Case Reports

Infections due to Phialemonium species: case report and review

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Infections caused by rarely encountered fungal pathogens have increased in recent decades. The present study describes a disseminated infection caused by Phialemonium curvatum, and reviews the literature in an effort to summarize prior experiences with this unusual pathogen. The clinical and microbiological characteristics of a new case due to Phialemonium are presented. The case is analysed with 19 other which have appeared in the literature since 1986. Ten cases were sporadic infections, while the others were associated with three small outbreaks. In all but our patient the skin’s natural barrier was compromised (15/20 [75%]) and immunosuppression was a factor in the majority of cases (14/20 [70%]). Dissemination was noted in 83% (5/6) of the immunocompetent patients and in 57% (8/14) of immunocompromised patients. Endocarditis was the most frequent form of infection (8/20 [40%]). Blood cultures were positive in 92% (12/13) of those with disseminated disease. The mortality rate was 54% (7/13) among those with disseminated infections, but fatal outcomes were not observed in patients receiving treatment with itraconazole, voriconazole or posaconazole. The in vitro susceptibility of Phialemonium indicated a more consistent level of activity for voriconazole and posaconazole. Although infections usually occur when there is a breakdown in the skin the skin barrier or host defences are weakened, our case points out that infections due to Phialemonium species may occur in patients without these risk factors. The most frequent form of Phialemonium infections is endovascular, often with endocarditis and positive blood cultures, associated with high mortality rates. Treatment with the new triazoles is associated with improved survival.

Keywords dematiaceous fungi, Phialemonium species, spondylodiscitis, psoas abscess, phaeohyphomycosis

Introduction

An increasing number of yeasts and moulds with the potential to cause human infections are described every year. In some of the cases, species identification of the etiologic agent is difficult to determine on the basis of classic methods of macro- and microscopic morphology. Furthermore, since laboratories do not have databases of in vitro susceptibility patterns, it is difficult to identify...
appropriate treatment methodologies for fungal infections. An effort must therefore be made to gather clinical and laboratory information that improves the current treatment of these mycoses.

This study describes a case of disseminated infection caused by *Phialemonium curvatum*. Furthermore, the literature is reviewed in search of available information on the clinical spectrum of infections caused by this unusual pathogen.

**Case report**

We present the case of a 46-year-old male with a history of alcohol abuse and no previous illnesses of note. The patient complained of low-back pain which had lasted for a month and was not associated with apparent trauma. He had been running a temperature of up to 39°C for 3 days. Physical examination only revealed pain in the low-back area. The following blood-test values were of interest: leukocytes, 12.1 × 10⁹/l erythrocyte sedimentation rate (ESR), 108 mm/h; and C-reactive protein, 81 mg/l. Liver function tests showed no alterations. A magnetic resonance imaging (MRI) of the lumbar spine indicated a change of signal intensity in the medullary cavities of the L1 and L2 vertebral bodies, with involvement of the L1-L2 intervertebral disc, and a small soft-tissue mass in the anterior paravertebral region. Following diagnosis of spondylodiscitis at the level of L1-L2, the patient was sent to hospital. His temperature at the time of admission was 38°C. Blood samples were taken for culture, and treatment with cloxacillin and cefotaxime was initiated. Six days later, after the patient’s fever had remitted, blood cultures revealed the presence of a yeast-like fungus. A puncture and aspiration of the L1-L2 intervertebral disc was performed under local anaesthesia, using a postero-lateral approach, a double-needle technique, and radiographic control. Chest x-rays, echocardiogram, HIV testing, and plasma immunoglobulin levels were normal or negative. On the 12th hospital day, when the intervertebral disc biopsy revealed the presence of a fungus that was morphologically identical to that found on blood cultures, antibiotic treatment was discontinued and replaced with fluconazole (400 mg/day IV). On day 21 it was determined that the isolate was consistent with a member of the genus *Acremonium* and treatment was changed to oral voriconazole (400 mg/12 h the first day, and 200 mg/12 h after that). The patient was also placed in a custom-made thoracic lumbosacral orthosis. During the next 3 weeks the patient remained free from fever, but continued to suffer from low-back pain as evidenced by a persistently increased ESR value (100 mm/h). A new MRI was taken, revealing a 1.8 × 3.3 × 7 cm abscess on the right psoas, in addition to the previously determined alterations. On day 47 the psoas abscess was drained percutaneously under computed tomography scan guidance, producing a purulent material which again yielded the same fungus in culture. A suction drain was left in place, and removed 4 days later. Subsequently the patient made good progress, and was discharged from hospital, after a total of 73 days, with persistent low-back pain and an ESR value of 19 mm/h. An x-ray performed 3 months after diagnosis revealed involvement of the superior end-plate of L3. MRI was once again performed, revealing further involvement of the medullary cavity of T12 and the upper half of L3, with highlighting after the administration of gadolinium and a markedly increased capture of contrast medium at the site of the previous lesion. There were no signs of recurrence of the psoas abscess or masses in the adjacent soft tissues. In spite of the patient’s radiological progress, we decided to continue with oral voriconazole therapy. At subsequent revision, no significant clinical changes were detected. Radiological improvement became apparent on an MRI taken 10 months after initiating treatment with voriconazole, which was administered for 16 months. Nine months after therapy completion, the patient still requires a stiff brace for low-back pain.

**Methods**

**Strains**

Two isolates were available for analysis, i.e., one that was recovered from a blood culture and the other from an intervertebral disc-space aspirate. Four strains were obtained from the culture collection of the CBS-Fungal Biodiversity Centre; three *P. curvatum* CBS 119451, CBS 365.61 and CBS 27136 and one *P. obovatum* CBS 279.76. The strains were subcultured in different media to ascertain their macroscopic and microscopic morphology. The media included malt extract agar (MEA, 2% malt extract, Oxoid), potato dextrose agar (PDA, Oxoid), oat meal agar (OMA, Oxoid), and potassium chloride agar (CIK, Oxoid).

All isolates were identified using conventional methods [1].

**PCR and DNA sequencing of internal transcribed spacer (ITS) region**

Moulds were cultured in GEPD medium (0.3% yeast extract, 1% peptone Difco, Madrid, Spain), 2% glucose (Sigma Aldrich Química, Madrid, Spain), for 24–48 h at
30°C. Genomic DNA was isolated using an extraction procedure that has previously been described [2]. DNA was purified using Chroma Spin + TE 200 columns (Clontech Laboratories, Inc., Becton Dickinson, Madrid, Spain) in accordance with the manufacturer's instructions. DNA segments comprising the ITS1 and ITS2 regions were amplified using primers ITS1 (5′-TCCGTAGGGTGAACCTGCGG-3′) and ITS4 (5′-TCCCTCCGCTATTGATATGC-3′). The reaction mixtures contained 0.5 μM of each primer, 0.2 mM of each deoxynucleoside triphosphate, 5 μl of PCR 10x buffer (Applied Biosystems), Madrid, Spain), 2.5 U Taq DNA polymerase (Amplitaq, Applied Biosystems), and 25 ng of DNA in a final volume of 50 μl. The samples were amplified in a GeneAmp PCR System 9700 (Applied Biosystems) using an initial cycle of 2 min at 94°C, followed by 35 cycles of 30 s at 94°C, 45 s at 56°C, 2 min at 72°C, and one final cycle of 5 min at 72°C. Reactions products were analysed in a 0.8% agarose gel. Sequencing reactions were obtained with 4 μl of a sequencing kit (BigDye terminator cycle sequencing, ready reaction: Applied Biosystems), 1 μM of the primers (ITS1 and ITS4), and 3 μl of the PCR product in a final volume of 10 μl.

**Sequences analysis**

Sequences were assembled and edited using the SeqMan II and EditSeq software packages (Lasergene: DNASTAR, Inc., Madison, Wis.). Identification was performed by comparison of the sequences with the sequences obtained from the CBS strains and ITS sequences of *Phialemonium* spp. obtained from the GenBank database.

**Phylogenetic analysis**

All phylogenetic analyses were conducted with Finger-printing II Informatix software, version 4.5 (Bio-Rad Laboratories, Madrid, Spain). The method employed was maximum parsimony clustering. Phylogram stability was assessed by means of parsimony bootstrapping with 2,000 simulations.

**Antifungal susceptibility testing**

Antifungal susceptibility testing was performed using the EUCAST antifungal susceptibility method for moulds. This is similar to the Clinical Laboratory Standards Institute M38A methodology [3], with the following modifications: (i) RPMI1640 is supplemented with 2% glucose, (ii) inoculum size is between 2×10⁶ to 5×10⁶ CFU/ml, and (iii) inoculum preparations involves counting spores in a hematocytometer [4–6]. *Aspergillus fumigatus* ATCC204305 and *A. flavus* ATCC204304 were used as quality control strains [3].

The antifungal agents used were amphotericin B (range 16–0.03 mg/l) (Sigma Aldrich Química), itraconazole (range 8–0.015 mg/l) (Janssen), voriconazole (range 8–0.015 mg/l) (Pfizer), posaconazole (range 8–0.015 mg/l) (Schering-Plough), caspofungin (range 16–0.03 mg/l) (Merck), micafungin (range 16–0.03 mg/l) (Astellas) and anidulafungin (range 16–0.03 mg/l) (Pfizer).

Endpoints were recorded at 48 h, and defined as the antifungal concentration that produced a complete inhibition of visual growth from amphotericin B and azole drugs. For the echinocandins the endpoint was the antifungal concentration that produces a visible change in the morphology of the hyphae compared with that noted in the control well (minimum effective concentration, MEC) [7,8]. Visual readings were performed with the help of a mirror.

**Review of the literature**

MEDLINE (National Library of Medicine, Bethesda, Maryland) was searched for cases of *Phialemonium* infections published in the international medical literature up to April 2008. Cases were included on the basis of the following two criteria, i.e., (i) presence of a clinical syndrome that was consistent with infection in any location, and (ii) confirmed mycological identification. A database was made with the following variables: year of publication, country, age, sex, underlying disease, predisposing factors, rupture of skin barrier, localized or disseminated infection, immunodepression, surgery, sporadic or outbreak case, species of *Phialemonium*, treatment and outcome. Infection was considered to be disseminated whenever *Phialemonium* was recovered from blood samples or evidence of infection at two or more non-contiguous sites was present. Localized infections were those in which *Phialemonium* was isolated from a clinically infected site without positive blood cultures or evidence of dissemination to systemic organs.

**Statistical analyses**

Data were analyzed using SPSS software, version 12.0. The Fisher’s exact test was used for the comparison of proportions. A P value of <0.05 was considered to be statistically significant. In addition, classification and regression trees (CART 6.0, Salford Systems, California, USA) was used to generate a predictive model for infection outcome. All variables in the database were included as potential predictors of prognosis.
Results

Identifications to levels species

Observation of macroscopic and microscopic characteristics suggested that isolates were members of the genus Phialemonium. Colonies did not exhibit aerial mycelia, but rather were moist, flat and diffuse. They were initially white, but became greyish throughout the period of incubation. Microscopic examination revealed lateral tapering phialides or lateral hyaline-producing collarettes, and smooth and thin-walled cylindrical to allantoid conidia that aggregated in slimy heads. Since these macroscopic and microscopic characteristics are common, with minor differences, to those found with other fungal genera such as the Acremonium, Phialophora or Lecythophora, molecular identification by means of DNA-fragment sequencing was performed [1]. The isolates were identified by means of maximum parsimony analysis as Phialemonium curvatum. ITS sequences obtained from clinical strains were compared with 3 P. curvatum ITS sequences from strains acquired to the CBS. P. rubigenum was used to root the tree. Bootstrap value after 2,000 replications was of 100.

Antifungal susceptibility testing

The minimum inhibitory concentrations (MICs) of antifungal agents for both clinical isolates were identical or showed a one- to two-fold dilution difference. The results found in the testing were: amphotericin B, 1 mg/l; itraconazole, 0.25–0.5 mg/l; voriconazole, 0.25 mg/l; posaconazole,0.25 mg/l; caspofungin, 8 mg/l; micafungin, >16 mg/l; and anidulafungin, 2 mg/l.

Review of the literature

Table 1 shows the main characteristics of cases of Phialemonium infection that have been published in the literature, as well as those noted in our case. The patients include 16 males and four females, with ages ranging from 7 weeks to 84 years (median, 48 years). Ten cases were sporadic infections, while the remaining 10 were associated with three different outbreaks. The first outbreak consisted of two patients in the same bone marrow transplant unit at a hospital in Brazil who developed fungemia due to the association of P. curvatum with central venous catheters [9]. In the second outbreak, four hemodialysis patients at a hospital in Chicago, IL, were found to have intravascular infections caused by P. curvatum [10]. Finally, in the third outbreak were four patients who had been treated for erectile dysfunction with syringes contaminated with P. curvatum [11,12]. Of all cases, ten came from the United States, five from Israel, three from Brazil, and two from Europe.

Of the 20 patients, 14 (70%) had comorbidities involving some degree of immune dysfunction. Terminal chronic renal failure was present in six patients (three of whom had undergone a renal transplant), four had hematologic malignancies (with bone marrow transplantation in three cases), four suffered from diabetes mellitus, one had solid-organ malignancy, and one case occurred in a 7-week-old premature infant. In 15 (75%) of the 20 cases, natural trauma of the skin barrier had occurred prior to infection. The probable portals of entry for the fungus were catheters in eight cases (four hemodialysis, three central venous, and one peritoneal dialysis), intracavernous injections in four, skin burns in one, discography in one, and joint puncture in one patient. In addition, three patients (15%) had heart prostheses. In five of the six immunocompetent patients (83%), a disruption of the skin barrier due to the factors noted above occurred prior to infection.

Disseminated infections were found in 13 patients (65%) (eight immunocompromised and five immunocompetent) but remained localized in seven remaining patients (35%) (six immunocompromised and one immunocompetent). The most frequent form of infection was endocarditis noted in eight cases (40%) (five involving a native valve, and three involving a prosthesis). Of these eight cases, six developed distant septic metastases located in the brain (three cases), the spleen (three cases), the vertebrae (two cases), the eyes (two cases), and the joints (one case).

Blood cultures were positive in 12 cases (60%). Frequency of fungemia was similar in immunocompromised and immunocompetent patients (57% [8/14] versus 67% [4/6], respectively; \(P=NS\)).

Of the 20 patients, 16 (80%) were treated with some kind of antifungal therapy. Amphotericin B was used as the initial drug in 14 cases (70%) (monotherapy in 11 patients, and combined with azoles in three). In five cases, amphotericin B monotherapy was followed by azole treatment. Altogether, amphotericin B was included in the treatment in 14 cases, and azoles were included in 10. In addition, 11 patients (55%) required surgical intervention.

Five (36%) of the 14 immunocompromised patients and two (33%) of the six immunocompetent patients died (\(P=NS\)) and all had disseminated infections. None of these patients were given antifungal treatment with itraconazole, voriconazole or posaconazole triazoles. In contrast, six patients with disseminated infection who survived did receive antifungal treatment (\(P=0.001\)). CART tree (Fig. 1) shows treatment as the most important variable for survival. The second most important was the type of
Table 1  Reported cases involving *Phialemonium* species.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age, sex</th>
<th>Predisposing condition</th>
<th>Type of infection</th>
<th>Species</th>
<th>Source of isolation</th>
<th>Surgery</th>
<th>Antifungal therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>[14]</td>
<td>4 mo, M</td>
<td>Burns</td>
<td>Sepsis</td>
<td><em>Obovatum</em></td>
<td>Skin, spleen</td>
<td>Debridement</td>
<td>None</td>
<td>Death</td>
</tr>
<tr>
<td>[29]</td>
<td>41 yr, M</td>
<td>Discography</td>
<td>Spondylodiscitis</td>
<td><em>Obovatum</em></td>
<td>L3-4 disc space</td>
<td>Discectomy</td>
<td>None</td>
<td>Cure</td>
</tr>
<tr>
<td>[19]</td>
<td>50 yr, F</td>
<td>Renal transplant</td>
<td>Mycetoma</td>
<td><em>Curvatum</em></td>
<td>Cyst fluid</td>
<td>Debridement</td>
<td>None</td>
<td>Cure</td>
</tr>
<tr>
<td>[19]</td>
<td>5 yr, F</td>
<td>Renal transplant Peritoneal catheter</td>
<td>Peritonitis</td>
<td><em>Obovatum</em></td>
<td>Peritoneal fluid</td>
<td>None</td>
<td>AMB + KTC, AMB + FC, FLC</td>
<td>Cure</td>
</tr>
<tr>
<td>[9]</td>
<td>41 yr, M</td>
<td>Acute lymphocytic leukemia CVC</td>
<td>Fungemia</td>
<td><em>Curvatum</em></td>
<td>Blood, skin</td>
<td>None</td>
<td>AMB</td>
<td>Death</td>
</tr>
<tr>
<td>[9]</td>
<td>37 yr, M</td>
<td>Hodgkins, SCT, CVC</td>
<td>Fungemia</td>
<td><em>Curvatum</em></td>
<td>Blood</td>
<td>None</td>
<td>ITC</td>
<td>Cure</td>
</tr>
<tr>
<td>[18]</td>
<td>30 yr, M</td>
<td>Multiple myeloma, SCT</td>
<td>Mycetoma</td>
<td><em>Curvatum</em></td>
<td>Cyst fluid</td>
<td>Debridement</td>
<td>AMB, KTC, AMB + KTC</td>
<td>Cure</td>
</tr>
<tr>
<td>[17]</td>
<td>7 wk, M</td>
<td>Prematurity, CVC Necrotizing enterocolitis</td>
<td>Endocarditis</td>
<td><em>Obovatum</em></td>
<td>Blood, vegetation, urine</td>
<td>Vegetation resection</td>
<td>AMB</td>
<td>Death</td>
</tr>
<tr>
<td>[10]</td>
<td>66 yr, M</td>
<td>CRF, AV graft</td>
<td>Endocarditis</td>
<td><em>Curvatum</em></td>
<td>Blood, AV graft</td>
<td>Valve resection</td>
<td>AMB + FLC</td>
<td>Death</td>
</tr>
<tr>
<td>[10]</td>
<td>35 yr, M</td>
<td>Renal transplant rejection CRF, AV fistula</td>
<td>Endocarditis</td>
<td><em>Curvatum</em></td>
<td>Blood, mitral and aortic valve, vitreous fluid</td>
<td>Valve replacement, vitrectomy</td>
<td>AMB, AMB + CAS</td>
<td>Death</td>
</tr>
<tr>
<td>[10]</td>
<td>70 yr, F</td>
<td>CRF, AV graft, DM</td>
<td>Endocarditis</td>
<td><em>Curvatum</em></td>
<td>AV graft</td>
<td>Graft resection</td>
<td>AMB, VOR</td>
<td>Curea</td>
</tr>
<tr>
<td>[31]</td>
<td>46 yr, M</td>
<td>Chronic myelogenous leukemia SCT</td>
<td>Lung nodule</td>
<td><em>Obovatum</em></td>
<td>Blood, lung</td>
<td>Nodule resection</td>
<td>AMB, ITC</td>
<td>Cure</td>
</tr>
<tr>
<td>[12]</td>
<td>70 yr, M</td>
<td>Intracavaneous injection, DM</td>
<td>Endophthalmitis</td>
<td><em>Curvatum</em></td>
<td>Vitreous fluid</td>
<td>Emulsification</td>
<td>Intravitreous AMB</td>
<td>Cure</td>
</tr>
<tr>
<td>[16]</td>
<td>64 yr, M</td>
<td>Articular injection, DM</td>
<td>Arthritis</td>
<td><em>Curvatum</em></td>
<td>Sinovial fluid</td>
<td>None</td>
<td>AMB</td>
<td>Cure</td>
</tr>
<tr>
<td>PR</td>
<td>46 yr, M</td>
<td>Alcoholism</td>
<td>Spondylodiscitis</td>
<td><em>Curvatum</em></td>
<td>Blood, L1-2 disc space, psoas abscess</td>
<td>Abscess drainage</td>
<td>FLC, VOR</td>
<td>Cureb</td>
</tr>
</tbody>
</table>

AMB, amphotericin B; AV, arteriovenous; CAS, caspofungin; CRF, chronic renal failure; CVC, central venous catheter; DM, diabetes mellitus; FC, flucytosine; FLC, fluconazole; ITC, itraconazole; KTC, ketoconazole; POS, posaconazole; PR, present report; SCT, stem cell transplant; VOR, voriconazole.

aLater death not attributable to the infection. bResidual pain.
strains had an MIC for amphotericin B $\geq$ 2 mg/l (43% of the *P. curvatum* strains and 83% of the *P. obovatum* strains), 100% (14) had an MIC for fluconazole $\geq$ 64 mg/l, 100% (18) had an MIC for fluconazole $\geq$ 16 mg/l, and 75% (6/8) had an MIC for caspofungin $\geq$ 16 mg/l. The MIC for itraconazole was $\leq$ 1 mg/l for 85% (17/20) of strains, and the same value was noted with voriconazole and posaconazole.

Table 2 shows the *in vitro* antifungal susceptibility data of the *Phialemonium* species associated with the cases reviewed in this study and of five additional strains studied by Guarro *et al.* [9]. Fifty-five per cent (11/20) of the tested

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**Fig. 1** Tree generated by CART and ROC curve for death. Splitter for node 1 are shown (+ is combined treatment/is sequential treatment) as well as the importance of the predictors variables in the model. AMB, amphotericin B; CAS, caspofungin; FC, fluconazole; FLC, fluconazole; ITC, itraconazole; KTC, ketoconazole; VOR, voriconazole.
relative to all isolates. The geometric mean MICs of itraconazole, voriconazole, and posaconazole were 0.39, 0.31, and 0.19 mg/l, respectively.

**Discussion**

*Phialemonium* is a fungus widely distributed in the environment and has been isolated from samples of air, soil, and industrial and waste waters [13]. However, since its first description as a human pathogen in 1986 [14], only 19 cases have been published in the literature and the majority of these in the last 10 years. The present study describes a new case of disseminated infection caused by this fungus.

*Phialemonium* was originally described by Gams and McGinnis in 1983 [13] as a fungus whose morphological characteristics were halfway between those of the hyaline *Acremonium*, and the pigmented *Phialophora*. Today it is considered a true dematiaceous fungus, having melanin on its cell wall [15]. However, the initial identification of this fungus as a hyaline filamentous mould in some cases [10–12,16–19] shows that the pigmentation of hyphae and spores is not always readily apparent in members of this genus. The incidence rate of *Phialemonium* infections could be underestimated because of the difficulty of its accurate identification. The availability of molecular methods to identify this genus to species level can provide a better understanding of the characteristics of infections caused by *Phialemonium* spp.

Most dematiaceous fungi have a low level of virulence, and their invasive ability depends mainly on the immune status of the host [20]. Therefore, localized infections of the skin and the soft tissues are the most common forms caused by these fungi [21,22]. Cases of disseminated infection generally occur in immunocompromised patients [23]. The majority (65%) of *Phialemonium* infections, in contrast with those caused by other dematiaceous fungi, have been invasive in both immunocompromised and immunocompetent patients. Only 10% of cases caused by *Phialemonium* were subcutaneous phaeohyphomycosis.

All cases of *Phialemonium* infection, with the sole exception of the clinical case reported here, involved patients with immune dysfunction or who had suffered a trauma of the natural skin barrier. Of particular relevance is the association of infection with the use of vascular catheters and heart prostheses as occurred in 50% of cases. This would suggest that *Phialemonium* is similar to *Acremonium*, a common cause of catheter infection [24], with respect to not just its morphologic characteristics, but also in its ability to adhere to plastic materials and foreign bodies. This would explain the endovascular nature of the infections in most cases, which are often associated with endocarditis and positive blood cultures. In our case, there was no previous trauma, invasive procedure or symptomatology to suggest the source of infection. The only theoretical factor that might raise doubts about the patient’s complete immunological integrity was his history of alcohol abuse.

One of the most important characteristics of infections caused by this fungus is the high rate of positive blood cultures in patients with disseminated infection (92%). It has been suggested that the ease by which *Phialemonium* disseminates through the blood could be due to the in vivo production of unicellular propagules [17] which mimic yeasts in blood culture gram stains. Other filamentous fungi with ability to sporulate in vivo, such as *Fusarium* or *Acremonium*, are more frequently isolated from blood than angioinvasive fungi like *Aspergillus* or *Mucor*. This may be due to the fact that these unicellular forms can enter into and travel in the blood more easily than hyphal structures [25,26].

Given the rarity of *Phialemonium* infections, there are no definitive data on which to base recommendations as to the treatment of choice. In the present review, we found that therapy with itraconazole, voriconazole or posaconazole was associated with a higher survival rate among patients with disseminated infections. As expected, all patients with focal infections survived. The most important predictor for outcome in CART analysis was treatment of the infections. Despite the limited number of cases for analysis, the statistical support of the model shown in Fig. 1 is relevant, especially the area under ROC curve. It seems that the triazole drugs must form the core of treatment. The limited available data on their in vitro sensitivity

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**Table 2 In vitro activity of antifungals against Phialemonium species**

<table>
<thead>
<tr>
<th>Phialemonium species</th>
<th>Number of isolates</th>
<th>MIC (range, mg/l)</th>
<th>Number of isolates</th>
<th>MIC (range, mg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMB</td>
<td>14</td>
<td>0.125–2</td>
<td>6</td>
<td>0.5–36.94</td>
</tr>
<tr>
<td>FC</td>
<td>9</td>
<td>&gt;64–256</td>
<td>5</td>
<td>&gt;64–322.75</td>
</tr>
<tr>
<td>MICO</td>
<td>6</td>
<td>0.5–10</td>
<td>2</td>
<td>0.5–1</td>
</tr>
<tr>
<td>KTC</td>
<td>6</td>
<td>0.25–&gt;40</td>
<td>4</td>
<td>0.8–2</td>
</tr>
<tr>
<td>FLC</td>
<td>12</td>
<td>16–&gt;40</td>
<td>6</td>
<td>16–80</td>
</tr>
<tr>
<td>ITC</td>
<td>14</td>
<td>0.06–&gt;40</td>
<td>6</td>
<td>0.5–1.25</td>
</tr>
<tr>
<td>VOR</td>
<td>8</td>
<td>0.25–0.5</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>POS</td>
<td>9</td>
<td>0.03–1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CAS</td>
<td>7</td>
<td>8–&gt;32</td>
<td>1</td>
<td>16</td>
</tr>
</tbody>
</table>

AMB, amphotericin B; CAS, caspofungin; FC, flucytosine; FLC, fluconazole; ITC, itraconazole; KTC, ketoconazole; MICO, miconazole; POS, posaconazole; VOR, voriconazole.

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confirm that these antifungals, especially voriconazole and posaconazole, exhibit the strongest level of activity against \textit{Phialemonium}, as is the case with most dematiaceous fungi [20,22,27,28].

Although \textit{Phialemonium} is an infrequent cause of infection, its incidence could increase due to the growing patient population that is susceptible to opportunistic fungal infections and to the increased ability to diagnose infections. Case reporting of successful and unsuccessful clinical experiences is important in attempting to better define optimal therapy for these infections.

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