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Addended Report

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Accession Number: **276233-21**

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Anatomic Pathology

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1 Whiskey - 314544 Canine German Shepherd Castrate

Tissue, Fixed

Digital Copper Quantification

Final Report

Digital Copper Quantification: 3,316ug/ gm dry weight basis (normal <400ug/gm dry weight basis)

The positive control (14,242ug/gm dry weight basis) and the negative control (214ug/gm dry weight basis) are appropriate with an intra-assay coefficient of variation of 7.1%.

Histopathology

Pathologist: Sean P. McDonough, DVM, Ph.D, Dipl. ACVP

Final Report

Morphological Diagnosis:

Hepatitis, chronic, mild, lymphohistiocytic with emerging back-to-back nodular regeneration, abundant hepatocellular copper and numerous copper granulomas (copper-associated hepatopathy).

Small intestine: Enteritis, moderate, chronic, diffuse, lymphoplasmacytic

Comments:

Although inflammation is rather modest, abundant copper accumulation is the most likely driver for the architectural remodeling observed in the biopsies. The duration and intensity of treatment for copper hepatopathy is based on the concentration of copper in the liver. If the sample of liver has not been submitted for copper determination, the amount of copper in the liver can be determined from a digitized image of the rhodanine stained section. If digital copper quantification is desired, please contact the pathology service office.

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The histologic findings in these gastrointestinal biopsies are consistent with inflammatory bowel disease (IBD). The cause of IBD remains unknown but current evidence suggests dysregulation of mucosal immunity in response to mucosal or luminal bacteria or bacterial products as central to the pathogenesis. The diagnosis of IBD is defined by a set of criteria and histopathologic assessment is only one of those criteria; histopathologic changes in the absence of other diagnostic criteria do not permit a diagnosis of IBD to be made (WASA. 2010. J Vet Intern Med. 24: 10-26). The severity of clinical signs does not always correspond to the degree of inflammatory cell infiltrates (Jergens et al. 2003. J Vet Intern Med. 17: 291-7).

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Histologic Description:

Examined on one slide are 3 sections of liver, location otherwise specified, of excellent diagnostic quality. Hepatic architecture is subtly remodeled with vague nodularity to the parenchyma. The nodules are composed of somewhat disorganized cords of hepatocytes with central portal tracts. At the periphery of the nodules, hepatocytes contain moderate to large numbers of red-brown, slightly refractile cytoplasmic granules, palpable with copper mixed with lipofuscin. Numerous nodular aggregates of macrophages that contains similar pigment are scattered between the regenerative nodules ("Copper granulomas" C). Kupffer cells lining the sinusoids often contain large amounts of hemosiderin. Portal tracts are infiltrated by sparse numbers of lymphocytes and a few hemosiderin-laden macrophages. These inflammatory cells do not target bile ducts nor do they breach the limiting plate.

A panel of histochemical stains was assessed to better characterize liver architecture (reticulin), fibrosis (Masson's trichrome) and heavy metal accumulation (Prussian blue for iron and Rhodanine for copper).

Reticulin: The reticulin stain Emphasizes a moderate degree of architectural remodeling with ill-defined nodules of proliferative hepatocytes separated by a narrow zones of parenchymal collapse. The foci of proliferative hepatocytes are mildly expansile, arranged in somewhat disorganized single and double white cords and have a reduction in the reticulin meshwork, compatible with nodular regeneration. Adventitia around large sub-lobular veins is mildly expanded. Portal tracts are also mildly expanded by extracellular matrix that very occasionally form sharp-plated trabeculae that end blindly in the parenchyma.

Mason's trichrome (type I collagen): The trichrome stain Demonstrates very occasional thin bands of central to central bridging fibrosis. Mild sinusoidal dilatation with a somewhat spotty distribution is also appreciated. No dissecting fibrosis, no necrotic hepatocytes and no bile retention are observed.

Prussian blue (iron): The Prussian blue Shows all hepatocytes contain moderate to large amounts of iron. Hepatocytes are devoid of stainable iron. Small amounts of iron are occasionally detected within the "copper granulomas".

Rhodanine (copper): The rhodanine stain For copper shows an estimated 2-thirds of the hepatocytes contain moderate to large numbers of coarse copper granules. Granules are more numerous in hepatocytes at the periphery of the regenerative nodules. Abundant copper is present within the macrophages of the copper granulomas between the regenerative nodules. These results correspond to a grade 4 out of 5 on a semiquantitative scale where grade 0 indicates no stainable copper and grade 5 corresponds to pan lobular copper accumulation.

Slides 2-4. Small intestine. Writing on the cassette is illegible and it cannot be determined which section corresponds to duodenum, jejunum and ileum. All sections of excellent diagnostic quality and have similar changes. The crypt villous ratio is estimated at 1:2 (within normal limits). The villi are lined by a uniform layer of columnar epithelial cells with a prominent brush border. The number of goblet cells varies between sections but is judged to be within normal limits. The lamina propria is infiltrated by small to moderate numbers of lymphocytes accompanied by a few large granular lymphocytes and rare plasma cells. Lacteals are within normal limits. The crypts are subtly splayed apart by very mild edema and a very mild increase in the number of plasma cells accompanied by a few eosinophils. An increased number of eosinophils accumulates beneath the base of the crypts forming a band up to 8 cells wide. The submucosa, muscularis and serosal layers are within normal limits.

Gross Submission Notes:

Gross description and trimming notes are available upon request.

NOTE: (12/14/2021) Cornell University, due to a surge of COVID-19 amongst its students, halted most educational activities. This does not affect AHDC operations. THE AHDC IS OPEN with regular business hours. Please see Holiday hours at <https://www.vet.cornell.edu/animal-health-diagnostic-center>

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