Diagnostic Exercise
From The Davis-Thompson Foundation*

Case #: 143 Month: April Year: 2020

Answer Sheet

Title: Dog, cerebral and spinal cryptococcal meningitis and radiculoneuritis

Contributors: Vanessa Tapia Barraza*, DVM, MS candidate, Mariana Martins Flores*, DVM, MS, Doctor in Veterinary Pathology. *Laboratory of Veterinary Pathology, Universidade Federal de Santa Maria (UFSM), Santa Maria, Rio Grande do Sul, Brazil.

Morphologic diagnosis: Brain and spinal cord, meningitis, histiocytic and lymphoplasmacytic, mild to moderate, chronic, multifocal, with intralesional yeasts. Spinal nerve roots (cervical, thoracic and lumbar), radiculoneuritis, histiocytic and lymphoplasmacytic, mild to moderate, chronic multifocal, with intralesional yeasts.

Etiology: Based on histologic morphologic features, including the presence of a thick capsule and of narrow-based budding, the etiology in this case is Cryptococcus sp. This was confirmed by culture of cerebrospinal fluid. The involved fungal species was not determined.

Description of the microorganism: In histologic sections of the brain, spinal cord and spinal nerve roots, there are multiple round to oval, 4-10 µm diameter microorganisms with a variably thick (1-30 µm) capsule that does not stain with Hematoxylin and Eosin. Occasionally, narrow-based budding is observed.

Special stains that could help in this case: Mayer’s mucicarmine and Alcian blue (Fig. 4) stains can be used to help demonstrate the yeast capsule of Cryptococcus spp., which is not readily visible with Hematoxylin and Eosin staining. Additionally, Gomori’s methenamine silver and Periodic acid-Schiff stains help visualizing the morphologic features of the yeast such as shape, size and budding, when present.
Discussion: Cryptococcosis is a non-contagious mycotic disease of domestic animals with worldwide distribution. It is caused by Cryptococcus neoformans or Cryptococcus gatti. Although the disease is most frequent in cats, other domestic species such as dogs, horses and cattle are occasionally affected as well. Humans may also get infected; however, the infection is not considered zoonotic. This fungus is a saprophyte, present in soil, pigeon feces and decaying organic material. It is most common in temperate and tropical climates. Animals generally get infected by inhalation, but direct cutaneous inoculation is also possible. Most infected animals are asymptomatic. Nonetheless, in some cases, the inhaled fungus replicates within the alveoli and subsequently spreads by hematogenous route, infecting various organs such as brain and spinal cord, eyes, lymph nodes and skin. In the case reported here, the infection was restricted to the nervous system. The main virulence factors of Cryptococcus spp. are the ability to grow at body temperature, a polysaccharide capsule, melanin production and the secretion of extracellular enzymes. The thick capsule of Cryptococcus spp. observed histologically is composed of mannose-rich polysaccharides and is considered a major virulence factor because it impairs phagocytosis and other immunologic functions. The associated granulomatous reaction is therefore generally minimal. Melanin or melanin-like compounds are produced via the enzyme laccase. They help modulate the host immunologic response as well as protect the
organism from oxidative damage and from both heat and cold. After production, melanin accumulates in the yeast wall. *Cryptococcus* spp. also produce extracellular enzymes that promote fungal survival within the host tissues and interfere with the host immune responses. Examples of these enzymes include lipases, proteases and DNases. Gross lesions of cryptococcosis classically consist of white to gray gelatinous masses in the organs involved. In the skin, swelling and ulceration are common. Histologically, yeast aggregates form masses that have a “soap bubble” appearance, since the thick and prominent yeast capsule does not stain with Hematoxylin and Eosin. In addition to this thick capsule (approximately 10-20 µm) and the overall minor accompanying inflammation, the fungus can be recognized in histologic sections based on other specific features, such as its shape and size (the yeasts are round to oval, measuring approximately 5-10 µm in diameter) as well as narrow-based budding. *Blastomyces dermatitidis* is relatively similar to *Cryptococcus* spp. but that fungus is generally associated with intense granulomatous inflammation, it does not have a capsule, and it is characterized by broad-based budding. Nonetheless, some strains of *Cryptococcus* may induce a more severe inflammatory response and occasionally do not have the classic thick capsule. In these cases, the presence of narrow-based budding is supportive of the diagnosis of *Cryptococcus*. Other fungi such as *Histoplasma capsulatum* and *Coccidioides immitis* may also somewhat resemble *Cryptococcus* although they are easier to distinguish. *H. capsulatum* var. capsulatum is much smaller (2-4 µm) and confined to the cytoplasm of macrophages. *C. immitis* is larger (20-200 µm) and contains endospores.

**References and Recommended literature:**


*The Diagnostic Exercises are an initiative of the Latin Comparative Pathology Group (LCPG), the Latin American subdivision of The Davis-Thompson Foundation. These exercises are contributed by members and non-members from any country of residence. Consider submitting an exercise! A final document containing this material with answers and a brief discussion will be posted on the CL Davis website ([http://www.cldavis.org/diagnostic_exercises.html](http://www.cldavis.org/diagnostic_exercises.html)).

**Associate Editor for this Diagnostic Exercise:** Mariana Flores  
**Editor-in-chief:** Vinicius Carreira