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Pathology

Necropsy - Companion & Exotic Animals

Gross Pathology

A 5.6-kg, 15-week-old, male intact, Vizsla dog with a history of lethargy, decreased appetite, dietary indiscretion, vomiting, and sudden death was submitted for necropsy. Other in-contact dogs were reported to have died suddenly and to have had clinical evidence of cardiomyopathy prior to death. The body condition score was 3/5, and the postmortem autolysis was moderate. The oral mucous membranes were mottled dark red, purple, and pink.

The thoracic cavity contained 15-20 ml of serosanguineous fluid. The left ventricular and septal myocardium had two, 3.0 x 2.5 cm and 1.2 cm x 0.5 cm, pale tan-yellow areas on cut surface. Within the endocardium of the right and left ventricle were similar, 0.5 cm to 1 cm in diameter, irregularly shaped, subvalvular, pale tan to yellow fouls. The lungs were diffusely mottled purple and red, had rib impressions on the pleural surface, and oozed serosanguineous fluid on cut surface. The trachea diffusely contained 5-10 ml of serosanguineous fluid, and the mucosa was diffusely reddened. The left and right thyroid glands were bilaterally enlarged and measured 3 x 1.2 cm x 2.5 x 1 cm, respectively.

The peritoneal cavity contained 5-10 ml of serosanguineous fluid. The liver was diffusely dark red-brown and oozed blood on cut surface. The stomach contained abundant partially digested ingesta. The duodenum and ileum contained a scant amount of thick yellow material. The jejunum contained scant amounts of yellow-brown liquid. The cecum and colon contained a large amount of soft, green-brown material.

Histopathology

Heart: In sections of left ventricle, up to 60% of the myocardium is obscured and effaced by multifocal to coalescing inflammatory foci composed of high numbers of lymphocytes, with fewer plasma cells, occasionally admixed with degenerate neutrophils, pyknotic and karyorrhectic cellular debris, edema, and hemorrhage, along with high numbers of fibroblasts and variable amounts of collagen. In one section of left ventricle, high numbers of similar inflammatory cells, edema, and hemorrhage, focally extend into and line the endocardium. Also in this section, subendocardial myocardium is locally replaced by a thick band of occasionally myxomatous granulation tissue. Within areas of inflammation and/or fibrosis, cardiomyocytes are atrophied, degenerate to necrotic, characterized by sarcoplasmic thinning, fragmentation, vacuolation, to rare hyper eosinophilia, with loss of cross-striation. In less affected areas of the left ventricle, occasional, there is multifocal loss of cardiomyocytes, and small groups of cardiomyocytes are degenerate to necrotic, with sarcoplasmic mineralization and surrounded by rare lymphocytes and satellite cells.

Within the right atrial subendocardial myocardium, occasional, small groups of cardiomyocytes have
Histopathology

large, intrasarcoplasmic clear vacuoles and/or sarcoplasmic hyper eosinophilia, with loss of cross-striation, and are occasionally surrounded by lymphocytes. Purkinje cells in this area are also markedly vacuolated.

Lungs: There is diffuse, moderate, intra-alveolar and perivascular edema. Alveoli also contain occasional fibrin, hemorrhage, and moderately increased numbers of alveolar macrophages. In one section, blood vessels are rarely surrounded by or associated with small numbers of lymphocytes and macrophages, occasionally forming aggregates.

Liver: There is diffuse, marked congestion. Centrilobular hepatocytes are mildly atrophied and contain fine, intracytoplasmic clear vacuoles (hydropic degeneration).

Spleen: Lymphoid follicles have prominent germinal centers.

Mesenteric lymph nodes: Lymphoid follicles have prominent germinal centers, and interfollicular lymphocytes are mildly depleted. With one lymph node, cortical lymphoid follicles are mildly depleted of lymphocytes.

Thymus: Multiple thymic lobules contain abundant hemorrhage.

Stomach: The mucosa multifocally contains rare, small aggregates of lymphocytes.

Small and large intestine: The lamina propria multifocally contains small numbers of lymphocytes and plasma cells.

The kidneys, adrenal glands, pancreas, thyroid glands, and brain have no significant tissue alterations.

Diagnosis

Heart: Myocarditis and mural endocarditis, lymphoplasma cellular and supplicative, chronic-active, multifocal, marked, with myocardial necrosis, mineralization, and fibrosis

Liver: Centrilobular congestion, degeneration and atrophy, acute

Lung: Severe pulmonary edema and fibrous alveolitis

Mild hydrothorax and ascites

Comments

The most significant finding and likely cause of death in this dog is the severe chronic-active myocarditis and endocarditis causing heart failure as evidenced by the pulmonary edema, centrilobular changes in liver, and hydrothorax and ascites. An infectious etiology is suspected given the inflammatory nature of the heart lesion and history of sudden death in multiple in-contact dogs. The concurrent endocarditis in this dog suggests that a bacterial etiology (such as Bartonella sp., Proteobacteria, Yersinia enterocolitica, Borrelia burgdorferi) may be more likely in this case. With viral (canine parvovirus-2, West Nile virus), fungal, or protozoal (Trypanosoma cruzi, Toxoplasma gondii, Neospora caninum, Hepatozoon americanum) agents representing possible, though less likely differentials. In this dog, the lesions appear confined to the heart, and there is no evidence of bacterial, fungal, or protozoal organisms by routine or gram-stain in the examined sections.

Immunohistochemistry for canine parvovirus-2 (CPV-2) was performed in order to rule out the possibility of the cardiac form of CPV-2 and was negative. This form is typified by non-suppurative myocarditis (ranging from lymphocytic to histiocytic, with fibrosis and granulation tissue), which was seen in this dog, and has been reported in dogs of up to 5 months of age, making it an important differential to consider in this case. It is possible, given the chronicity of the lesion, that viral antigen was no longer present which could explain the negative results on immunohistochemistry.

Immunohistochemistry for Bartonella sp. may be valuable in this case and can be ordered through
Necropsy - Companion & Exotic Animals

Comments
our laboratory, at an additional cost, if desired.

Additional special stains are pending in order to visualize possible bacterial organisms; results will follow in an addendum.


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Addendum

Comments
Additional special stains did not reveal bacterial organisms within sections of heart.

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ADDENDUM 2

Comments
PCR was performed on formalin-fixed, paraffin-embedded sections of heart tissue and was negative for canine parvovirus-2, suggesting that infection due to this viral agent is unlikely. Further testing, such as PCR for Bartonella henselae, can be performed, if desired, through our diagnostic laboratory, at an additional cost.
Though a specific causative agent is currently undetermined, the nature of the inflammation is highly
ADDENDUM 2

Comments
suggestive of a bacterial infection, and less likely an acute viral disease. These changes are, however, not typical of a drug toxicity. This animal was administered Trifexis, and although there is concern from the owner that a drug-associated toxicity may have led to the changes noted histologically and acute death of this puppy as well as other puppies, cardiotoxicity has not been reported as a side-effect in clinical trials for this drug or anecdotally. The follow adverse reactions have been reported with Trifexis: lethargy, inappetence, seizures, blindness, vomiting, diarrhea, pruritus, dermatitis, and skin reddening. Vomiting and subsequent acute death have been reported anecdotally with some frequency, and common necropsy lesions include liver and kidney disease.

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Molecular Biology

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Reported By
Sarah Bales, Lab Technician III
Report Date
2013-10-29
Test Interpretation

Results authorized by Dr. Susan Sanchez, Section Head.