis, a phenomenon already demonstrated for *Fusarium, Acremonium,* and *Paecilomyces* species in cases of invasive infection [38]. Nonculture methods have rarely been used for the diagnosis of *Trichoderma* infection. Gautheret et al. [11] mentioned antigen detection by use of a kit for the detection of the *Aspergillus* galactomannan antigen, a result not found in our cases. Einsele et al. [39], in describing primers for the detection of DNA from numerous pathogenic fungi in serum or blood, did not test *Trichoderma* in their report. We found that their primers amplified the target sequence on DNA extracted from our 2 stains (data not shown). Thus, their protocol could be tested for *Trichoderma* DNA detection in patients supposed to be infected with *Trichoderma* species. The identification of *Trichoderma* isolates at the species level may be difficult in the case of a positive result, as demonstrated in some reports in which identification that relied only on conventional methods led to erroneous species identification [11, 24, 40]. With use of molecular tools, Kulhs et al. [24] showed that most *Trichoderma* infections in humans are due to *T. longibrachiatum* and, more rarely, to *Trichoderma citrinoviride* [24]. Our cases and a previous case of otitis externa concur with this idea [26].

Regardless of the clinical presentation, the prognosis of these infections was poor. In patients with CAPD-related infections, recovery occurred in association with removal of the catheter alone in 1 case [20]. Nevertheless, the role of antifungal therapy in the management of these infections should not be underestimated, because persistent infections have been documented despite the removal of the catheter [9, 15]. It is difficult to determine optimal therapeutic management from these observations, but, while not scientifically demonstrated, it seems reasonable to remove the catheter concomitantly with the prescription of an antifungal drug. The latter should be defined according to susceptibility (see below) and pharmacokinetics of the drugs, notably peritoneal diffusion. Five of 9 patients with cancer-associated infection died, among whom $\geqslant$4 had a persistent fungal infection (table 2). There is a trend showing that disseminated forms had a poor prognosis: all 3 patients with disseminated infection died, whereas there were 2 deaths

Table 2. Prognostic factors and outcome for invasive fungal *Trichoderma* infections in immunocompromised patients.

Reference	Antifungal prophylaxis[a]	Type of infection	Neutropenia[a]/ recovery of normal PMNL count	Therapy	Outcome	Attributable mortality with persistent infection
[12]	None	D	NS/NA	None	Died	Yes
[10]	None	S	NS/NA	Amphotericin B and surgical debridement, followed by itraconazole and amphotericin B and maxillary irrigation	Cured	NA
[14]	IV amphotericin B, 25 mg every other day	S	Yes/NS	Amphotericin B and surgical debridement, followed by fluconazole	Died	Yes
PR, case 1	None	S	Yes/No	Surgical debridement and povidone iodine	Cured	NA
PR, case 2	Itraconazole, 400 mg/day	S	No/NA	Lipid-associated amphotericin B	Died	No
[18]	Amphotericin B nasal spray, fluconazole, 200 mg/day	D	Yes/No	Amphotericin B, followed by itraconazole, followed by lipid-associated amphotericin B	Died	Yes
[16]	Fluconazole, 100 mg/day	S	Yes/No	Amphotericin B lipid complex	Cured	NA
[21]	None	S	Yes/No	Amphotericin B, ketoconazole, and surgical resection, followed by itraconazole	Cured	NA
[11]	None	D	Yes/No	Amphotericin B and flucytosine	Died	Yes

NOTE. D, disseminated (i.e., ⩾2 noncontiguous organs involved); NA, not applicable; NS, not specified; PMNC, polymorphonuclear cell; PR, present report; S, systemic (i.e., 1 organ involved).

[a] At onset of fungal infection.

among 6 patients with localized infections, a clinical feature already reported with invasive fusariosis [36]. Once again, no therapeutic regimen has clearly demonstrated its superiority over the others.

Although correlation between in vitro test results and clinical response remains difficult to interpret, the clinical failures may be partly due to the low susceptibility of these fungi to both amphotericin B and available azole derivatives. Even if breakpoints have not yet been defined for these uncommon fungi, isolates recovered from our patients as well as from patients with previous cases exhibited, regardless of the species tested and the method of evaluation used, high MICs against amphotericin B (⩾1 mg/L), flucytosine (>64 mg/L), and available azole derivatives, including itraconazole (⩾4 mg/L). More recently, voriconazole and Sch56592, new triazole antifungal agents, have been shown to be effective in vitro against filamentous fungi, including a strain of *Trichoderma* with an MIC of voriconazole of 0.25 mg/L [41, 42]. Our results, although slightly more elevated, warrant further investigations of clinical efficacy of voriconazole in case of *Trichoderma* infection.

Acknowledgments

We thank A. M. Le Flohic and H. Raberin, for providing additional clinical details on unpublished cases; Pfizer and Janssen Laboratories, for providing us with antifungal powders; and Pr. B. Papierok (Pasteur Institute, Mycologic Collection), for giving us the reference strains.

References

1. Larsen FO, Clementsen P, Hansen M, et al. Volatile organic compounds from the indoor mould *Trichoderma viride* cause histamine release from human bronchoalveolar cells. Inflamm Res **1998**; 47:S5–6.
2. Perfect JR, Schell WA. The new fungal opportunists are coming. Clin Infect Dis **1996**; 22:S112–8.
3. Groll AH, Walsh TJ. Uncommon opportunistic fungi: new nosocomial threats. Clin Microbiol Infect **2001**; 7:8–24.
4. Kuhls K, Lieckfeldt E, Samuels G, Meyer W, Kubicek C, Börner T. Revision of *Trichoderma* sect. *longibrachiatum* including related teleomorphs based on analysis of ribosomal DNA internal transcribed spacer sequences. Mycologia **1997**; 89:442–60.
5. National Committee for Clinical Laboratory Standards (NCCLS). Reference method for broth dilution antifungal susceptibility testing of conidium-forming filamentous fungi: proposed standard. NCCLS document M38-P. Villanova, PA: NCCLS, **1998**.
6. Espinel-Ingroff A, Bartlett M, Bowden R, et al. Multicenter evaluation of proposed standardized procedure for antifungal susceptibility testing of filamentous fungi. J Clin Microbiol **1997**; 35:139–43.
7. Bren A. Fungal peritonitis in patients on continuous ambulatory peritoneal dialysis. Eur J Clin Microbiol Infect Dis **1998**; 17:839–43.
8. Bustamante-Labarta MH, Caramutti V, Allende GN, Weinschelbaum E, Torino AF. Unsuspected embolic fungal endocarditis of an aortic conduit diagnosed by transesophageal echocardiography. J Am Soc Echocardiogr **2000**; 13:953–4.
9. Campos-Herrero M, Bordes A, Perera A, Ruiz M, Fernandez A. *Trichoderma koningii* peritonitis in a patient undergoing peritoneal dialysis. Clin Microbiol Newslett **1996**; 18:150–2.

10. Furukawa H, Kusne S, Sutton DA, et al. Acute invasive sinusitis due to *Trichoderma longibrachiatum* in a liver and small bowel transplant recipient. Clin Infect Dis **1998**; 26:487–9.
11. Gautheret A, Dromer F, Bourhis JH, Andremont A. *Trichoderma pseudokoningii* as a cause of fatal infection in a bone marrow transplant recipient. Clin Infect Dis **1995**; 20:1063–4.
12. Guarro J, Antolin-Ayala MI, Gene J, Gutierrez-Calzada J, Nieves-Diez C, Ortoneda M. Fatal case of *Trichoderma harzianum* infection in a renal transplant recipient. J Clin Microbiol **1999**; 37:3751–5.
13. Guiserix J, Ramdane M, Finielz P, Michault A, Rajaonarivelo P. *Trichoderma harzianum* peritonitis in peritoneal dialysis. Nephron **1996**; 74:473–4.
14. Jacobs F, Byl B, Bourgeois N, et al. *Trichoderma viride* infection in a liver transplant recipient. Mycoses **1992**; 35:301–3.
15. Loeppky CB, Sprouse RF, Carlson JV, Everett ED. *Trichoderma viride* peritonitis. South Med J **1983**; 76:798–9.
16. Munoz FM, Demmler GJ, Travis WR, Ogden AK, Rossmann SN, Rinaldi MG. *Trichoderma longibrachiatum* infection in a pediatric patient with aplastic anemia. J Clin Microbiol **1997**; 35:499–503.
17. Ragnaud JM, Marceau C, Roche-Bezian MC, Wone C. Infection péritonéale à *Trichoderma koningii* sur dialyse continue ambulatoire. Med Mal Infect **1984**; 14:402–5.
18. Richter S, Cormican MG, Pfaller MA, et al. Fatal disseminated *Trichoderma longibrachiatum* infection in an adult bone marrow transplant patient: species identification and review of the literature. J Clin Microbiol **1999**; 37:1154–60.
19. Robertson MH. Fungi in fluids—a hazard of intravenous therapy. J Med Microbiol **1969**; 3:99–102.
20. Rota S, Marchesi D, Farina C, de Bievre C. *Trichoderma pseudokoningii* peritonitis in automated peritoneal dialysis patient successfully treated by early catheter removal. Perit Dial Int **2000**; 20:91–3.
21. Seguin P, Degeilh B, Grulois I, et al. Successful treatment of a brain abscess due to *Trichoderma longibrachiatum* after surgical resection. Eur J Clin Microbiol Infect Dis **1995**; 14:445–8.
22. Tanis BC, van der Pijl H, van Ogtrop ML, Kibbelaar RE, Chang PC. Fatal fungal peritonitis by *Trichoderma longibrachiatum* complicating peritoneal dialysis. Nephrol Dial Transplant **1995**; 10:114–6.
23. Venugopal PL, Venugopal TL, Gomathi A, Ramakrishna ES, Ilavarasi S. Mycotic keratitis in Madras. Indian J Pathol Microbiol **1989**; 32: 190–7.
24. Kuhls K, Lieckfeldt E, Borner T, Gueho E. Molecular reidentification of human pathogenic *Trichoderma* isolates as *Trichoderma longibrachiatum* and *Trichoderma citrinoviride.* Med Mycol **1999**; 37:25–33.
25. Walsh TJ, Hiemenz JW, Seibel NL, et al. Amphotericin B lipid complex for invasive fungal infections: analysis of safety and efficacy in 556 cases. Clin Infect Dis **1998**; 26:1383–96.
26. Hennequin C, Chouaki T, Pichon JC, Strunski V, Raccurt C. Otitis externa due to *Trichoderma longibrachiatum.* Eur J Clin Microbiol Infect Dis **2000**; 19:641–2.
27. Escudero GM, Pino CE, Munoz MR. Pulmonary mycoma caused by *Trichoderma viride* [in Spanish]. Actas Dermosifiliogr **1976**; 67:673–80.
28. Saran R, Goel S, Khanna R. Fungal peritonitis in continuous ambulatory peritoneal dialysis. Int J Artif Organs **1996**; 19:441–5.
29. Goldie SJ, Kiernan-Tridle L, Torres C, et al. Fungal peritonitis in a large chronic peritoneal dialysis population: a report of 55 episodes. Am J Kidney Dis **1996**; 28:86–91.
30. Cheng IK, Fang GX, Chan TM, Chan PC, Chan MK. Fungal peritonitis complicating peritoneal dialysis: report of 27 cases and review of treatment. Q J Med **1989**; 71:407–16.
31. Warris A, Gaustad P, Meis J, Verweij P, Abrahamsen T. Water as a source of filamentous fungi in a childhood bone marrow transplantation unit [abstract 1909]. In: Program and abstracts of the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy (San Francisco). Washington, DC: American Society for Microbiology, **1999**:578.
32. Bouakline A, Lacroix C, Roux N, Gangneux JP, Derouin F. Fungal contamination of food in hematology units. J Clin Microbiol **2000**; 38:4272–3.
33. Ammari LK, Puck JM, McGawan KL. Catheter-related *Fusarium solani* fungemia and pulmonary infection in a patient with leukemia in remission. Clin Infect Dis **1993**; 16:148–50.
34. Stewart WK, Anderson DC, Wilson MI. Hazard of peritoneal dialysis: contaminated fluid. Br Med J **1967**; 1:606–7.
35. Daisy JA, Abrutyn EA, MacGregor RR. Inadvertent administration of intravenous fluids contaminated with fungus. Ann Intern Med **1979**; 91:563–5.
36. Hennequin C, Lavarde V, Poirot JL, et al. Invasive *Fusarium* infections: a retrospective survey of 31 cases. French "Groupe d'Etudes des Mycoses Opportunistes" GEMO. J Med Vet Mycol **1997**; 35:107–14.
37. Boutati EI, Anaissie EJ. *Fusarium,* a significant emerging pathogen in patients with hematologic malignancy: ten years' experience at a cancer center and implications for management. Blood **1997**; 90:999–1008.
38. Liu K, Howell DN, Perfect JR, Schell WA. Morphologic criteria for the preliminary identification of *Fusarium, Paecilomyces,* and *Acremonium* species by histopathology. Am J Clin Pathol **1998**; 109:45–54.
39. Einsele H, Hebart H, Roller G, et al. Detection and identification of fungal pathogens in blood by using molecular probes. J Clin Microbiol **1997**; 35:1353–60.
40. de Hoog G, Guarro J, Gené J, Figueras M. Hyphomyces: *Trichoderma.* In: Atlas of clinical fungi. Utrecht, The Netherlands: Centraalbureau voor Schimmelcultures, Universitat Rovira i Virgili, **2000**:943.
41. Marco F, Pfaller MA, Messer SA, Jones RN. In vitro activity of a new triazole antifungal agent, Sch 56592, against clinical isolates of filamentous fungi. Mycopathologia **1998**; 141:73–7.
42. Marco F, Pfaller MA, Messer SA, Jones RN. Antifungal activity of a new triazole, voriconazole (UK-109,496), compared with three other antifungal agents tested against clinical isolates of filamentous fungi. Med Mycol **1998**; 36:433–6.