# Three Cases of Catheter-related Bloodstream Infection Caused by *Phialemonium curvata*

## *A Case Report and Literature Review*

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**Background:** With recent developments in the field of microbiology, an increasing number of yeasts and molds with the potential to cause infections in humans are identified every year. In addition to the challenges in identifying clinical isolates, there is limited antifungal susceptibility data available for *Phialemonium* species, leading to uncertainty in optimal treatment recommendations.

**Methods:** In this article, catheter-related bloodstream infections caused by *Phialemonium curvata* (previously *Phialemonium curvatum*) in 3 immunosuppressed patients are presented. Furthermore, the literature was reviewed to identify the clinical spectrum and treatment approaches for the reported infections.

**Results:** The cases presented here were analyzed along with 24 cases reported in the literature. Among all cases, 21 (77.7%) patients had an underlying condition. Nine (33.3%) patients had hematologic/oncologic malignancies and solid organ transplants. Twenty-two (81.4%) patients had a history of device or invasive interventions. Surgical procedures, removal of contaminated devices or tissue were found to reduce the risk of death by 86.7%. Correspondence analysis revealed a significant association between antifungal treatment and outcome ($P < 0.001$). The correspondence analysis could explain 53.9% of this relationship. Monotherapy and combination therapy were associated with survival. While salvage treatment or no antifungal therapy was associated with mortality, intravitreal injection or topical application of voriconazole was associated with sequelae.

**Conclusions:** Surgical intervention and removal of contaminated devices or tissue should be considered at an early stage.

**Key Words:** *Phialemonium curvata*, pediatric, immunosuppressed, treatment, surgery

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Owing to recent advances in the field of microbiology, an increasing number of pathogens potentially causing infections in humans are being identified every year. The genus *Phialemonium* was first described by Gams and McGinnis.[1] The *Phialemonium* species have been increasingly reported in humans as agents causing opportunistic invasive fungal infections. *Phialemonium* spp. is an anamorphic fungus commonly found in the environment such as air, soil, sewage and industrial water. Although they form pale colonies in vitro, melanin can be demonstrated in fungal cell walls using the Fontana-Masson stain, hence they are considered *Dematiaceous* fungi. Originally described as an intermediate genus between *Acremonium* and *Phialophora* genera, *Phialemonium* once included 3 species: *Phialemonium curvata*, *Phialemonium obovatum* and *Phialemonium dimorphosporum*. However, *P. dimorphosporum* was later considered to be the same pathogen as *P. curvata*. *P. curvata* and *P. obovatum* can be distinguished based on colony color, conidial morphology and molecular markers.[2–4] *P. curvata* has been reported as the causative agent in both immunosuppressed and immunocompetent patients. Common infections associated with *P. curvata* species include fungemia, endocarditis, endophthalmitis and mycetoma.[2,4–7]

Fatal infections have also been reported in the literature.[2,6] Since laboratories lack databases of in vitro susceptibility patterns for *P. curvata*, it is difficult to provide appropriate treatment recommendations. Therefore, this report aims to contribute to the literature by presenting 3 cases of catheter-related bloodstream infections (CRBSIs) caused by *P. curvata*, a rare fungal pathogen, in immunosuppressed patients. Additionally, a review of the literature was conducted to obtain current information on the clinical spectrum and therapeutic approaches for the reported infections.

## MATERIALS AND METHODS

A retrospective analysis involving 3 patients diagnosed with CRBSI caused by *P. curvata* was conducted between November 2019 and March 2023 at Ankara Bilkent Children's Hospital. In this report, after presenting each case identified at our center separately, all cases of *P. curvata* reported in the literature were analyzed collectively.

The diagnosis of CRBSI was considered based on the following: (1) the occurrence of chills accompanied by fever (>38°C) within 1 hour after catheter manipulation or flushing, (2) isolation of the same pathogen from both catheter and peripheral blood cultures, (3) the catheter culture showing growth at least 2 hours before peripheral blood culture.[8]

First-line treatment was classified as monotherapy if a single systemic antifungal drug was used alone or consecutively after another antifungal drug. Combination therapy was defined as the simultaneous administration of 2 systemic antifungal drugs. Salvage therapy was defined as any treatment administered to patients who did not respond to or tolerate the initial treatment.

### Culture and Antimicrobial Susceptibility

The biopsy specimen was cultured on Sabouraud dextrose agar (SDA; Oxoid, Hampshire, England) and potato dextrose agar (PDA; Oxoid, Hampshire, England), and both media were aerobically incubated

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at 35 and 25°C. Fungal growth became apparent after 12 days of incubation at 25°C in the PDA medium. The isolate's growth was less at 35°C on SDA/PDA than at 25°C on SDA/PDA.[9,10] Colonies on PDA at 25°C initially appeared white and moist, later turning olivaceous-brown with grayish aerial mycelium, exhibiting a velvety texture with a nearly black reverse (Fig. 1). Microscopic examination of the slide culture with Corn Meal Tween 80 agar revealed septate hyphae that were initially hyaline and later turned pale brown. Penicillate branches of phialides produced oval, curved conidia, while chlamydoconidia were not observed (Fig. 2). Mold colonies from the PDA cultures of patient samples were subjected to matrix-assisted laser desorption ionization-time of flight analysis using Microflex LT/SH Smart MS (Bruker Daltonics-Germany) and the mold library (MBT Filamentous Fungi Library 3.0) software, resulting in identification as *Phialemoniopsis curvata* with scores of 1.79, 1.8, 1.72 and 1.77.

## Antifungal Susceptibility Testing

Antifungal susceptibility testing was conducted using the broth microdilution method in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines.[11] The antifungals tested included amphotericin B (Sigma, St. Louis, MO), micafungin (Astellas, Spain), voriconazole (Pfizer, Spain), itraconazole and posaconazole (Merck-Sharp-Dohme, Spain). Stock solutions were prepared using water (for micafungin) or dimethyl sulfoxide for other antifungals, and serial 2-fold dilutions were made in RPMI 1640 medium (Sigma) buffered to pH 7.0 with 0.165 M MOPS (morpholinepropanesulfonic acid) buffer (Sigma). The isolates were grown on PDA for 10 days and incubated at 25°C to promote sporulation. The minimum inhibitory concentrations (MICs) of amphotericin B and the 3 triazoles (defined as the lowest drug concentrations that produced complete growth inhibition (100%) and the minimum effective concentrations of micafungin at 48 hours for the isolate were determined at the PHIT-UMRL using the CLSI broth microdilution method. Final inoculum concentrations ranged from $1 \times 10^4$ to $5 \times 10^4$ CFU/mL (M38-3rd ed). Reference quality control strains of *Aspergillus flavus* ATCC 204304 and *Aspergillus terreus* ATCC MYA-3633 were used.[12] Categorical endpoints and epidemiologic cutoff values have not been established for *Phialemoniopsis curvata*.[13] In vitro antifungal susceptibility testing performed at PHIT-NMRL using the CLSI broth microdilution method showed low MICs for micafungin (0.06–0.25 μg/mL), posaconazole (0.25–1 μg/mL) and voriconazole (0.25–0.5 μg/mL). The isolates exhibited low MIC values for all 3 antifungal agents.

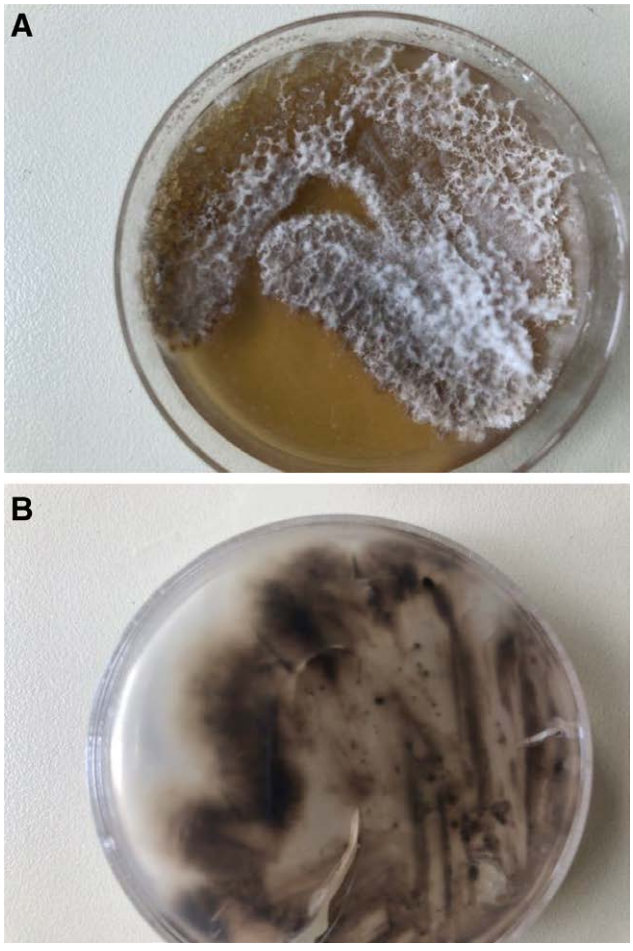



**FIGURE 1.** A: The *Phialemonium curvata* colonies on potato dextrose agar, 25°C, 12 days. Surface of colony. B: *Phialemonium curvata* colonies on potato dextrose agar, 25°C, 12 days. Reverse of colony. full color online



**FIGURE 2.** Micromorphologic appearance on the potato dextrose agar: Adelophialides with straight to allantoid conidia (×40 magnification). full color online

MEDLINE (National Library of Medicine, Bethesda, Maryland) and Google Scholar were searched for reports of cases of *Phialemonium* infection published in international medical literature through August 2023. The terms used for the search included *Phialemonium* and *P. curvata.* Clinical cases were selected. A database was created with the following variables: First author, year of publication, age, sex, underlying disease, risk factors (device or invasive intervention), presence/absence of immunosuppression, medical therapy, surgical treatment and outcome.

## Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics software, version 25.0 (IBM Corp., Armonk, NY). The

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Euclidean distance measure and symmetrical normalization were employed for analysis. Likelihood ratio test was used for analyzing categorical data. Results were presented as frequencies and percentages. Binary logistic regression was employed to estimate the risk of mortality. The relationship between antifungal therapy and outcomes was assessed using correspondence analysis (CA). A $P < 0.05$ was considered statistically significant.

## RESULTS

Our 3 cases are presented below.

### Case #1

A 17-year-old female patient diagnosed with alveolar rhabdomyosarcoma in September 2022 was receiving chemotherapy at our pediatric oncology unit at certain intervals. After completing the eleventh cycle of chemotherapy, the patient presented with complaints of fever during home follow-up. She was diagnosed with febrile neutropenia based on fever (38°C), anal mucositis, and an absolute neutrophil count of 30 cells/mm$^3$. The patient was admitted to the oncology service where treatment with teicoplanin and piperacillin-tazobactam was initiated. Upon receiving reports of yeast signals in both central and peripheral blood cultures, fluconazole (12 mg/kg/d) was added to the treatment regimen. The use of the port catheter was discontinued. Echocardiography, abdominal ultrasound and ocular examinations were all normal. Gram staining revealed both hyphal and yeast-like forms. Slow-growing mold-like colonies with white and occasionally brown areas were detected on SDA culture. Microscopic examination with lactophenol cotton blue revealed hyphal structures and conidia resembling *Acremonium* spp., but identification could not be made. Clinical specimens were sent to the National Mycology Reference Laboratories for analysis. Antifungal therapy was switched to caspofungin (70 mg/m$^2$/d on Day 1, 50 mg/m$^2$/d thereafter). The port catheter was removed. On the sixth day of caspofungin treatment, due to the presence of growth in the follow-up blood culture and the need for ongoing chemotherapy, voriconazole (6 mg/kg twice daily, later changed to 4 mg/kg twice daily) was added to the treatment regimen. The culture result was reported as *P. curvata*. The MICs for posaconazole, voriconazole, itraconazole, micafungin and amphotericin B were 1, 0.5, 8, 0.06 and 8 μg/mL, respectively. The patient received a total of 6 weeks of treatment, including 3 weeks of combined antifungal therapy and 3 weeks of oral voriconazole.

### Case #2

A 3-year-old male patient diagnosed with ependymoma developed fever (38.5°C), chills and tachycardia during his second cycle of chemotherapy administered through a central venous catheter. Catheter use was discontinued due to suspected CRBSI. Central and peripheral blood cultures were obtained, and the patient was started on cefoperazone/sulbactam treatment. After 48 hours, as the fever persisted, teicoplanin was added to the treatment regimen. Yeast signals were reported for both the port catheter and peripheral blood cultures, and fluconazole (12 mg/kg/d) was added to the treatment regimen. Echocardiography, abdominal ultrasound and eye examinations were unremarkable. Since the microbiologic phenomenon observed in Case #1 was also identified in this patient, the isolates were sent to the National Mycology Reference Laboratories for analysis. Antifungal therapy was switched to voriconazole (6 mg/kg twice daily, later changed to 4 mg/kg twice daily). The port catheter was removed. The MICs for posaconazole, voriconazole, itraconazole, micafungin and amphotericin B were 1, 0.5, 8, 0.06 and 8 μg/mL, respectively. Due to the absence of growth in repeated cultures, the patient received a total of 6 weeks of antifungal treatment, including 2 weeks of intravenous voriconazole and 4 weeks of oral voriconazole.

As part of the hospital infection prevention and control management, a series of measures were immediately taken considering the 2 cases occurring 8 days apart in the same block, both involving CRBSI. Briefly, these measures included providing education on hand hygiene, use of gloves, isolation measures, cleaning and disinfection practices and catheter usage to all staff working in the block. Family members of the patients were advised against bringing outside food, emphasizing the importance of not drying laundry inside the room. Samples were obtained from ventilation filters. *Aspergillus* spp. growth was detected in 3 samples, leading to the implementation of comprehensive preventive measures.

### Case #3

A 15-year-old female patient diagnosed with Hodgkin's lymphoma developed febrile neutropenia following chemotherapy. Liposomal amphotericin B was added to her ongoing teicoplanin and cefoperazone/sulbactam therapies upon receiving reports of yeast signals in the central catheter culture at 12 hours and peripheral blood culture at 14 hours. We were informed that the colonies, where species differentiation could not be clearly made, might be *P. curvatum*. Abdominal ultrasound, echocardiography and eye examinations showed normal results. The patient's port catheter was removed. She was also being treated with enoxaparin sodium. Discontinuation of enoxaparin sodium was considered for the patient by the hematology department and imaging was requested. Pulmonary artery computed tomography angiography performed at that time revealed newly developed, branching, nodular lesions with irregular borders at the superior and posterobasal segments of the lower lobe of the right lung, superior segment as well as laterobasal and posterobasal segments of the lower lobe of the left lung, involving distal vascular structures. Galactomannan antigen was negative. Bronchoalveolar lavage fluid tested negative for *Mycobacterium tuberculosis* (TBC) acid-fast bacillus, cytomegalovirus and galactomannan. TBC plasma polymerase chain reaction was negative. Fungal and bacterial cultures of bronchoalveolar lavage fluid, and the syndromic respiratory panel were all negative. Due to the patient's immunosuppressed status and detection of lesions on lung tomography suggestive of fungal infections, she was considered to have a possible invasive fungal infection and treated with liposomal amphotericin B for a total duration of 6 weeks. Antifungal susceptibility testing revealed the following MICs: 2 μg/mL for liposomal amphotericin B, 0.125 μg/mL for itraconazole, 0.25 μg/mL for posaconazole, 0.25 μg/mL for voriconazole. Since the patient was scheduled to undergo bone marrow transplantation, prophylactic treatment with voriconazole was initiated. Follow-up lung tomography showed the resolution of the nodular lesions.

Literature search revealed a total of 24 reported cases, including 14 case reports and 4 case series. All reported cases involved adults. The clinical characteristics of all cases from the literature as well as our cases are summarized in Table 1. Twenty-one (77.7%) patients had an underlying medical condition (alcoholism was excluded). Nine (33.3%) patients had hematologic/oncologic malignancies and solid organ transplants. Twenty-two (81.4%) patients had a history of device use or invasive intervention. Surgical intervention and removal of contaminated devices or tissue were found to reduce the risk of death by 86.7% (Tables 2 and 3).

CA showed a significant relationship between antifungal treatment and outcome ($P < 0.001$). The CA analysis could explain only 53.9% of this relationship. While antifungal monotherapy and combination therapy were associated with survival, salvage



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**TABLE 1.** Reported Cases and Our Cases Involving *Phialemonium curvata*

| First Author | Year | No | Sex/Age | Presence of Immunosuppression | Underlying Disease | Risk Factors (Device Use or Invasive Intervention) | Immunosuppressive Therapy | Type of Infection | Sampling Site (s) | Coinfection | Surgery | Antifungal Therapy | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| King et al.[5] | 1993 | 1 | F/50 years | Yes | Renal transplant | No | Steroid, azathioprine, cyclosporine | Mycetoma | Cyst fluid | No | Repeated debridement | No | Cure |
| Schonheyder et al.[6] | 1996 | 2 | F/63 years | – | Colon cancer | Bioprosthetic aortic valve | No | Endocarditis | Blood, aortic valve | *Streptococcus sanguis* | No | No | Death |
| Guarro et al.[2] | 1999 | 3 | M/41 years | Yes | Acute lymphocytic leukemia | CVC | NA | Fungemia | Blood, skin | No | No | AMB | Death |
| | | 4 | M/37 years | Yes | Hodgkin's lymphoma, HSCT | CVC | NA | Fungemia | Blood | *Exophiala jeanselmei* | No | ITC | Cure |
| Heins-Vaccari et al.[7] | 2001 | 5 | M/30 years | Yes | Multiple myeloma, HSCT | CVC | Steroid | Mycetoma | Cyst fluid | No | Debridement | AMB, KTC, AMB+KTC | Cure |
| Proia et al.[4] | 2004 | 6 | M/66 years | – | Chronic renal failure | AV graft | No | Endocarditis | Blood, graft tissue specimen | No | Graft resection | AMB+FLC | Death |
| | | 7 | M/35 years | Yes | Renal transplant rejection, chronic renal failure | AV fistula | Steroid, cyclosporine | Endophthalmitis, endocarditis, splenic abscess | Blood, mitral and aortic valve, vitreous fluid | No | Valve replacement, vitrectomy | AMB, AMB+-CAS | Death |
| | | 8 | F/70 years | – | Chronic renal failure, cerebrovascular accident, type II diabetes mellitus, peripheral vascular disease | AV graft | No | Graft infection | Graft tissue specimen | No | Graft resection | AMB, VOR | Cure |
| | | 9 | M/77 years | – | Chronic renal failure, type II diabetes mellitus | AV graft | No | Endocarditis | Blood, AV graft | No | Graft resection | AMB+VOR, VOR | Cure |
| Strahilevitz et al.[14] | 2005 | 10 | M/84 years | – | Chronic renal failure, hypertension | Bioprosthetic aortic valve, intracavernous injection | No | Spinal osteomyelitis, endocarditis | Blood, biopsy from L5 vertebra | No | No | AMB | Death |
| | | 11 | M/55 years | – | – | Intracavernous injection | No | Endocarditis, splenic abcess, septic arthritis | Blood, aortic valve, sinovial fluid | No | Valve replacement, splenectomy | AMB, VOR, POS | Cure |
| Zayit-Soudry et al.[15] | 2005 | 12 | M/71 years | – | Hypertension | Bioprosthetic aortic valve, coronary artery bypass grafting, intracavernous injection | No | Endocarditis, endophthalmitis | Blood, aortic valve, vitreous fluid | No | Valve replacement, vitrectomy | AMB, VOR | Sequelae (blind) |
| Dan et al.[16] | 2006 | 13 | M/64 years | – | Type II diabetes mellitus, hypertension, ischemic heart disease | Articular injection | No | Arthritis | Sinovial fluid | No | No | AMB | Cure |
| Weinberger et al.[17] | 2006 | 14 | F/70 years | – | Type II diabetes mellitus, hypertension | Intracavernous injection | No | Endophthalmitis | Vitreous biopsy | No | Vitrectomy | Intravitreal injections of AMB | Sequelae (eye enucleation) |

*(Continued)*

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**TABLE 1.** *Continued*

| First Author | Year | No | Sex/Age | Presence of Immunosuppression | Underlying Disease | Risk Factors (Device Use or Invasive Intervention) | Immunosuppressive Therapy | Type of Infection | Sampling Site (s) | Coinfection | Surgery | Antifungal Therapy | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Rivero et al.[18] | 2009 | 15 | M/46 years | – | Alcoholism | No | No | Spondylodiscitis | Blood, L1-2 disc space, psoas abscess | No | Abscess drainage | FLU, VOR | Cure |
| Rao et al.[19] | 2009 | 16 | M/60 years | – | Chronic renal failure | CVC | NA | Fungemia | Blood | NA | NA | NA | NA |
| | | 17 | M/70 years | – | Chronic renal failure | AV fistula | NA | Fungemia | Blood | NA | NA | NA | NA |
| Escamilla et al.[20] | 2011 | 18 | F/71 years | – | Type II diabetes mellitus, liver cirrhosis (hepatitis C virus), cardiac arrhythmia, hypertension | No | No | Sphenoid sinusitis | Sinus | No | Sphenoidectomy | VOR | Cure |
| Persy et al.[21] | 2011 | 19 | F/54 years | Yes | HSCT, GVHD | NA | Cyclosporine A, mycophenolate mofetil, steroid | Fungemia | Blood | NA | No | VOR+FLC, AMB+CAS, POS, POS+-CAS | Death |
| Freda et al.[22] | 2011 | 20 | M/84 years | – | – | Cataract surgery | No | Corneoscleral wound infection | Corneal scraping | No | Corneal keratoplasty, necrotic area excision | Topical AMB +KTC, Intravitreal injections of AMB | Sequelae (evisceration) |
| Anagnostakos et al.[23] | 2012 | 21 | M/64 years | – | – | Joint prosthesis | No | Periprosthetic knee joint infections | Joint biopsy | No | Debridement and prosthesis removal | VOR | Cure |
| Zou et al.[24] | 2014 | 22 | M/42 years | – | – | History of head injury at age 19 | No | Meningitis | BOS | No | No | VOR, FLC, AMB, FLC | Sequelae (acroanesthesia) |
| Roszkowska et al.[25] | 2021 | 23 | F/54 years | – | – | Daily disposable silicone hydrogel contact lenses | NA | Keratitis | Corneal scraping | Acanthamoeba | No | Topical VOR | Cure |
| Navaratnam et al.[26] | 2022 | 24 | F/68 years | – | Type II diabetes mellitus, psoriatic arthritis, goiter | No | Methotrexate | Endophthalmitis | Vitreous biopsy | NA | Vitrectomy | VOR | Sequelae (retinal detachment, macular hole>evisceration) |
| Our case #1 | 2022 | 25 | F/17 years | Yes | Rhabdomyosarcoma | CVC | Etoposide, mesna, ifosfamide | CRBSI | Blood | No | Catheter removed | FLC, CAS+VOR | Cure |
| Our case #2 | 2022 | 26 | M/3 years | Yes | Ependymoma | CVC | Vincristine, carboplatin, cyclophosphamide | CRBSI | Blood | No | Catheter removed | FLC, VOR | Cure |
| Our case #3 | 2023 | 27 | F/15 years | Yes | Hodgkin's lymphoma | CVC | Bendamustine | CRBSI | Blood | No | Catheter removed | AMB, VOR | Cure |

AMB indicates amphotericin B; AV, arteriovenous; CAS, caspofungin; CRBSI, catheter-related bloodstream infection; CSF, cerebrospinal fluid; CVC, central venous catheter; F, female; FLC, fluconazole; GVHD, graft-versus-host disease; HSCT, hematopoietic stem cell transplantation; ITC, itraconazole; KTC, ketoconazole; M, male; NA, not applicable; VOR, voriconazole.



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**TABLE 2.** Relationship of Variables With Survival

| Variables | Cure n = 19% | Death n = 6% | *P* value* |
|---|---|---|---|
| Sex (%) | | | |
| Female | 8 (42.1%) | 2 (33.3%) | 0.702 |
| Male | 11 (57.9%) | 4 (66.7%) | |
| Presence of immunosuppression | | | |
| No | 13 (68.4%) | 3 (50%) | 0.419 |
| Yes | 6 (31.6%) | 3 (50%) | |
| Immunosuppressive therapy | | | |
| No | 11 (64.7%) | 3 (60%) | 0.848 |
| Yes | 6 (35.3%) | 2 (40%) | |
| Presence of coinfection | | | |
| No | 16 (88.9%) | 4 (80%) | 0.617 |
| Yes | 2 (11.1%) | 1 (20%) | |
| Surgery | | | |
| No | 4 (21.1%) | 4 (66.7%) | 0.042 |
| Yes | 15 (78.9%) | 2 (33.3%) | |
| Presence of underlying disease | | | |
| No | 6 (31. 6%) | 0 (0.0%) | 0.050 |
| Yes | 13 (68.4%) | 6 (100%) | |
| Risk factors (device or invasive intervention) | | | |
| No | 5 (26.3%) | 0 (0.0%) | 0.103 |
| Yes | 14 (73.7%) | 5 (100%) | |

Patients with missing data were excluded from the statistical analyses.
*Likelihood ratio was used.

**TABLE 3.** Binary Logistic Regression Analysis Results of Variables

| Variables | OR | Univariate 95% CI | *P* value |
|---|---|---|---|
| Sex | 1.455 | 0.212–9.984 | 0.703 |
| Presence of immunosuppression | 2.167 | 0.334–14.057 | 0.418 |
| Immunosuppressive therapy | 1.222 | 0.158–9.467 | 0.848 |
| Presence of coinfection | 2 | 0.143–27.99 | 0.617 |
| Surgery | **0.133** | **0.018–1.009** | **0.042** |

CI indicates confidence interval; OR, odds ratio.
Patients with missing data were excluded from the statistical analyses.
Bold values indicate statistically significant.

treatment or no antifungal treatment was associated with mortality. Intravitreal injection or topical application of voriconazole was associated with sequelae (Fig. 3).

## DISCUSSION

*P. curvata* is gaining recognition as an invasive fungal pathogen due to increased awareness of its pathogenic potential as well as technologic advances in microbiology. Although *P. curvata* spp. rarely cause disease in humans, cases resulting in sequelae or mortality have been reported.[2,6,14,15,17] *Phialemonium* infections may involve multiple systems, and most commonly include endocarditis, endophthalmitis and fungemia.[2,4,14,17,19]

Many of our patients were immunocompromised or had underlying diseases. History of intravascular device use or invasive procedures emerged as a significant risk factor (22/27, 81.5%). Among the 5 patients with no history of invasive procedures, 3 had a history of immunosuppressive treatment, while no risk factors were identified in the other 2 patients.[5,18,20,21,26] *P. curvata* infections involving the eye are associated with serious complications such as blindness, eye enucleation and evisceration. Therapeutic success in ocular fungal infections depends primarily on (1) early diagnosis of the fungal infection, (2) accurate identification of the etiologic agent and (3) timely initiation of antifungal treatment.[4,17,22,26] In our study, invasive procedures such as valve replacement, vitrectomy, graft resection, debridement and catheter removal were found to reduce the risk of mortality by 86.7%. According to the CA results, intravitreal injection or topical application of voriconazole was associated with sequelae. Particularly in patients with endophthalmitis, early vitrectomy and initiation of appropriate systemic and intravitreal antifungal therapy seem necessary.

The *Phialemonium* species are isolated from various environments such as air, soil, industrial water and sewage. *P. curvata* infections were reported in the form of isolated case reports or case clusters. In a study by Strahilevitz et al.,[14] an epidemiologic surveillance study was initiated in Israel in March 2002 after a patient died as a result of endocarditis caused by *P. curvata*. Subsequently, 2 additional cases were identified, and the common feature among the 3 patients was the use of syringes for intracavernous penile injections obtained from the same impotence clinic. Cultures of used and unused syringes collected from the patients' homes and clinic, as well as environmental cultures, were analyzed. Both prefilled, unused syringes and used syringes were found to be contaminated with *P. curvata*. In a study by Proia et al.,[4] endovascular *P. curvata* infections were identified in 4 clusters of patients undergoing chronic hemodialysis. No epidemiologic surveillance study was undertaken. Rao et al.[19] conducted an epidemiologic surveillance study after the detection of *P. curvata* in the blood culture of a patient undergoing hemodialysis at the Hines VA Hospital, a hemodialysis center in Illinois, in 2005. Blood, water, surface, and dialysate samples were cultured. Two patients with *P. curvata*-associated bloodstream infections were identified. Both patients were found to use of the same device attached to a contaminated faucet for dialysis sessions on different occasions. Since *P. curvata* was isolated from both patient blood and dialysis product water, it was concluded that the likely source of mold was biofilms in the dialysis product water distribution system. At our clinic, infection prevention and control measures were implemented and samples were collected from ventilation filters upon detection of *P. curvata*-associated CRBSI in 2 of our cases 8 days apart. However, no environmental cultures or samples were obtained from used port flushing syringes, which is a limitation of our study. In centers where *P. curvata* infections are identified, an epidemiologic surveillance study can help identify both the source and new cases.

It was observed that voriconazole and posaconazole exhibit low MIC values against *Phialemonium* organisms. In Proia et al.'s[4] study, 2 patients treated with high-dose amphotericin B deoxycholate plus caspofungin or amphotericin B deoxycholate plus intravenous fluconazole died, while the other 2 patients were successfully treated with different regimens. One patient was treated with amphotericin B deoxycholate followed by oral voriconazole, and the other patient received combination therapy with amphotericin B deoxycholate and voriconazole followed by oral voriconazole. In a case report by Heins-Vacari et al.,[7] painful, purplish nodular lesions were detected on the right ankle of a patient 2 months after bone marrow transplantation. *P. curvata* was identified in a culture from spontaneous drainage. Successful treatment was achieved with surgical debridement followed by amphotericin B and ketoconazole. In Case #1, the patient was successfully treated with caspofungin plus voriconazole, in Case #2 with voriconazole, and in Case# 3 with liposomal amphotericin B. In addition to the challenges in identifying clinical isolates, there is limited antifungal susceptibility data available for *Phialemonium* species, which contributes to the uncertainty in optimal treatment recommendations. With increased reporting of cases of *P. curvata*, treatment guidelines providing solid recommendations for optimal treatment duration and appropriate antifungal therapy are likely to

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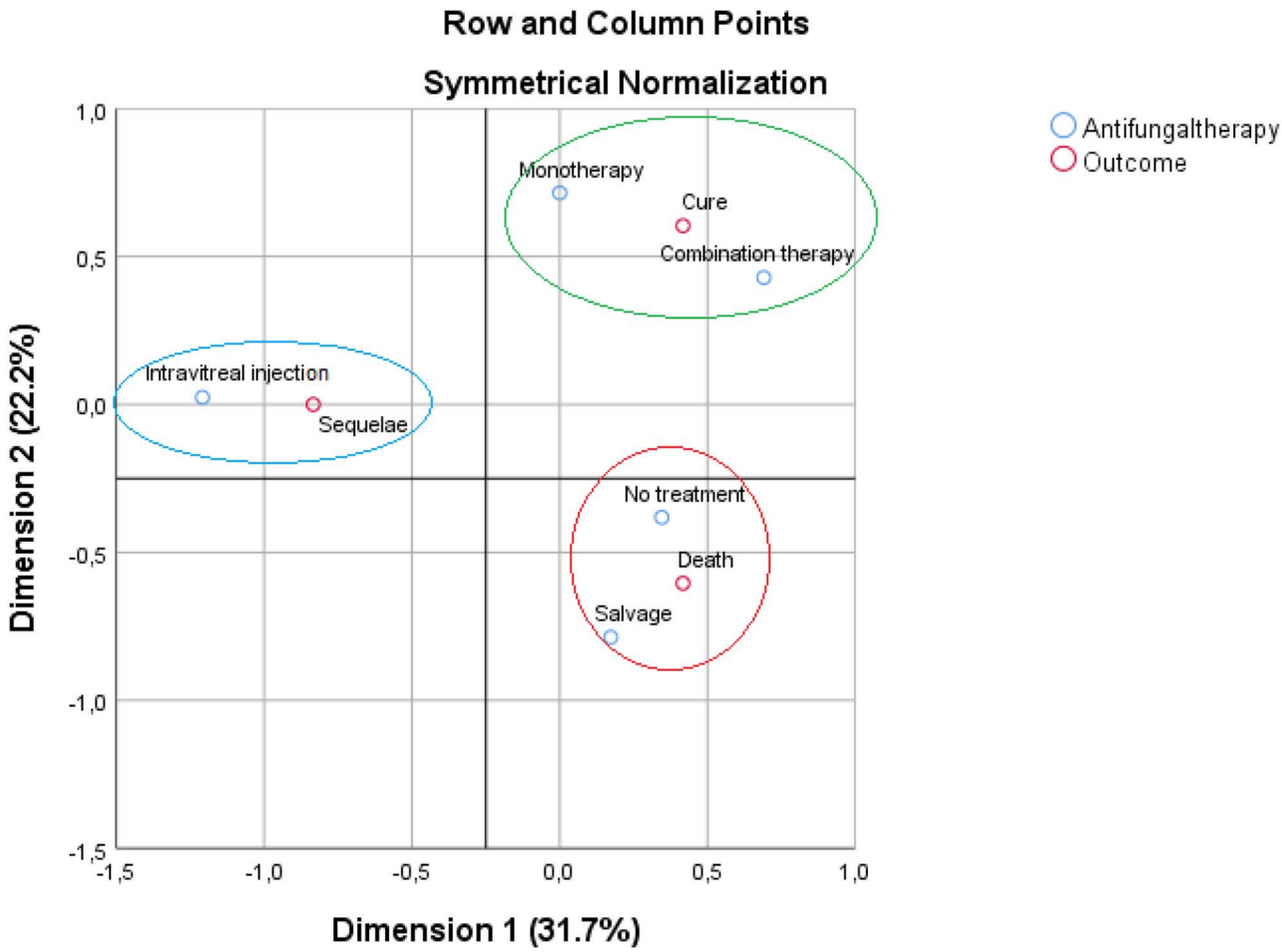



**FIGURE 3.** Relationship between antifungal treatment and outcome. full color online

emerge. Among fatal cases, endovascular infections are the most reported. In addition to antifungal therapy, early surgical intervention and removal of contaminated devices or tissue affect prognosis. Absence of neutropenia or other immunosuppressive conditions, and removal of the catheter or infected tissue may be important host factors for survival.

*P. curvata* can grow in routine blood culture bottles. The organism is often confused with yeast on Gram staining. Yeast-like forms are free conidia or spores of *Phialemonium* species. Similar phenomena have been observed in cases caused by *Fusarium* and *Acremonium* molds.[27] In such cases, *P. curvata* infections should also be considered as a possible causative agent.

In conclusion, *Phialemonium* species are increasingly recognized as invasive fungal pathogens among immunocompromised individuals and patients with underlying diseases. Early consideration of surgical intervention and removal of contaminated devices or tissues is essential. *P. curvata* infections can be acquired from both healthcare settings and the community, and may occur in clusters or sporadically. Due to the absence of databases of in vitro susceptibility patterns for *P. curvata*, it is difficult to establish appropriate treatment methodologies for fungal infections. Therefore, efforts should be directed toward gathering clinical and laboratory data that enhance the current understanding of treating these mycoses. Conducting epidemiologic surveillance studies can assist in the identification of additional cases, providing insights into the true prevalence and pathogenicity of *P. curvata* and associated mortality rates.

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