Fungal Infections of the Central Nervous System in Small Animals

Clinical Features, Diagnosis, and Management

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KEYWORDS

• Dog • Cat • Brain • *Aspergillus* • *Blastomyces* • *Cladophialophora* • *Coccidioides* • *Cryptococcus*

KEY POINTS

- Central nervous system (CNS) fungal infections in small animals often present as multifocal meningoencephalomyelitis, intracranial lesions that accompany sinonasal lesions, ventriculitis, or a solitary brain or spinal cord granuloma.
- Systemic clinical signs vary; there is often no detectable extraneural involvement in CNS granuloma cases.
- Surgery may have a diagnostic and therapeutic role in CNS granuloma cases.
- Recent advances have occurred in serology for the systemic mycoses, but for the rarer fungi demonstration of the organism remains obligatory for definitive diagnosis (eg, cytology, histology or culture).
- Fluconazole, voriconazole, and posaconazole cross the blood-brain barrier, but voriconazole is neurotoxic to cats. Liposomal and lipid-encapsulated formulations of amphotericin B improve renal safety and the distribution to the CNS.

INTRODUCTION

Mycotic infections of the central nervous system (CNS) of dogs and cats are, depending on geographic location, a very rare to sporadic but severe cause of disease.

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Cases may present with multifocal meningoencephalomyelitis, intracranial lesions accompanying sinonasal lesions, ventriculitis, or a solitary CNS granuloma. Each of these presentations has its own features, incidence of multisystemic mycosis, differential diagnoses, pertinent diagnostic tests, and appropriate management, and is discussed separately in this article. Many organisms have been implicated in CNS mycosis and their predispositions vary. *Cryptococcus* spp have been associated with each of these clinical patterns but ventriculitis is atypical. *Blastomyces dermatitidis* often presents as an intracranial mass extending from the nasal cavity, but is also a chief cause of canine ventriculitis. *Cladophialophora bantiana* is neurotropic, often presenting as brain granulomas without extraneural lesions.

Much information is available regarding life cycles and microbiological features of the systemic mycoses.[1–5] Canine fungal discospondylitis has been studied, especially *Aspergillus* and *Paecilomyces*.[6–10] This article focuses on the clinical features, diagnosis, and management of fungal infections of the brain and spinal cord in dogs and cats.

SIGNALMENT, HISTORY, AND CLINICAL PRESENTATION

Fungal infections more often occur in younger animals, animals spending more time outdoors, and larger dogs.[1,2,11] Young German Shepherd dogs are overrepresented for aspergillosis.[10,12] However, indoor-only cats can develop mycoses.[3,5] Disease also occurs in older animals, including CNS cryptococcosis in cats[5,13] and many cases of solitary CNS granulomas (discussed later). Exposure to bird or bat feces sitting on soil (including house plants) is pertinent.[3,14]

Geographic location and travel history are critical. *Cryptococcus neoformans* is worldwide. *Cryptococcus gattii* is common around Vancouver Island and the northwestern United States, and is now recognized as a distinct species to *C neoformans*.[5] Most coccidioidomycosis cases are in animals that live in Arizona, in a neighboring state, or in animals that lived there up to 6 years previously.[1,15] Many blastomycosis cases are in the Midwest, the Ohio and Mississippi river valleys, or certain other clusters; proximity to bodies of water is a risk factor for dogs.[2,11,16] Most histoplasmosis cases are associated with the Mississippi, Ohio, or Missouri river valleys.[3]

Many CNS mycosis cases have progressive neurologic clinical signs over 0 to 14 days.[10,13,16–22] Transitory steroid responsiveness is common.[16,18] Longer neurologic histories occur, especially with cryptococcosis.[13] Neurologic clinical signs depend on localization. With multifocal meningoencephalomyelitis, forebrain and central vestibular deficits are common. In sinonasal mycosis with intracranial extension, seizures and other forebrain deficits are typical. With a solitary CNS granuloma, neurolocalization is often focal and forebrain or spinal. A cerebral mass with brain herniations may cause diffuse intracranial deficits. Cases with ventriculitis often have rapidly progressive brainstem disease.

When present, systemic signs precede the neurologic signs or occur concurrently. Systemic clinical signs are often present for days or a few weeks. However, cats with CNS cryptococcosis had extended extraneural histories (median 52 days, up to 4 years), which was significantly longer than in dogs (median 7 days).[13] There may be no clinical evidence of extraneural involvement. Specifics regarding extraneural disease are discussed later.

Multifocal Meningoencephalomyelitis Accompanying Systemic Disease

Multifocal meningoencephalomyelitis is especially common with hematogenous brain infection by *Cryptococcus* (**Box 1**). Usually, extraneural involvement is apparent