Diagnostic Exercise

From The Davis-Thompson Foundation*

Case #: 132 Month: November Year: 2019

Answer Sheet

Title: Acute Liver Failure in a 4 mo. old Mastiff.

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Three Possible Causes: The biochemistry and blood coagulation panels combined indicate acute liver necrosis/failure. In the dog, one possible cause would be Leptospirosis (which was tested for by snap test and negative). Other reasonable possibilities for acute liver failure are toxicoses (Amanitin, Microcystin, Aflatoxin). Among these possibilities, Amanitin is most likely given the necrosis of the intestinal tract (hemorrhage) and the kidney.

Diagnosis: Acute massive centrilobular and bridging hepatic necrosis.

Cause: Amanitin toxicosis.

Typical Gross Findings: In this case, the changes in the liver, aside from the friability, were subtle. In some cases, the massive necrosis can cause microhepatica. The mottling in this case corresponded to regions of collapse that were congested.
Microscopic Findings: The predominant histopathologic finding is severe centrilobular to panlobular hepatic necrosis. There was lobular collapse and parenchymal loss with replacement by swollen, dissociated hepatocytes, hypereosinophilic fibrillar material, pyknotic nuclei and karyorrhectic debris. Hepatocytes were frequently microvesiculated and/or contained aggregates of intracytoplasmic, brown to golden granules (hemosiderin). In the kidney, there was acute individual or segmental cell necrosis of the proximal and distal tubular epithelium characterized by cytoplasmic vacuolation, pyknotic nuclei, hypereosinophilia, and occasional cell sloughing into the tubular lumen.
Morphologic Diagnosis:

1. Liver: Massive centrilobular to panlobular hepatic necrosis, with mild periportal bridging fibrosis and pigment-laden hepatocytes.


3. Gastrointestinal tract: Melena (Gross diagnosis); Acute necrotizing enteritis.

Ancillary Diagnostics (Toxicology):
Liver: Trace Aminitin detected; Liver: No Alfatoxin detected; Stomach content: No microcystin detected.

Discussion: Amanitin, also known as alpha-amanitin or α-amanitin, is an amatoxin that, along with phallotoxins and virotoxins, is a hepatotoxic cyclopeptide toxin found in some mushroom species. Amanitin ingestion initially results in an asymptomatic incubation period, which in dog ranges from 6 to 24 hours, followed by gastrointestinal and hepatotoxic phases. If untreated, ingestion eventually leads to multiorgan failure and death. Amanitins enact their toxic effect through inhibition of RNA polymerase II, leading to decreased protein synthesis and eventual cell death. Therefore, cells with high metabolic activity, such as hepatocytes, crypt cells and renal tubular epithelial cells, are most susceptible. This explains why animals, such as this patient, that have ingested amanitin classically present with liver failure, gastrointestinal signs, and/or renal failure.

References:

*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).

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