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## Fungal pyogranulomatous encephalitis in a dog with leishmaniosis

### Encefalite piogranulomatosa micótica em um cão com leishmaniose

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#### -NOTE-

#### ABSTRACT

A case of pyogranulomatous micotic encephalitis in a one-year old, female, Fila Brasileiro dog is reported. Gross examination of the cerebrum revealed a softened haemorrhagic area in the right frontal cortex and on the cut surface of the left hemisphere, which affected the white matter and deep cortical areas. The diagnosis of multifocal mycotic pyogranulomatous encephalitis was obtained by the histopathological examination, which showed the presence of macrophages, giant cells, haemorrhage and brownish septate hyphae diffusely distributed within the tissue and invading vessel lumina. Identification of amastigotes forms in popliteus lymphonode imprint confirmed infection by *Leishmania* sp. Mycotic infection in the brain of this dog was related to a concurrent leishmaniosis, an immunosuppressive disease.

**Key words:** leishmaniasis, mycotic encephalitis, dog.

#### RESUMO

É relatado um caso de encefalite piogranulomatosa em um cão fêmea de um ano de idade, da raça Fila Brasileiro. Ao exame macroscópico do cérebro, evidenciou-se área amolecida e hemorrágica no córtex frontal direito e na superfície de corte do hemisfério esquerdo, afetando a substância branca e áreas corticais profundas. O diagnóstico de encefalite piogranulomatosa micótica multifocal foi realizado através de exame histopatológico, que mostrou a presença de macrófagos, células gigantes, focos de hemorragia e hifas septadas de coloração marrom, com distribuição difusa e

invadindo a luz de vasos. A identificação de formas amastigotas "no imprint" de linfonodo poplíteo confirmou o diagnóstico de leishmaniose. A infecção micótica no cérebro deste cão foi relacionada com a ocorrência concomitante de leishmaniose, uma doença imunossupressora.

**Palavras-chave:** leishmaniose, encefalite micótica, cão.

Several different fungal organisms have been shown to cause meningitis and encephalitis in both large and small animals. Fungal organisms commonly reported to infect the central nervous system of small animals are *Cryptococcus neoformans* (WILKINSON 1979; O'TOOLE et al., 2003), *Blastomyces dermatitidis* (BREIDER et al., 1988), *Histoplasma capsulatum* (MEADOWS, 1992), *Coccidioides immitis* (BURTCH, 1998) *Cladophialophora bantiana* (AÑOR et al., 2001), several species of *Aspergillus* including *A. fumigatus* and *A. terreus* (MULLANEY et al., 1983), and *Fusarium solani* (EVANS et al., 2004).

Phaeohyphomycosis is a human and animal infection caused by dematiaceous (darkly pigmented) fungi, defined as those that have melanin or melanin-like pigment in their cell walls (DILLEHAY et al., 1987;

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BOULJIHAD et al., 2002). The infection with aggressive fungus has a high mortality rate, primarily related to its poor response to currently available antifungal therapy (TUNUGUNTLA et al., 2005). Most reported cases of cerebral phaeohyphomycosis have occurred in immunocompetent patients; however, some case reports and experimental data have suggested that cellular immune deficiency is a risk factor (BRANDT & WARNOCK, 2003). Being a parasite, *Leishmania* ensures its own survival by modulating the host immune system either by inducing immunosuppression or by promoting pro-parasitic host functions (AWASTHI et al., 2004). Studies of *Leishmania* infections in mice indicate that resistance or susceptibility to the disease is associated with the development of Th1 or Th2-type response, respectively (LOCKSLEY & SCOTT, 1991). Visceral leishmaniasis presents vigorous Th2 immune response, which is mainly characterized in human by augmented expression of IL-4, polyclonal B cell activation, intense hypergammaglobulinemia and production of antileishmanial IgE antibodies (ALMEIDA et al., 2005). Prolonged latent infection with *Leishmania sp* results in cell-mediated immunosuppression that could be related to the expression of IL-10 (SANTOS-GOMES et al., 2002). Compromised hosts with impaired T-lymphocyte or macrophage function are prone to develop CNS infections caused by intracellular pathogens as bacteria (e.g., *Nocardia*), viruses (e.g. herpesvirus), parasites (e.g., *T. gondii*) and fungus as *Aspergillus sp* (CUNHA, 2001).

A one-year old female dog of the Fila Brasileiro breed, had been presenting clinical signs of apathy, ataxy and cough for 8 days and eventually died before clinical attendance. Icterus, swollen lymph nodes, splenomegalia, pulmonary congestion and whitish dots in the kidney cortex were observed at necropsy. Cytology for leishmaniasis was positive at popliteus lymphonodus imprint stained with *Panótico rápido* (similar to Diff Quik®, a Giemsa stain). In the brain, meninges were diffusely opaque and congested; the superficial blood vessels of the cerebral cortex were hyperemic; a softened haemorrhagic area was observed in the right frontal cortex and on the cut surface of the left hemisphere, which affected the white matter and deep cortical areas. Oral cavity and teeth, ear canals and nasal sinuses, were examined, and no evidence of inflammation or trauma was found in any of these locations. Pulmonary lesions suggestive of mycotic infection were not observed. Only alveolar congestion was observed in the histopathological examination of lungs. Microscopically, numerous brown, oblong, segmented branching hyphae and extensive

pyogranulomatous inflammation were identified throughout the cerebral lesion and in adjacent blood vessels. Hyphae was easily visualized in hematoxylin-eosin stain.

Seizures are common reflection of a variety of intracranial physiologic abnormalities in dogs. The localization and extension of lesion in frontal lobes are also associated with seizures (BAGLEY & GAVIN, 1998). Whereas intracranial tumours can occur in young dogs and cats they typically occur in middle aged to older animals (MOORE et al., 1996). Since the lesion of the brain of this dog at gross examination suggested a diagnosis of neoplasia, complementary tests were not performed. The diagnosis of multifocal mycotic pyogranulomatous encephalitis was obtained by histopathological examination, which was characterized by the presence of neutrophils, mononuclear and giant cells, haemorrhage and brownish septate hyphae diffusely distributed within the tissue (Figure 1) and invading vessel lumina. Much of the nervous tissue damage is caused by vascular invasion of the organism and associated with inflammatory reaction, leading secondarily to infarction.

The source of infection in this case was not identified. The route of entry has been speculated to be nasal, as suggested by KROHNE (2000) as the principal route of infection. In this case, no systemic spread was identified, indicative of lack of hematogenous spread. Although fungal infections themselves are relatively frequent, actual granulomatous masses due to fungal infections are rare (DUBEY et al., 2005). *Cladophialophora* species are highly neurotropic, and *Cladophialophora bantiana* (synonym = *Xylohypha bantiana* or *C. trichoides*) is the most commonly identified agent (OSIYEMI et al., 2001). The immune response during *L. infantum* infection has been widely studied. Susceptible dogs show poor lymphoproliferative responses to specific antigen (PINELLI et al., 1994; MARTINEZ-MORENO et al., 1995) and the immunosuppressive nature of the disease, though antigen-specific, is an early event following infection (DE LUNA et al., 1999). Based on the morphologic aspects, the agent is believed to be a fungus of the *Cladosporium* gender, which, in the case under discussion, had no trouble to invade the encephalon due to down regulation of protective T-helper type 1 adaptive immune responses associated with visceral leishmaniasis.

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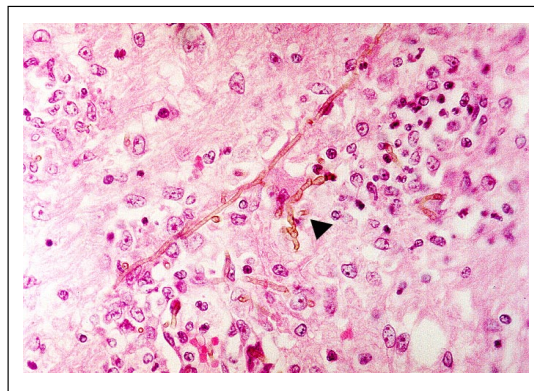


Figure 1 - Histological section of brain cortex where brownish hyphae (arrow head), gliosis and neutrophils are observed (H-E). Objective 40X.

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