



Diagnostic Exercise

From The Davis-Thompson Foundation*

Case #: 71 Month: August Year: 2016

Answer Sheet

Contributors: Federico Giannitti, DVM. "Instituto Nacional de Investigacion Agropecuaria" (INIA), La Estanzuela, Colonia, Uruguay; and University of Minnesota Veterinary Diagnostic Laboratory, Saint Paul, Minnesota, USA.

1-Gross descriptions:

- Figure 1: Brain, sagittal section: the ventricular system (lateral, third and fourth ventricles) is diffusely and mildly dilated (ectasia) and filled with abundant (several milliliters) homogeneous, yellowish, creamy (viscous) exudate (pus).
- Figure 2: Brain, coronal section, right thalamic area: scattered randomly throughout the neuroparenchyma there are 2 well-demarcated, approximately 0.5 x 0.5 x 0.5 cm, irregularly ovoid, bright red foci (malacia/hemorrhage/infarction).
- Figure 3: Heart, left ventricular free wall and papillary muscle: there is a focally extensive, poorly demarcated, irregularly shaped, approximately 3 x 3 cm area of yellowish/tan and bright red discoloration of the myocardium.

2-Morphologic diagnoses:

- Brain: severe diffuse suppurative ventriculitis, with multifocal random necrotizing meningoencephalitis, vasculitis, thrombosis (infarction) and intralesional/intravascular bacteria (cocci/bacilli), subacute.
- Heart: severe suppurative and necrotizing myocarditis with mineralization, vasculitis, thrombosis (infarction), and intralesional bacteria (cocci/bacilli), subacute.

3-Cause

- *Histophilus somni*.

4-Etiologic diagnoses:

- Cerebral histophilosis (*Histophilus* encephalitis).
- Cardiac histophilosis (*Histophilus* myocarditis).

5-Name of the disease

- Infectious Thrombotic Meningoencephalitis (ITME), Thrombotic Meningoencephalitis (TME).

6-Ancillary diagnostic tests to confirm the etiology

- Bacterial culture: *H. somni* is a fastidious facultative anaerobic bacterium. It grows on enriched media such as blood agar, and most isolates need increased concentrations of CO₂ to grow. The bacterium is quite slow-growing and reaches a colony size of 1-2 mm after 24-48 hours of incubation at 37°C. It can therefore be easily overgrown by the resident or contaminating bacteria in a clinical sample. Isolates of *H. somni* can have different appearances on blood agar, as they can be beta-haemolytic, alpha-haemolytic or non-haemolytic.
- PCR: species-specific PCR tests targeting the 16S rDNA are readily available.
- Immunohistochemistry (IHC): *H. somni* antigen can be demonstrated intralesionally by IHC in formalin-fixed paraffin-embedded tissues.
- Tissue gram stain would help differentiate *H. somni*, a gram-negative short coccobacillus, from gram-positive bacteria that can also cause suppurative/neutrophilic/necrotizing lesions such as *Listeria monocytogenes*.

Discussion:

All the gross and microscopic lesions depicted in this diagnostic exercise are highly compatible with those caused by *Histophilus somni* in cattle. The agent was isolated from the heart and brain in this case, confirming the etiologic diagnoses.

Histophilus somni (formerly *Haemophilus somnus*, *Histophilus ovis* and *Haemophilus agni*) is a member of the family *Pasteurellaceae*, which is recognized as an opportunistic pathogen of cattle and sheep. The only known habitats of *H. somni* are the mucosal surfaces of ruminants. While some strains are associated with disease, others are commensals. However, since very few *H. somni* strains have been sequenced, the genetic differences between virulent and avirulent strains (i.e., genes responsible for virulence factors) are poorly known.

H. somni is a normal inhabitant of the male and female bovine genital tract, and to a lesser extent the bovine nasal cavity. Calves are infected by carrier cows in the first months of life. The mechanisms and circumstances by which *H. somni* invades the bloodstream are not known. *H. somni* is responsible for a wide variety of syndromes, including sudden (unexpected) death, septicemia and fever, thrombotic meningoencephalitis, myocarditis/pericarditis,

pneumonia/pleuritis and laryngitis, arthritis/polyarthritis, reproductive disease (including abortion and metritis), mastitis, ocular disease (endophthalmitis) and otitis.

Although *H. somni* is capable of causing local inflammation at the sites of infection and is toxic to epithelial and phagocytic cells, vasculitis and thrombosis are the hallmark lesions induced by this agent. The pathogenetic mechanisms of the vasculitis are associated with the cytotoxic effects of the bacteria's lipo-oligosaccharide on endothelial cells, which induces apoptosis, inflammatory response, activation of platelets, and histamine production. The endothelial cells of the blood-brain barrier are particularly vulnerable to the cytotoxic effects, but vasculitis can develop in most organs. Additionally, *H. somni* is considered a facultative intracellular pathogen as it survives within monocytes, impairs the phagocytic function of neutrophils and macrophages, and induces degeneration of macrophages and apoptosis of neutrophils. As a result, the typical lesions induced by the agent are vasculitis, thrombosis, hemorrhage, necrosis and suppurative/fibrinosuppurative inflammation.

References and Recommended literature:

- Jubb, Kennedy and Palmer's Pathology of Domestic Animals, 6th edition, Ed. M. Grant Maxie, Elsevier, 2015.
- O'Toole D, Allen T, Hunter R, Corbeil LB. Diagnostic exercise: myocarditis due to *Histophilus somni* in feedlot and backgrounded cattle. Vet Pathol 2009; 46:1015-7.
- O'Toole D, Sondgeroth KS. Histophilosis as a natural disease. Curr Top Microbiol Immunol 2016; 396:15-48.

*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).

Associate Editor for this Diagnostic Exercise: Santiago Diab
Editor-in-chief: Vinicius Carreira