A 3-month-old male mixed-breed dog was submitted for necropsy. The puppy was in an animal shelter with 4 other dogs and died suddenly 2 days after being found as a stray. The other dogs did not develop any evidence of clinical disease.

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The dog died during the night with no previous clinical signs, and therefore no physical examination was performed by the referring veterinarian. Grossly, the carcass had mild autolysis and weighed 2.7 kg (5.9 lb). The oral and ocular mucosal surfaces as well as the subcutaneous tissues and skeletal muscles were all markedly pale. The thoracic cavity was completely filled with 25 to 30 mL of blood, and the lungs were diffusely small and red because of compressive atelectasis (Figure 1). Expanding the thymus and adjacent fibroadipose tissue, there was a dark red and gelatinous hematoma that extended multifocally through the esophageal serosa. No other areas of hemorrhage were observed in other organs. The small intestine contained small amounts of yellow semifluid material and a few cestodes morphologically consistent with *Dipylidium caninum*.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →
Histopathologic and Toxicological Findings

Various tissue samples were collected for histologic examination, including samples of the thymus, mediastinal lymph nodes, and lungs. Microscopically, there were extensive areas of hemorrhage primarily expanding the thymic capsule and interlobular septa but also extending into the thymic cortex and medulla and adjacent fibroadipose tissue (Figure 2). Hemorrhage was admixed with large amounts of fibrillar eosinophilic material (fibrin), edema fluid, and neutrophils and macrophages with fewer lymphocytes and plasma cells. Hemorrhagic foci throughout the cortex and medulla contained extensive accumulations of nuclear debris resulting from lymphoid necrosis (Figure 3). The mediastinal lymph nodes contained extensive areas of accumulations of neutrophils and macrophages with cytoplasmic erythrocytes and nuclear debris. Pulmonary alveolar spaces were diffusely collapsed as a result of atelectasis. Frozen samples of gastric contents and liver tissue were tested for anticoagulant rodenticides.

Toxicological analyses were completed at the Michigan State University Diagnostic Center for Population and Animal Health, East Lansing, Mich, by means of a high-performance liquid chromatography screening procedure. The method of Chalermchaikit et al1 was used. In brief, 2 g of the sample (liver tissue or stomach contents) was extracted with acetonitrile followed by solid-phase cleanup. Identification and quantitation of 10 anticoagulant rodenticides were achieved by reverse-phase separation with both UV and fluorescence detectors (acidic chromatography and basic chromatography) in tandem to provide primary and confirmatory analysis. Detection limits per sample were 0.002 mg/kg (0.0009 mg/lb) for brodifacoum; 0.02 mg/kg (0.009 mg/lb) for bromadiolone, coumachlor, coumatetralyl, difenacoum, and warfarin; 0.07 mg/kg (0.03 mg/lb) for difethialone; 0.20 mg/kg (0.091 mg/lb) for chlorphacinone and diphacinone; and 1.0 mg/kg (0.45 mg/lb) for coumafuryl. Brodifacoum was detected in both samples, with concentrations of 0.028 mg/kg (0.013 mg/lb) in the gastric contents and 1.180 mg/kg (0.5364 mg/lb) in the liver.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: diffuse, severe thymic hemorrhage, with secondary hemothorax and secondary pulmonary atelectasis and extensive, mild catarrhal enteritis with multiple cestodes (*Dipylidium caninum*).

Case summary: thymic hemorrhage secondary to anticoagulant rodenticide toxicosis in a dog.

Comments

Severe thymic hemorrhage or thymic hematoma is a well-recognized and highly fatal condition that has been reported most commonly for young dogs.2–14 Many affected dogs die suddenly because of hypovolemic shock secondary to massive mediastinal hemorrhage.2,5–9 No clinico-pathologic data were available for the dog of this report, although the marked pallor observed in multiple organs during necropsy was consistent with anemia, most likely secondary to hypovolemic shock as a result of massive blood loss into the...
thymus and thorax. The mild intestinal cestodiasis was considered an incidental finding in this case.

Thymic hemorrhage in dogs has been associated with a wide variety of causes, including physical trauma to the thorax, excessive pulling on a dog’s collar, rupture of dissecting aortic aneurysms, underlying neoplasia such as thymic lymphoma or thymoma, and ingestion of anticoagulant rodenticides.5,10,11,13,15 In addition, cases of spontaneous thymic hemorrhage with no evident cause have also been reported.4,6–8,12,14,17 The proposed underlying mechanisms for the development of fatal thymic hemorrhage in these idiopathic cases rely on the assumption that thymic involution was developing in affected dogs before the onset of hemorrhage.12,14,17 Thymic involution is a physiologic process that begins with puberty, which occurs between 6 and 12 months of age in dogs.3 Thus, it is hypothesized that a regressing thymus containing a fragile, thin-walled vascular bed that lacks support from the adjacent fibroadipose tissue might be predisposed to fatal hemorrhage after a sudden increase in blood pressure or even after a minor traumatic event.4,17 Morphologic evidence of thymic involution includes depletion of cortical lymphocytes, replacement of the parenchyma by adipose tissue, and an increase in the number of thymic corpuscles.7 The age of the dog of this report indicates that it had not reached puberty at the time of death. Moreover, no evidence of thymic regression was observed in the multiple examined sections of thymus. Thus, the lack of morphologic evidence for thymic regression and the absence of trauma or other gross and microscopic abnormalities that could be associated with severe thymic hemorrhage warranted toxicologic screening for anticoagulant rodenticides. The presence of toxic concentrations of brodifacoum in the gastric contents and liver tissue confirmed the diagnosis of fatal thymic hemorrhage secondary to anticoagulant rodenticide toxicity in this dog.5,10,11,13,15

Anticoagulant rodenticide toxicosis is a fairly common problem in dogs and has been associated with either disseminated hemorrhages9–11 or localized fatal thymic hemorrhage1 similar to that observed in the dog of this report. First-generation anticoagulant rodenticides (eg, warfarin and dicumarol) contain small amounts of their active compound and therefore are usually associated with low risk of toxic effects following ingestion of a single dose. However, second-generation anticoagulant rodenticides (eg, diphenacine and brodifacoum) have enhanced toxicity and contain a high concentration of their toxic substance.4,10,13,15,16 Brodifacoum has been reported as highly toxic after ingestion, with an LD₅₀ of 0.25 to 3.5 mg/kg (0.11 to 1.6 mg/lb) for dogs.16 Following oral absorption, brodifacoum strongly binds to plasma proteins within approximately 12 hours, and it is metabolized in the liver and excreted through the urine.16 The mechanism of action of anticoagulant rodenticides involves the inhibition of hepatic vitamin K–epoxide reductase, with consequent decreased synthesis of clotting factors II, VII, IX, and X.9–11 Because vitamin K and its dependent clotting factors are progressively consumed without replacement by the animal, the clinical signs of poisoning are delayed for a few days following exposure to the toxic substance.16 The dog of the present report was the only one that died in a group of 4 other dogs in the same environment, and it had been caught as a stray 2 days before death. Thus, it is most likely that this puppy was exposed to the anticoagulant rodenticide before it arrived at the animal shelter.

Similar to the features of the case described in this report, sudden death due to massive internal bleeding is very common in cases of anticoagulant rodenticide toxicosis in dogs.5 However, clinical signs including dyspnea, lethargy, pallor, hemoptysis, epistaxis, melena, lameness due to hemarthrosis, and disseminated hemorrhages may also develop.10 Typical clinicopathologic abnormalities in affected dogs reflect disorders in the intrinsic, extrinsic, and common coagulation systems, with prolonged activated partial thromboplastin time (intrinsic and common systems), prolonged prothrombin time (extrinsic and common systems), and prolonged activated clotting time (intrinsic and common systems).11,16 In addition, thrombocytopenia, prolonged thrombin clotting time, and fibrin-fibrinogen degradation products may develop after severe internal bleeding has occurred.10,16 Necropsy findings are usually evident and may include pallor with disseminated or localized hemorrhages mainly in the thoracic and abdominal cavity.9–11 Although fatal thymic hemorrhage in dogs can occur with no apparent cause, examination for evidence of thymic involution and screening of fresh samples of gastric contents and liver tissue for anticoagulant rodenticides may contribute to a final diagnosis.9,10,11,13,15,16

References