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ESCMID and ECMM joint clinical guidelines for the diagnosis and management of systemic phaeohyphomycosis: diseases caused by black fungi

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Abstract

The aetiological agents of many invasive fungal infections are saprobes and opportunistic pathogens. Some of these fungi are darkly pigmented due to melanin production and traditionally have been named 'dematiaceous'. The melanized fungi cause a wide array of clinical syndromes ranging from superficial to deep-seated infections. Diagnosis relies on histopathological examination of clinical specimens and on examination of cultures. Sequencing is recommended for accurate species identification, especially for unusual or newly described pathogens. In cases of mycetoma and chromoblastomycosis, pathognomonic histological findings are useful and the Fontana–Masson stain, specific for melanin, usually confirms the diagnosis. There are no standardized therapies but voriconazole, posaconazole and itraconazole demonstrate the most consistent *in vitro* activity against this group of fungi. Oral itraconazole has been considered the drug of choice, given the extensive clinical experience with this drug. However, voriconazole may presumably be superior for central nervous system infections

because of its ability to achieve good levels in the cerebrospinal fluid. Posaconazole is a well-tolerated alternative drug, backed by less clinical experience but with excellent salvage treatment results after failure of other antifungals. Amphotericin B has been useful as alternative therapy in some cases. Combination antifungal therapy is recommended for cerebral abscesses when surgery is not possible and for disseminated infections in immunocompromised patients.

Keywords: Clinical presentation, diagnosis, guideline, mycosis, phaeohyphomycosis, prophylaxis, treatment
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Introduction

A panel of experts of the European Fungal Infection Study Group (EFISG) of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) undertook a data review and compiled guidelines for the diagnosis and management of infections caused by melanized (black) fungi. The deep-seated infection caused by these fungi is often referred to as phaeohyphomycosis. Many infections, however, are superficial and mild, or cause cutaneous or pulmonary colonization only. In addition, many species of black fungi have a cosmopolitan presence and are widely distributed in the environment and the possibility that a suspected clinical isolate might be a contaminant must be considered. The course of infection differs with the species, so for clinical management it is paramount to obtain an accurate species identification. Although sizeable numbers of these rare fungal pathogens have been implicated in human infections, we have reviewed only the most common ones.

Methods

The guideline development followed the AGREE II method (Appraisal of guidelines for research and evaluation II; http://www.agreetrust.org/resource-centre/agree-ii/, accessed 13 December 2013). The overall objective of the guidelines has been on the diagnosis and management of deep-seated phaeohyphomycosis, including disseminated infections. In addition, superficial and allergic manifestations caused by these fungi are also briefly discussed. The definition of the strength of recommendation and the quality of the published evidence are defined in Table 1. The health questions covered by the guidelines are specifically described in the Tables 2–4. The population to whom the recommendations are meant to apply is any patient suffering from phaeohyphomycosis. The expert panel (35 members) was set up by ESCMID/EFISG and European Confederation of Medical Mycology (ECMM) including clinical microbiologists, infectious diseases experts, paediatricians, haematologists and intensive care unit experts taking into account the target users of these guidelines. Competing interests of guideline development group members were recorded and addressed. An expert subgroup (AC, MCE, JG, SDH, SK, OAC, JFM) reviewed the available literature. The other experts of the panel acted as external reviewers. The members actively shared their views and documents by email, teleconferences and face-to face meetings during 2012–2013.

TABLE 1. System for grading strength of recommendation and quality of evidence about diagnostic procedures and therapy of infections by black fungi

Grade of recommendation	Definition
Strength of recommendation	
Grade A	ESCMID (EFISG) and ECMM strongly support a recommendation for use
Grade B	ESCMID (EFISG) and ECMM moderately support a recommendation for use
Grade C	ESCMID (EFISG) and ECMM marginally support a recommendation for use
Grade D	ESCMID (EFISG) and ECMM support a recommendation against use
Level of evidence	**Definition**
Quality of evidence accepted	
Level I	Evidence from at least one properly designed randomized, controlled trial
Level II	Evidence from at least one well-designed clinical trial, without randomization; from cohort or case–control analytical studies (preferably from more than one centre); from multiple time series; or from dramatic results of uncontrolled experiments
Level III	Evidence from opinions of respected authorities, based on clinical experience, descriptive case studies, or reports of expert committees