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Pyogranulomatous meningoencephalitis associated with dematiaceous fungal (*Cladophialophora bantiana*) infection in a domestic cat

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Abstract. A 6-month-old, castrated male domestic cat with progressive neurological signs of 2–3 weeks duration was necropsied. Macroscopic findings were restricted to the brain and included irregularly shaped, well-delineated but unencapsulated areas of intense black pigmentation involving the rostral portion of both cerebral hemispheres. Microscopically, numerous brown, oblong, segmented branching hyphae and conidial-like structures and extensive pyogranulomatous inflammation were identified throughout the cerebral lesion and in adjacent blood vessels. Hyphae and oval conidia were best demonstrated with either Gomori methenamine silver or periodic acid–Schiff stain. Fungal infection in the brain of this cat was unrelated to any concurrent immunodeficiency syndrome or immunosuppressive treatment. This report deals with a case of cerebral phaeohyphomycosis from which a different species of dematiaceous fungus, *Cladophialophora bantiana*, was isolated and identified.

Cladophialophora bantiana is a fungus that, on culture, possesses melanin-like pigment on the wall of hyphae and/or spores.¹⁰ Dematiaceous fungi include members in the form family Dematiaceae of the *Hyphomycete*, form order Sphaeropsidales of the *Coelomycetes*, and various unitunicate *Ascomycytes* and other groups.¹⁷ Clinical infections by dematiaceous fungi that are superficial, cutaneous, subcutaneous, cerebral, or systemic⁴ are designated as phaeohyphomycosis, an umbrella term introduced in 1974.¹⁰ In humans, primary cerebral phaeohyphomycosis is well documented dating back to 1952,³ and associated lesions were described as brain abscess,¹⁶ meningoencephalitis and brain abscess,⁶ or chronic meningitis.¹ In comparison, primary phaeohyphomycosis of the brain of animals is seldom reported. Cerebral phaeohyphomycosis is rare in domestic animals, having been previously described in only 5 cats (4 from the USA and 1 from South Africa)^{5,9,11,15,18} and 4 dogs.^{5,13,14} In addition, most of the previously published cases of cerebral phaeohyphomycosis in animals were diagnosed only on the basis of histopathologic features, without isolation and identification of the fungal agent. This report documents a case of feline cerebral phaeohyphomycosis from which *Cladophialophora bantiana*, a dematiaceous fungus, was isolated and identified.

A 6-month-old castrated male domestic medium-haired cat was referred to the University of Minnesota Veterinary

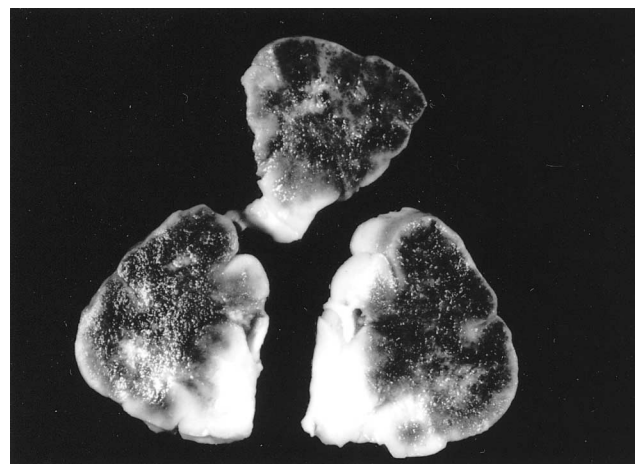


Figure 1. Brain; cat. Cross-sections of the rostral cerebrum and meninges. Well-demarcated areas of black discoloration and softening caused by *C. bantiana*.

Teaching Hospital because of progressive neurological signs for 2–3 weeks. Anisocoria, vertical nystagmus, mentation deficits, right-sided rigidity, weakness, inability to stand or eat, and superficial oral erosions were noted on examination. Following euthanasia, a necropsy was performed at the Minnesota Veterinary Diagnostic Laboratory in St. Paul, Minnesota. Gross lesions were confined to the brain, where black pigmented areas involved a 4 × 3-cm area of the rostral half of the left cerebral hemisphere and a 1.5 × 1-cm area of the cranial portion of the right frontal lobe. Cross-sections of formalin-fixed brain revealed well-delineated black lesions extending from the meninges deep into the brain (Fig. 1).

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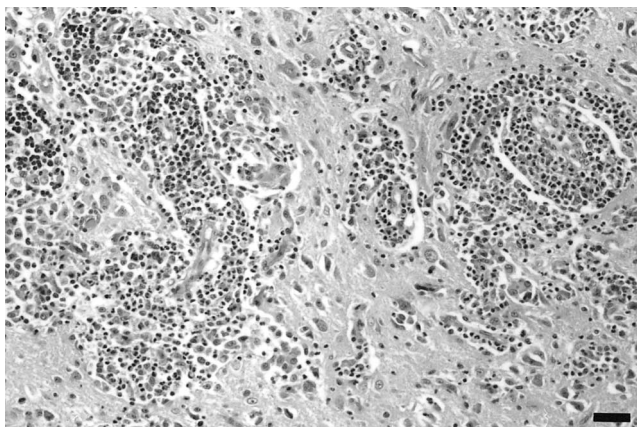


Figure 2. Brain; cat. Extensive pyogranulomatous inflammation with perivascular cuffing in the rostral cerebral cortex. HE stain. Bar = 38 μ m.

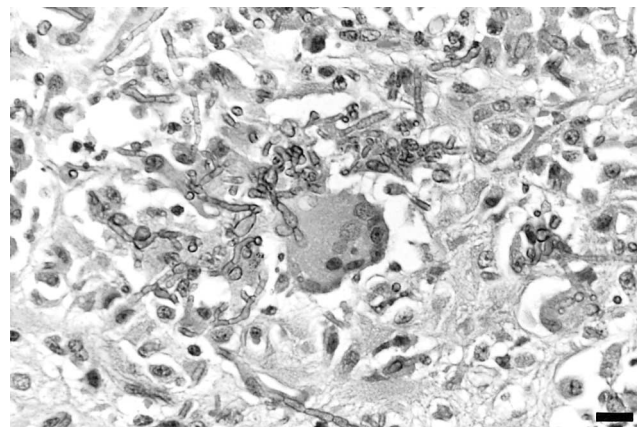


Figure 3. Brain; cat. Section of cerebrum revealing severe granulomatous inflammation comprised mainly of macrophages and multinucleated giant cells, with many ovoid, branching septate hyphae. HE stain. Bar = 15 μ m.

Tissue samples from the brain, heart, lung, liver, kidney, and spleen were fixed in 10% neutral buffered formalin, routinely processed, embedded in paraffin, sectioned at 4–5 μ m, and stained with hematoxylin and eosin (HE), Gomori methenamine silver (GMS), periodic acid–Schiff (PAS) reaction, and acid-fast stain (Kinyoun's method for acid fast bacteria).

Microscopic lesions were confined to the brain. In the brain, extensive pyogranulomatous inflammation involved both the meninges and cerebral cortex. The inflammatory cell infiltrate included large numbers of histiocytes, epithelioid macrophages, neutrophils, multinucleated giant cells, plasma cells, lymphocytes, and a few eosinophils. Inflammatory cells were dispersed around many oblong, branching septate hyphae (3–5 μ m in diameter) and conidial-like structures (Figs. 2, 3). Fungi were best visualized in GMS- and PAS-stained tissue sections (Fig. 4). Acid-fast stain did not reveal acid-fast bacilli. Thrombi in meningeal and cerebral vessels contained fungal elements. Blood vessels were often surrounded by lymphocytic cuffs of various thickness that contained a few eosinophils. Foci of liquefactive necrosis, neovascularization, neutrophilic infiltration, mineralization, and intense astrocytic proliferation were distributed throughout the area of granulomatous inflammation.

After 10–15 days of incubation, cultures from cerebral lesions revealed a slowly growing, dark pigmented fungus. Colonies on Sabouraud dextrose agar had a velvety dark olive-brown surface. Lactophenol cotton blue wet mount preparation revealed brown septate hyphae with long, sparsely branched wavy chains of smooth oval conidia, which did not display dark scars of attachment. Based on the colony characteristics, growth rate, good growth at 37 C, and the morphology, the Bacteriology Section of the Minnesota Veterinary Diagnostic Laboratory tentatively identified this fungus as *C. bantiana*. Fungal identification was verified by The Ohio Department of Health Laboratories in Columbus, Ohio, and the Fungus Testing Laboratory in San Antonio, Texas.

This report describes the pathologic findings in a 6-month-old castrated male cat with *C. bantiana* infection localized

to the brain and surrounding meninges. *Cladophialophora bantiana* and closely related fungal agents (*Cladosporium bantianum*, *Cladosporium trichoides*, *Xylophylpha emmonsii*)⁸ are classified in the subphyla Ascomycotina and Deuteromycotina, which constitute a group of ubiquitous dematiaceous fungi with melanin pigment in their hyphal elements, conidia, or both.¹² Dematiaceous fungal infection of the brain and/or meninges have been reported previously in humans,^{1,3,6,16} dogs,^{5,13,14} and cats.^{5,9,11,16,18,19} Recently, an ocular form of the disease was described in 2 cats and a dog.² Microscopic lesions in this case are similar to those reported previously from cats and other species.^{1,3,5,6,9,13–16,18,19} The most consistent lesions are seen in the brain and consist of conspicuous suppurative and granulomatous meningoencephalitis with foci of necrosis, perivascular cuffs, fungal invasion of blood vessels, and marked proliferation of reactive astrocytes. Based on microscopic examination of other organs, there was no evidence of a systemic infection in this cat. The pathogenesis of infection in this cat is uncertain, but fungi were likely introduced via the oronasal route. Pre-

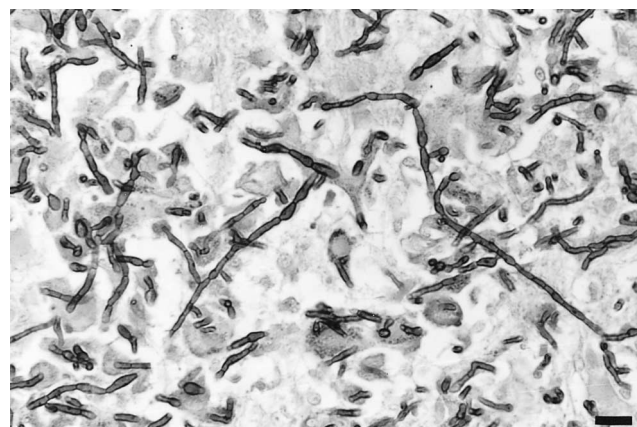


Figure 4. Brain; cat. Section of cerebrum showing myriads of oblong, septate, branching hyphae and a few macrophages. PAS stain. Bar = 15 μ m.

vicious reports indicated that dematiaceous fungi generally gain access to the host through broken skin, either directly due to trauma or indirectly by contamination of a preexisting wound.^{2,7,9,11} The source of infection was most likely environmental since dematiaceous fungi are mostly soil organisms associated with plant material as plant pathogens.¹⁰ No predisposing factors were identified in this case; the cat was young, serologically negative for both feline leukemia virus and feline immunodeficiency virus, and had no history of long-term therapy with corticosteroids and/or antibiotics, of neoplasia, or of chronic debilitating disease. In addition, no obvious lymphoid depletion that would suggest immune suppression was noted histologically.

Despite the rare occurrence of feline or canine cerebral phaeohyphomycosis, it should be included in the list of the differential diagnoses of companion animals with a history of neurologic signs. Macroscopically, locally extensive dark-pigmented lesions involving the brain could include other mycetomas, hematoma, telangiectasia, and melanoma. In tissue sections, the dematiaceous fungal organisms appear as either darkly pigmented individual hyphae, conidia, or yeast-like structures. Furthermore, the pigmented fungi of dematiomycosis should be differentiated from eumycotic black-grain mycetomas, whose causative agent forms distinct compact aggregates of mycelia.¹⁹ Dematiaceous fungal infection in domestic animals may pose a public health problem because of a risk of exposure during necropsy or when handling this organism.¹² Definitive diagnosis of cerebral dematiaceous mycotic infection requires identification by culture. Fungi cultured from the brain of this cat were identified as *C. bantiana*, and lesions observed in the brain were consistent with documented pathology associated with dematiaceous fungal infection.

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