

## Sticks and bones: Traumatic phaeohyphomycosis presenting as an epidural scalp abscess and cranial osteomyelitis



Richard L. Oehler<sup>a,b,\*</sup>, Ju Hee Katzman<sup>b</sup>, Natan Kraitman<sup>b</sup>, Vivian Vega-Rodriguez<sup>a,b</sup>, John F. Toney<sup>a,b</sup>

<sup>a</sup> James A Haley Veterans Hospital, 13,000 Bruce B Downs Blvd, #111J, Tampa, FL 33612, USA

<sup>b</sup> University of South Florida Morsani College of Medicine, 4202 East Fowler Avenue, Tampa, FL 33612, USA

### ARTICLE INFO

#### Keywords:

Phaeohyphomycosis  
Cranial  
Osteomyelitis  
Cladospirium  
*Cladophialophora bantiatum*

### ABSTRACT

The pigmented molds can cause soft tissue and invasive disease (phaeohyphomycosis) in immunocompetent patients. We describe a 76-year-old male patient who developed a *Cladophialophora bantiatum* posterior scalp abscess and cranial osteomyelitis following an incidental scalp exposure with a tree branch. Management requires extensive surgical debridement followed by prolonged antifungal therapy.

### 1. Introduction

Phaeohyphomycosis is a term used to refer to infections caused by dematiaceous or darkly pigmented fungi. The pigmented molds (Table 1) can produce soft tissue and invasive disease independent from a patient's underlying immune or metabolic disorders [1]. Derived from the Greek word *phaeo*, meaning “dark,” the term “phaeohyphomycosis” includes superficial (black piedra, tinea nigra), cutaneous, corneal or mycotic keratitis, subcutaneous, and systemic disease (including invasive and cerebral). All have melanin-like pigmented hyphae in tissue. They are often found in the soil and are generally distributed worldwide.

The development of phaeohyphomycosis has been associated with several major risk factors: (1) Disruption of the skin barrier, including trauma, chronic damage to skin or mucosa, surgery, intravenous drug use, and prosthetic devices. (2) Depressed cellular immunity as seen in neutropenia associated with hematological malignancies, bone marrow and organ transplant recipients, and immunosuppressive therapy. Lastly, (3) increased environmental exposure can result in elevated risk. Although the routes of infection for all dematiaceous fungi are not entirely understood, known mechanisms include inhalation, ingestion, or soft tissue trauma. Inhalation-related infections typically occur in immunocompromised patients or those with chronic lung disease. Manifestations can include pneumonia, nodular lung disease, and endobronchial lesions. Severity often depends upon the ability of the patient to resolve their underlying immune system deficits. Gastrointestinal disease is less common but has been reported [2].

Skin and soft tissue syndromes are among the most common manifestations of the phaeohyphomycoses. Infection may develop indolently until it is noticed as a slow-growing subcutaneous mass. Lesions may also appear superficially as cystic or papular nodules. Superficial disease commonly involves the skin of the extremities or uncovered feet [3].

When it occurs, the extension of a soft tissue infection can vary from the localized involvement of underlying fascia and bone to more distant hematogenous dissemination. Although immunocompromised patients may be at greater risk, phaeohyphomycosis may occur in patients who have no immunodeficiency [4].

Cranial involvement is a rare manifestation and can be seen in greater proportion among immunocompetent individuals. Many infections occur hematogenously or can be spread as a result of sinusitis or a surgical procedure [5]. Local soft tissue extension to the cranial area is rare, given that traumatic inoculation to the head is poorly described in the literature and requires direct exposure of the scalp. Several species can have greater neurotropic potential, including *Cladophialophora bantiana*, *Exophiala dermatitidis*, *Dactylaria gallopava*, *Rhinochlaidiella mackenziei*, and others. *Cladophialophora bantiana* encompasses several strains including *Cladospirium trichoides*, *Xylohypha bantiana*, and *Cladospirium bantianum* [6]. *C. bantiana* can cause brain abscesses in both immunocompromised and immunocompetent individuals. In a 2002 retrospective review of 1620 immunocompromised solid organ transplant recipients in which 17 cases of fungal brain abscess were identified, *Aspergillus* spp. predominated (65%). Only one case of *C. bantiana* occurred (and was fatal) [7]. A second case in the medical literature

\* Corresponding author. James A Haley Veterans Hospital, 13,000 Bruce B Downs Blvd, #111J, Tampa, FL 33612, USA.

E-mail address: [richard.oehler@va.gov](mailto:richard.oehler@va.gov) (R.L. Oehler).

<https://doi.org/10.1016/j.mmcrr.2019.04.011>

Received 13 February 2019; Received in revised form 12 April 2019; Accepted 24 April 2019

Available online 27 April 2019

2211-7539/ Published by Elsevier B.V. on behalf of International Society for Human and Animal Mycology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Table 1**  
Classification of agents of phaeohyphomycosis [12]<sup>a</sup>.

Order	Genus or Species
Chaetothyriales	<i>Exophiala</i> spp. <i>Cladophialophora</i> <i>Phialospora</i> spp.
Pleosporales	<i>Alternaria</i> spp. <i>Bipolaris</i> spp. <i>Curvularia</i> spp. <i>Exserohilum</i> spp.
Capnodiales	<i>Cladosporium</i> spp.

<sup>a</sup> This list is not inclusive.

involved a non-immunocompromised male farm worker who developed a *C. bantiana* brain abscess. He received surgical debridement accompanied by a three-week duration of amphotericin and itraconazole followed by further debridement and a subsequent six-week course of voriconazole. Unfortunately, this also resulted in a fatal outcome [8].

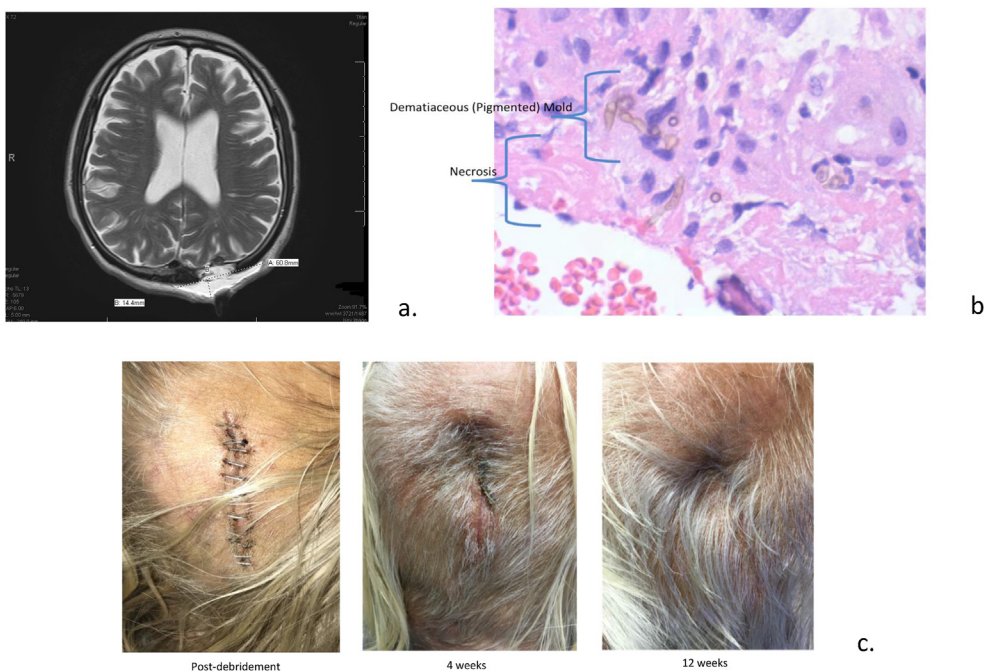
We describe a 76-year-old male patient who developed a *Cladophialophora bantiana* posterior scalp abscess and cranial osteomyelitis over several months following an incidental scalp exposure with a tree branch. To our knowledge, the unique circumstances of this exposure have not been previously reported in the literature.

**2. Case**

A 76-year-old male was admitted with a several-month history of a slowly enlarging posterior scalp abscess. The patient recalled experiencing minor scalp trauma five months earlier when a sharp-ended tree branch struck his temple while he was on a riding mower. He denied any superficial laceration. A couple of weeks later, he noted a gumball-sized soft tissue mass near the occipital vertex. Over 1–2 months, it slowly doubled in size. He presented to his primary care provider with complaints of the mass and was referred to a plastic surgeon. His surgeon felt that the mass probably reflected a lipoma or cyst and scheduled an excision under local anesthesia. Intraoperatively, he was found to have a five-centimeter thick-walled abscess with the bony erosion up to the level of the dura mater. Excision of the mass resulted in a 2.2 cm × 1.8 cm bony defect. Copious amounts of pus were found, but

initial gram stain and culture results were negative. Post-excision MRI results (Fig. 1a) demonstrated the extension of the abscess to the epidural space. Following wound closure, the patient was discharged on a 7–10-day course of oral linezolid. Five days later, the infectious diseases team received the histopathology results. They revealed a “large abscess cavity lined by suppurative granulomatous inflammation with numerous pigmented (dematiaceous) fungal organisms” with septate hyphae and budding yeast-like forms. Cultures from the biopsy ultimately returned positive for *Cladophialophora bantiana* (identification at Quest Diagnostics, San Juan Capistrano, California).

After readmission to the hospital five days after the initial surgery, he was seen by the infectious diseases consultation service. We felt that the patient likely had a soft-tissue phaeohyphomycosis complicated by extension to the dura, likely necessitating further debridement. Three days later, the patient received an occipital scalp wound irrigation and debridement. An additional large fluid collection was found intraoperatively which was sent for diagnostic studies. Histopathology demonstrated pigmented mold organisms overlying necrotic tissue (Fig. 1b) with some well-demarcated areas of acute inflammation, histiocytosis, and adjacent bony fragments. Postoperatively (Day 0), liposomal amphotericin B, 5 mg/kg/day IV daily (including pre- and post-hydration) plus voriconazole 200 mg by mouth twice a day were initiated. Oral voriconazole was used due to the risk of acute kidney injury with the intravenous formulation. Unfortunately, within 48 hours of initiating liposomal Amphotericin B, the patient developed acute kidney injury, and laboratory studies documented an increase in his creatinine from 1.5 mg/dl to 2.5 mg/dl. His liposomal amphotericin B was discontinued, and he was discharged home on oral voriconazole 200mg BID (5mg/kg/day). On the following day, *Cladophialophora bantiana* species again was isolated. The specimen was submitted for antifungal susceptibilities to the Fungus Testing Laboratory (Reference Laboratory) at the University of Texas Health Science Center for CLSI M38-A2 Macrodilution. Six weeks later, *Cladophialophora bantiana* was reported with likely susceptibility (as there are no established break-points) to amphotericin B, 5-flucytosine, itraconazole, and voriconazole. Over the next several months, the patient has done well on voriconazole therapy, drug levels ranging from 2.7 to 4.9 mcg/mL (therapeutic 2.0–5.5mcg/mL). Clinic visits at 4 weeks and 12 weeks (Fig. 1c) post-debridement revealed progressive healing and resolution of his scalp wound. The patient has since completed his 6 months of



**Fig. 1.** a. T2-weighted MRI image after the initial debridement procedure showing extension of the scalp abscess through the cranium into the epidural space b. Post-biopsy photomicrograph showing pigmented mold organisms alongside areas of adjacent tissue necrosis.c. Gross photos of the scalp wound following initial debridement and after 4 and 12 weeks on Voriconazole.

antifungal therapy and reports only a small quarter-sized defect on his calvarium as a residual manifestation of his infection.

### 3. Discussion

Our elderly patient had no significant health issues or exposures other than a recent history of glucose intolerance and a remote minor scalp injury. His *Cladophialaphora bantiana* infection presented as an initial “subcutaneous cyst” which then developed into an indolent slowly progressive nodular process on his scalp occiput. However, given the neurotropic potential of *C. bantiana*, he developed erosion of the infection through the calvarium extending to the epidural space. He required extensive surgical debridement of the abscess. Postoperatively, the patient experienced liposomal amphotericin B associated acute kidney injury. Fortunately, he continued to tolerate the voriconazole after his hospital discharge. After three weeks, he showed evidence of having a good response to his antifungal therapy, to be continued for a total of 6 months.

Phaeohiphomycosis infections presenting with combined soft tissue and CNS involvement because of local inoculation of the scalp are not widely reported. The relatively slow progression of the lesion from a subcutaneous cyst to a 5 cm mass extending to the epidural space in a patient with absent CNS symptoms is remarkable. Although phaeohiphomycosis infections can be extremely aggressive and recurrence despite aggressive surgical intervention is possible, so far, the patient has responded well to treatment. This may reflect the excellent CNS penetration of voriconazole in addition to the meticulous debridement by our neurosurgical team.

The management of phaeohiphomycosis infections can depend upon the site, the overall immune system status, and the extent of disease progression. With limited soft-tissue disease, surgical excision alone may be curative, although it is frequently accompanied by systemic antifungal therapy, especially in immunocompromised patients. Azole antifungals are typically utilized, usually for 3–6 months. Choices include itraconazole and voriconazole [4,9]. Isavuconazonium should also be effective, although there is less clinical experience with this agent. Small single pulmonary nodules may respond to surgical excision alone. With more extensive disease, liposomal Amphotericin B with or without an anti-mold oral azole is appropriate initial therapy [4]. The resolution of any underlying immune system defects is critical [9].

The management of CNS-associated phaeohiphomycosis relies on a dual approach. Patients should receive debridement of the abscess plus effective antifungal therapy with good CNS penetration [4,10]. Complete surgical excision is preferred to simple CT-guided aspiration. Biopsy of the involved tissue for organism identification is also important, although susceptibility testing has not been fully standardized. Initial antifungal therapy for CNS disease should include liposomal amphotericin B plus an azole antifungal (itraconazole, voriconazole, posaconazole, or isavuconazole). The CNS penetration of voriconazole is excellent, and in recent years, this agent has been favored over itraconazole. Both voriconazole and isavuconazole are available as IV formulations, which may have initial pharmacokinetic advantages. Transition to an oral azole is possible when a clinical response is seen. Treatment for CNS phaeohiphomycosis for at least six months is

customary but can extend to 12 months or longer [11]. Other antifungal agents with more limited experience include the echinocandins, terbinafine, and flucytosine [4,10,11].

Clinicians should consider phaeohiphomycosis in anyone regardless of immune status who presents with the growth of single or multiple non-tender subcutaneous soft tissue nodules. Although distribution on the extremities is most likely, other more centrally located body areas may also be involved. When the infection involves the CNS, it can be aggressive and invasive, and may go on to progress to cerebral disease, which can have a fatal outcome. Effective management of CNS phaeohiphomycosis requires debridement and excision of the abscess or lesions with prolonged antifungal therapy utilizing agents with excellent CNS penetration.

### Author conflicts of interest

None.

### Acknowledgement

We greatly appreciate the assistance of Dr. Corinne Stobaugh, Supervisory Pathologist, Cytology Section, Pathology and Laboratory Medicine Service, James A Haley VA Hospital, with the preparation of photomicrographs used in this publication.

### References

- [1] S.M. Hussey, R. Gander, P. Southern, M.P. Hoang, Subcutaneous phaeohiphomycosis caused by *Cladophialaphora bantiana*, Arch. Pathol. Lab Med. 129 (6) (2005) 794–797.
- [2] M. Sudhadham, S. Prakitsin, S. Sivichai, R. Chaiyarat, G.M. Dorrestein, S.B. Menken, et al., The neurotropic black yeast *Exophiala dermatitidis* has a possible origin in the tropical rain forest, Stud. Mycol. 61 (2008) 145–155.
- [3] H. Ochiai, H. Kawano, S. Minato, T. Yoneyama, Y. Shima, Cerebral phaeohiphomycosis: case report, Neuropathology 32 (2) (2012) 202–206.
- [4] A. Chowdhary, J.F. Meis, J. Guarro, G.S. de Hoog, S. Kathuria, M.C. Arendrup, et al., ESCMID and ECMM joint clinical guidelines for the diagnosis and management of systemic phaeohiphomycosis: diseases caused by black fungi, Clin. Microbiol. Infect. 20 (Suppl 3) (2014) 47–75.
- [5] S. Nandedkar, T. Bajpai, G.S. Bhatambare, P. Sakhi, Cerebral phaeohiphomycosis: a rare case from central India, Asian J. Neurosurg. 10 (2) (2015) 142–144.
- [6] A.S. Kantarcioglu, J. Guarro, S. De Hoog, H. Apaydin, N. Kiraz, An updated comprehensive systematic review of *Cladophialaphora bantiana* and analysis of epidemiology, clinical characteristics, and outcome of cerebral cases, Med. Mycol. 55 (6) (2017) 579–604.
- [7] J.W. Baddley, D. Salzman, P.G. Pappas, Fungal brain abscess in transplant recipients: epidemiologic, microbiologic, and clinical features, Clin. Transplant. 16 (6) (2002) 419–424.
- [8] A. Fica, M.C. Diaz, M. Luppi, R. Olivares, L. Saez, M. Baboor, et al., Unsuccessful treatment with voriconazole of a brain abscess due to *Cladophialaphora bantiana*, Scand. J. Infect. Dis. 35 (11–12) (2003) 892–893.
- [9] J.S. Schieffelin, J.B. Garcia-Diaz, G.E. Loss Jr., E.N. Beckman, R.A. Keller, C. Staffeld-Coit, et al., Phaeohiphomycosis fungal infections in solid organ transplant recipients: clinical presentation, pathology, and treatment, Transpl. Infect. Dis. 16 (2) (2014) 270–278.
- [10] S.G. Revankar, D.A. Sutton, M.G. Rinaldi, Primary central nervous system phaeohiphomycosis: a review of 101 cases, Clin. Infect. Dis. 38 (2) (2004) 206–216.
- [11] M.K. Lyons, J.E. Blair, K.O. Leslie, Successful treatment with voriconazole of fungal cerebral abscess due to *Cladophialaphora bantiana*, Clin. Neurol. Neurosurg. 107 (6) (2005) 532–534.
- [12] S.G. Revankar, D.A. Sutton, Melanized fungi in human disease, Clin. Microbiol. Rev. 23 (4) (2010) 884–928.