

Journal of Feline Medicine and Surgery

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Journal of Feline Medicine and Surgery 2013 15: 628

DOI: 10.1177/1098612X13489227

The online version of this article can be found at:

<http://jfm.sagepub.com/content/15/7/628>

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What is This?

RARE OPPORTUNISTIC MYCOSES IN CATS: PHAEOPHYCOMYCOSIS AND HYALOPHYCOMYCOSIS

ABCD guidelines on prevention and management



Albert Lloret, Katrin Hartmann, Maria Grazia Pennisi, Lluís Ferrer*, Diane Addie, Sándor Belák, Corine Boucraut-Baralon, Herman Egberink, Tadeusz Frymus, Tim Gruffydd-Jones, Margaret J Hosie, Hans Lutz, Fulvio Marsilio, Karin Möstl, Alan D Radford, Etienne Thiry, Uwe Truyen and Marian C Horzinek

Overview: Phaeohiphomycoses and hyalohyphomycoses are rare opportunistic infections acquired from the environment. More cases have been reported in recent years in humans and cats.

Disease signs: Single or multiple nodules or ulcerated plaques (which may be pigmented) in the skin are the typical lesions. In some cases the infection disseminates or involves the central nervous system (CNS).

Diagnosis: Diagnosis is based on fungal detection by cytology and/or histology. Culture provides definitive diagnosis and species identification.

Treatment: Treatment involves surgical excision in cases of localised skin disease followed by systemic antifungal therapy, with itraconazole as the agent of first choice. Relapses after treatment are common. Itraconazole and other systemic antifungal agents have been used to treat systemic or neurological cases, but the response is unpredictable. The prognosis is guarded to poor in cats with multiple lesions and systemic or neurological involvement.

Zoonotic risk: There is no zoonotic risk associated with contact with infected cats.

Fungal properties and epidemiology

Phaeohiphomycoses are rare opportunistic fungal infections caused by numerous genera of fungal moulds that characteristically produce melanin-pigmented 'dematiaceous' (dark-coloured) hyphal elements in tissues and in culture (Figures 1 and 2); yeast-like forms have also been found in some cases.¹ Hyalohyphomycoses are caused by several genera of fungi that are non-pigmented, being transparent or hyaline in tissues.¹

Both are ubiquitous saprophytic agents. The number of reports of infections is increasing in humans and animals, often associated with immunosuppressive treatment or an immunosuppressive condition. In human medicine, they are currently considered emerging fungal infections.^{2,3}

Infections are acquired from traumatic implantation from the environment (soil and decomposed plants). Direct transmission between hosts does not occur.¹

The taxonomy of the aetiological agents is complicated, and names have often been changed. More than 100 species classified within 60 genera have been described as agents of phaeohiphomycosis in animals and humans. Pathogens for dogs and cats include species from *Alternaria*, *Bipolaris*, *Cladophialophora* and *Curvularia*. Genera with species causing disease in cats, but not in dogs, are *Exophiala*, *Fonsecaea*, *Macrophomina*, *Microsphaerosis*, *Moniliella*, *Phialophora*, *Phoma*, *Scolecobasidium* and *Stemphylium*.

European Advisory Board on Cat Diseases

The European Advisory Board on Cat Diseases (ABCD) is a body of experts in immunology, vaccinology and clinical feline medicine that issues guidelines on prevention and management of feline infectious diseases in Europe, for the benefit of the health and welfare of cats. The guidelines are based on current scientific knowledge of the diseases and available vaccines concerned.

The latest version of the rare opportunistic mycoses in cats guidelines is available at www.abcd-vets.org

*The ABCD is grateful to Professor Lluís Ferrer, of the Foster Hospital for Small Animals, Cummings School of Veterinary Medicine, Tufts University, USA, who, though not a member of the Board, contributed to this article.

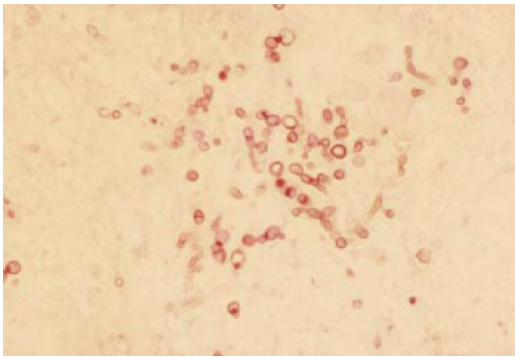


Figure 1 Dark-coloured, periodic acid-Schiff-positive, fungal structures in a tissue sample. Courtesy of Alessandra Fondati

Genera with species causing hyalohyphomycosis in dogs and cats include *Fusarium*, *Acremonium*, *Paecilomyces*, *Pseudallescheria*, *Sagemonella*, *Phialosimplex* and *Scedosporium*.

Feline phaeohyphomycosis probably has a worldwide distribution as sporadic cases have been reported from North America, Spain,⁴ Italy,^{5,6} Australia,⁷ Canada,⁸ the UK^{9,10} and Japan.¹¹

A retrospective study from the UK evaluating 77 cats with nodular granulomatous skin lesions caused by fungal infection found that the most frequent cause was hyalohyphomycosis. Phaeohyphomycosis and deep pseudomycetomas were less frequently diagnosed.⁹

Pathogenesis

Infection occurs mainly through contact or skin puncture, especially through trauma involving wood.¹ Respiratory tract colonisation is suspected to occur in systemic cases. In the rare cases of CNS infection, the route of exposure has not been elucidated, but an extension from sinuses, the orbit and middle ear has been suggested.^{1,12} Local infections are rarely associated with systemic diseases or immunosuppression.¹ The infrequent cases of systemic disseminated infection may or may not be associated with immunosuppression.

Clinical presentation

Nodules or masses in the skin or nasal mucosa are the most common clinical problem. Ulcerated, crusting or fistulating nodules, non-ulcerated subcutaneous nodules and/or plaques, which can be focal or multifocal and locally invasive, are typical lesions.⁴⁻¹¹ The lesions may appear pigmented,¹ but are otherwise not different from chronic bacterial infection or cystic skin lesions. In most cases they

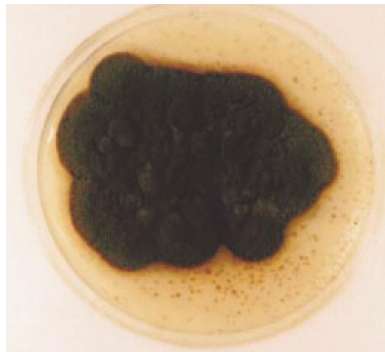


Figure 2 'Dematiaceous' (dark-coloured) colony. Courtesy of Alessandra Fondati

In human medicine, these are currently considered emerging fungal infections.



EBM grades
The ranking system for grading the level of evidence of various statements within this article is described on page 533 of this Special Issue.

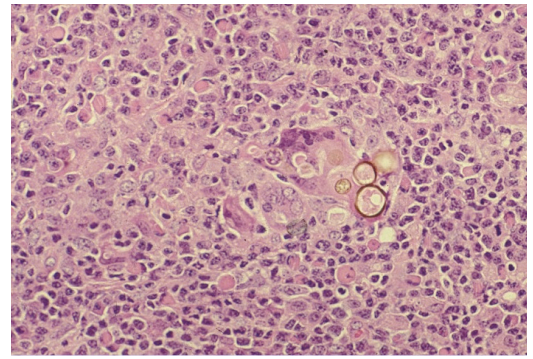


Figure 3 Pigmented fungal structures in a tissue sample. Courtesy of Lluís Ferrer

are found in the facial region, and on the distal part of the extremities or the tail. A typical presentation is a nodule on the bridge of the nose.⁴ A case of a focal pulmonary granuloma caused by *Cladophialophora bantiana* has been reported in a cat.¹³

A few cases in the literature concern fungal infections that were responsible for multifocal neurological signs due to encephalitis or brain abscesses¹² or for disseminated disease,^{14,15} especially in association with immunosuppression. In these cases the causative organism has been identified as *Cladosporium* species. Most cases have been diagnosed post mortem.

Diagnosis

Diagnosis is based on visualisation of the fungal organism on cytology and/or histology, which usually shows a nodular to diffuse pyogranulomatous inflammation pattern. In tissue, the presence of pigmented fungal structures in the centre of the pyogranulomatous reaction is highly suggestive of phaeohyphomycosis (Figure 3).^{1,4-11} Special fungal stains such as Gomori methenamine silver or periodic acid-Schiff can enhance the diagnostic sensitivity.

Definitive diagnosis relies on fungal culture and identification of the fungal species based on morphology and pigmentation features by specialised laboratories.¹

Molecular techniques have only seldom been used to identify pathogenic fungal species.¹¹

Treatment

No prospective studies exist on the treatment of feline phaeohyphomycosis or hyalohyphomycosis. Recommendations are based on case reports.

The approach for local lesions is aggressive surgical excision, as these rarely respond to antifungal treatment. After surgery of a single lesion, if multiple lesions exist or in cases of disseminated infection, itraconazole is the treatment of choice [EBM grade IV].

Table 1 Treatment of phaeohyphomycosis and hyalohyphomycosis

Drug/treatment	Dose and frequency	Comments
Surgical excision		Radical surgery with wide margins
Itraconazole	10 mg/kg PO q24h	Consider if multiple lesions or post-surgery
Posaconazole	5 mg/kg q24h PO	Consider in severe or disseminated disease
Amphotericin B	0.25 mg/kg q48h IV to a total	Consider in severe or disseminated disease

Disseminated or neurological cases are poorly responsive to treatment. Ketoconazole, amphotericin B and posaconazole have been used in a few cases [EBM grade IV].^{1,13}

Table 1 lists the treatment options for these infections.

Funding

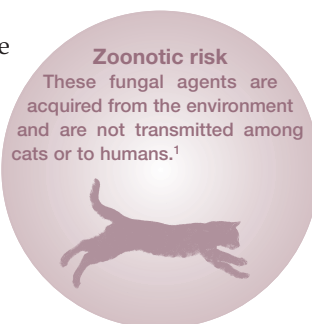
The authors received no specific grant from any funding agency in the public, commercial or not-for-profit sectors for the preparation of this article. The ABCD is supported by Merial, but is a scientifically independent body.

Conflict of interest

The authors do not have any potential conflicts of interest to declare.

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KEY POINTS

- ❖ Sporadic cases of these fungal diseases have been reported in cats.
- ❖ Skin nodules and ulcers, especially involving the facial area, distal extremities and tail, are the most frequent lesions.
- ❖ Dissemination and CNS signs may occur in rare cases, especially with *Cladosporium* species infection.
- ❖ Histology and culture are the most useful diagnostic tests. Some fungi show a typical pigmentation, which is helpful for diagnosis.
- ❖ A combination of surgery and systemic antifungal treatment (itraconazole) may cure cases with localised lesions.
- ❖ Cases of disseminated skin disease or systemic disease have a poor prognosis; new azole drugs like posaconazole should be considered in these cats.

