Dematiaceous Molds

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KEYWORDS

• Dematiaceous • Phaeohyphomycosis • Amphotericin B • Itraconazole
• Voriconazole • Isavuconazole • Posaconazole

KEY POINTS

- Phaeohyphomycosis refers to infections due to dematiaceous, or darkly pigmented fungi that are distinguished from other fungal species by the presence of melanin.
- They are ubiquitous and commonly found in soil. Transmission is generally by inhalation or by direct contact in the presence of trauma to skin or mucous membrane.
- Although they are rare causes of infection, they can cause superficial and disseminated infection in both immunocompromised and immunocompetent individuals and are often difficult to treat, requiring both surgical intervention and prolonged medical therapy.
- Standard therapies are lacking; management is based on in vitro data, animal studies, and clinical experience and expert opinions derived primarily from descriptive case studies.

INTRODUCTION

Dematiaceous, or darkly pigmented fungi, are the cause of phaeohyphomycosis, the general term used to describe a variety of infections ranging from superficial infections, allergic disease, pneumonia, brain abscess, and disseminated infection. These fungi are uncommon causes of human disease but can be responsible for life-threatening infections in both immunocompromised and immunocompetent individuals. They are commonly found in the soil and are generally distributed worldwide, which suggests that most if not all individuals are exposed to them, presumably from inhalation. However, phaeohyphomycosis should be distinguished from other specific pathologic conditions associated with dematiaceous fungi, which include chromoblastomycosis and mycetoma. Chromoblastomycosis is caused by a small group of fungi that produce characteristic sclerotic bodies in tissue and is usually seen in tropical regions.[1] Mycetoma is a deep tissue infection, typically of the lower

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extremities, characterized by the presence of mycotic granules.[1] These clinical syndromes are discussed in detail in other reviews.[1–3]

Dematiaceous molds have become increasingly recognized as important pathogens. The spectrum of diseases they are associated with has also broadened. Although they are commonly seen in immunocompromised patients, for some infectious syndromes in immunocompetent individuals, such as allergic fungal sinusitis and brain abscess, they are among the most common etiologic fungi.

MYCOLOGY

More than 150 species and 70 genera of dematiaceous fungi have been implicated in human disease.[3] As the number of immunocompromised patients increases because of conditions, such as diabetes, organ transplantation, and novel medical therapy (eg, monoclonal antibodies), additional species are being reported as causes of human disease, expanding an already long list of potential pathogens.[4–6] Common genera associated with specific clinical syndromes are listed in **Table 1**. The distinguishing characteristic common to all these various species is the presence of melanin in their cell walls, which imparts the dark color to their conidia or spores and hyphae. The colonies are typically brown to black in color as well. In tissue, they will stain strongly with the Fontana-Masson stain, which is specific for melanin.[2] This stain can be helpful in distinguishing these fungi from other species, particularly *Aspergillus*. In addition, hyphae typically appear more fragmented in tissue than seen with *Aspergillus*, with irregular septate hyphae and yeastlike forms.[2]

Guidelines are available regarding the handling of potentially infectious fungi in the laboratory setting. It is suggested that cultures of certain well-known fungi, such as *Coccidioides immitis* and *Histoplasma capsulatum*, are to be worked with in a biosafety level 3 facility, which requires a separate negative pressure room. Recently agents of phaeohyphomycosis, in particular *Cladophialophora bantiana*, have been included in the list of fungi that should be kept under biosafety level 2 containment.[7] This requirement seems reasonable given their propensity, albeit rarely, for causing life-threatening infection in normal individuals.

Table 1
MIC distribution of isavuconazole tested against dematiaceous fungi based on CLSI broth microdilution M38-A2 method

Organism (Number of Isolates)	Range	MIC_{50} (μg/mL)	MIC_{90} (μg/mL)	Mean
Cladophialophora carrionii (81)	0.016–1.0	0.125	0.25	0.136
Cladophialophora bantiana (37)	0.008–1.0	0.25	0.5	0.259
Fonsecaea monophora (25)	0.063–1.0	0.125	0.25	0.184
Fonsecaea pedrosoi (21)	0.063–0.25	0.25	0.25	0.226
Madurella mycetomatis	≤0.016–0.125	0.031	0.063	0.037
Scedosporium prolificans (6)	>32.0	—	—	—
Exophiala sp environmental (106)	0.25–16.0	2.0	4.0	1.78
Exophiala dermatitidis (66)	0.031–1.0	0.5	1.0	0.418
Exophiala jeanselmei	0.25–>2.0	2.0	—	—
Exophiala spinifera	2.0	—	—	—

Abbreviation: CLSI, clinical & laboratory standards institute; MIC, minimal inhibitory concentration.
Data from Ref.[75–84]