Anicteric gallbladder rupture in dogs: 5 cases (2007–2013)

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Objective—To describe clinical, laboratory, and surgical findings in dogs with confirmed gallbladder rupture and in which serum total bilirubin concentration was within reference limits.

Design—Retrospective case series.

Animals—5 dogs.

Procedures—Medical records were searched to identify dogs with gallbladder rupture that underwent treatment at the Kansas State University Veterinary Health Center from November 2007 through November 2013. Dogs were included if they had undergone abdominal ultrasonography, serum total bilirubin concentration was ≤ 0.4 mg/dL, and abdominal exploratory surgery confirmed the presence of gallbladder upture.

Results—An exploratory celotomy was performed in all dogs because of ultrasonographic findings of mild to marked abdominal effusion and either an unidentifiable gallbladder (n = 1 dog) or a distended gallbladder with a suspected gallbladder mucocele (4 dogs). Serum total bilirubin concentration was within reference limits (median, 0.2 mg/dL; range, 0.1 to 0.4 mg/dL; reference range, 0.1 to 0.4 mg/dL) in all dogs before surgery. In 1 dog, bile acids concentrations in serum and in peritoneal fluid were compared and the results (48 µmol/L and 1,070 µmol/L, respectively) were supportive of the diagnosis of gallbladder rupture.

Conclusions and Clinical Relevance—Results indicated that even when serum total bilirubin concentration is within reference limits, gallbladder rupture should be considered in dogs with acute signs of abdominal pain when a mucocele is suspected on abdominal imaging and free abdominal fluid is present. Results suggested that a comparison of serum to peritoneal fluid bile acids concentrations may provide additional support for a diagnosis of gallbladder rupture. (*J Am Vet Med Assoc* 2015;247:1412–1414)

Gallbladder rupture is a surgical emergency, and diagnosis of this disease must be rapid and accurate. Ultrasonography is neither 100% sensitive nor 100% specific for the diagnosis of gallbladder rupture; therefore, a need for confirmato y testing is evident.[1–3] Clinicopathologic abnormalities associated with gallbladder or biliary tract disease include high serum alanine aminotransferase activity, alkaline phosphatase activity, and total bilirubin concentration. Furthermore, high serum total bilirubin concentration is traditionally considered the hallmark of biliary tract disease.[3] Gallbladder rupture without the presence of high serum total bilirubin concentration has been reported but with a low incidence and lack of detail on clinical evaluation.[4–9]

The purpose of the study reported here was to describe clinical, laboratory, and surgical findings in dogs with surgically and histologically confirmed gallbladder rupture, free abdominal fluid, serum total bilirubin concentration within reference limits, and no apparent icterus that were evaluated at a veterinary teaching hospital.

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Materials and Methods

Case selection—Electronic veterinary medical records were searched to identify all dogs evaluated at the Kansas State University Veterinary Health Center between January 1, 2007, and December 31, 2013, that had a confirmed diagnosis of gallbladder rupture. Dogs were included in this retrospective study if an abdominal ultrasonographic examination was performed prior to surgery that documented the presence of abdominal effusion, if total serum bilirubin concentration was ≤ 0.4 mg/dL (laboratory reference range, 0.1 to 0.4 mg/dL), and if there was surgical confirmation of gallbladder rupture during exploratory laparotomy.

Medical records review—Electronic and hard copy medical records were reviewed, and information on breed, age, sex, reproductive (neuter) status, and body weight was recorded. Other information collected from the record included history, physical examination findings, clinicopathologic data (results of CBC, serum biochemical analysis, and peritoneal fluid analysis), diagnostic imaging (abdominal radiography and ultrasonography performed and reviewed by a board-certified veterinary radiologist) and surgical findings, results of microbial culture of peritoneal fluid and gallbladder tissue samples, histopathologic data (reviewed by a veterinary clinical pathologist), and outcome. Follow-up

information was obtained from the medical records and by contacting the dog owners. Descriptive statistics (mean, median, and range) were calculated for age, body weight, and clinicopathologic data.

Surgical procedures—All dogs underwent cholecystectomy by use of a standard open approach, as previously described.[10] Liver biopsies were performed at the time of exploratory laparotomy. Anesthetic protocols, perioperative analgesia, and antimicrobials were administered at the discretion of the attending clinician.

Results

Dogs—Records of 9 dogs that had gall bladder rupture were identified over the 7-year study period. Of these 9, 4 were excluded: 3 because of the presence of hyperbilirubinemia and 1 because of an incomplete minimum database. Five dogs met the criteria for study inclusion (2 spayed females and 3 castrated males). The breeds included mixed (n = 2), Pomeranian (1), Shetland Sheepdog (1), and Bichon Frise (1). Mean age at the time of diagnosis was 10 years (median, 10 years; range, 8 to 12 years). Mean and median body weights were 15.3 and 14 kg (33.7 and 30.8 lb), respectively.

History and physical examination finding —One patient was referred by a primary care veterinarian for evaluation of signs of abdominal pain. The remaining 4 dogs were seen on an emergency basis because of vomiting (n = 2 dogs), lethargy (2), and anorexia (2). All patients had clinical signs present for ≤ 72 hours prior to examination at the veterinary teaching hospital (median, 24 hours; range, 12 to 72 hours) and had signs of abdominal pain on initial physical examination, as determined by annotations indicating reaction to cranial abdominal palpation (n = 5 dogs) and hunched posture in the medical record (2 dogs). High body temperature was noted in the records of 2 dogs (39.7° and 39.2°C [103.5° and 102.7°F]; reference range, 37.2° to 39.16°C [99° to 102.5°F]. Panting was noted for 2 dogs. None of the patients had evidence of icterus on physical examination.

Clinicopathologic data—A CBC and serum biochemical analysis were performed for all patients at hospital admission. The most common abnormalities on CBC included leukocytosis (median, 26.5 × 10^3 WBCs/µL; range, 20.4 × 10^3 WBCs/µL to 28.5 × 10^3 WBCs/µL; reference range, 6 × 10^3 WBCs/µL to 17 × 10^3 WBCs/µL), which was present in all 5 dogs, with a high band neutrophil count (median, 0.4 × 10^3 band neutrophils/µL; range, 0 × 10^3 band neutrophils/µL to 0.8 × 10^3 band neutrophils/µL; reference range, 0 × 10^3 band neutrophils/µL to 0.3 × 10^3 band neutrophils/µL) in 3. All 5 patients also had lymphopenia (median, 0.8 × 10^3 lymphocytes/µL; range, 0.6 × 10^3 lymphocytes/µL to 1.4 × 10^3 lymphocytes/µL; reference range, 1.5 × 10^3 lymphocytes/µL to 5 × 10^3 lymphocytes/µL) and monocytosis (median, 1.9 × 10^3 monocytes/µL; range, 1 × 10^3 monocytes/µL to 3.4 × 10^3 monocytes/µL; reference range, 0.1 × 10^3 monocytes/µL to 0.8 × 10^3 monocytes/µL). One patient had a high Hct (64%; reference range, 37% to 55%), hemoglobin concentration (21.3 g/dL; reference range, 12 to 18 g/dL), and erythrocyte count (10 × 10^6 RBCs/µL; reference range, 5.5 × 10^6 RBCs/µL to 8.5 × 10^6 RBCs/µL), which was considered consistent with dehydration or possibly normal patient variance.

Abnormal serum biochemical findings included hypoalbuminemia (median, 2.9 g/dL; range [for all patients], 2.2 to 3.4 g/dL; reference range, 3.4 to 4.2 g/dL) in 4 dogs, high alkaline phosphatase activity (median, 1,101 U/L; range, 477 to 2,069 U/L; reference range, 1 to 142 U/L) in 5, high alanine aminotransferase activity (median, 221 U/L; range, 166 to 298 U/L; reference range, 28 to 171 U/L) in 3, and high creatine kinase activity (median, 379 U/L; range, 95 to 6,791 U/L; reference range, 128 to 328 U/L) in 3. Notably, the serum total bilirubin concentration was within the reference range for all 5 dogs (median, 0.2 mg/dL; range, 0.1 to 0.4 mg/dL; reference range, 0.1 to 0.4 mg/dL).

Diagnostic imaging finding —Abdominal radiographic images obtained prior to surgery (n = 2 dogs) showed decreased serosal detail in both dogs and no other pertinent findings. Ultrasonographic findings included a mild to moderate amount of abdominal effusion either throughout the abdomen (n = 4) or focally near the liver (1). A round, hypoechoic, stellate structure was also visualized either within the gallbladder (n = 4 dogs, each with a subjectively distended gallbladder) or free within the abdomen (in 1 dog with no identifiable gall bladder seen during an ultrasonographic examination). Peritoneal fluid analysis was performed for 2 dogs. The fluid obtained from both patients was an exudate type with a bilirubin concentration of 0.4 mg/dL (serum total bilirubin concentration in these patients was 0.1 and 0.4 mg/dL). Abdominal fluid of one of these dogs was tested for the presence of bile acids, and the fluid concentration of these products was substantially greater at 1,070 µmol/L, compared with a serum bile acids concentration of 46 µmol/L on the same day.

Surgical and histologic finding —Gallbladder rupture was confirmed during laparotomy in all 5 dogs. One dog had a liver nodule found during laparotomy. Histologic evaluation of the liver nodule from this patient revealed periportal inflammation with mild multifocal vacuolar degeneration. The remaining 4 dogs had otherwise unremarkable abdominal exploratory surgeries, except for the gallbladder rupture and secondary bile peritonitis. All patients, regardless of gross appearance of the liver at the time of surgery, had liver biopsies performed. Bacteriologic culture of abdominal fluid samples yielded no growth in 4 dogs and was positive for a *Streptococcus* sp and an *Actinomyces* sp in 1 dog. Histologic evaluation (n = 5 dogs) of the gallbladder revealed evidence of gallbladder necrosis in 4 dogs and fibrinolytic, suppurative cholecystitis in 1 dog. Histologic evaluation of the liver biopsy samples revealed mild to moderate periportal inflammation, with bile stasis in all 5 patients and mild vacuolar degeneration in 1 dog.

Outcomes—Four of the 5 dogs survived to discharge from the hospital. One patient, a 12-year-old neutered male Shetland Sheepdog, developed acute respiratory distress and was euthanized because of declining clinical condition. Two patients were lost to follow-up. One patient was euthanized 2 years later for reasons un-

related to the gallbladder rupture. One dog was alive at the time of the study and reportedly doing well with no complications related to gallbladder rupture.

Discussion

This retrospective case series included 5 dogs with gallbladder rupture, mild to moderate abdominal effusion, and serum total bilirubin concentrations within reference limits. All dogs described in this report had free abdominal flui detected during an ultrasonographic examination and surgically confirmed gallbladder rupture. Although hyperbilirubinemia is typically considered a key part of the diagnosis in patients with biliary disease,[5] results of this case series show that patients can have a ruptured gallbladder without evidence of icterus, with serum total bilirubin concentrations within reference limits, and with unremarkable peritoneal fluid bilirubin concentration (< 2 times the concentration in serum).

Gallbladder mucocele is a disease that has been recognized with increasing frequency in veterinary medicine.[1,3,4] It can be a cause of morbidity or a benign, incidental fin - ing.[1,3,4] On ultrasonography, the classic appearance of a gallbladder mucocele is characterized by immobile, echogenic bile with a finely striated or stellate pattern within the lumen of the gallbladder.[2] The pathogenesis of gallbladder mucoceles is unknown.[3,11] In cases of gallbladder rupture or leakage, bile that is released into the abdomen contains concentrated bile acids and bilirubin. Abdominal fluid analysis can be a key component to diagnostic evaluation of any patient with signs of abdominal pain and free fluid on abdominal ultrasonography.[3,11] Interestingly, when the abdominal fluid from 2 dogs in this report was analyzed with standard methodology (reporting total nucleated cell count, protein, and cytologic descriptions), a diagnosis of gallbladder rupture was not made. Furthermore, analysis of the total bilirubin concentration of abdominal fluid was not helpful in achieving a diagnosis of ruptured gallbladder in these patients. However, when a bile acids assay was performed retrospectively on the abdominal fluid from 1 dog, the concentration was markedly increased, compared with the serum bile acids concentration from the same dog on the same day, which would have been confirmato y for gallbladder rupture in that case. This patient had a peritoneal fluid bilirubin concentration of 0.4 mg/dL.

Bilirubin presumably diffuses freely across the peritoneum, and other contents found in bile (eg, cholesterol) would be insensitive for testing, leaving bile acids as a logical choice for testing of abdominal fluid in patients with suspected biliary rupture.[3,11] Anicteric gallbladder rupture may occur in patients with serum total bilirubin concentrations within reference limits and should be considered a distinct entity from bile duct rupture. With gallbladder rupture, the common bile duct is not disturbed, and bile can still form in the liver and be transported to the intestines for excretion. This may result in sufficient elimination to prevent hyperbilirubinemia. Bile that traverses through the cystic duct and into the ruptured gallbladder would then enter the peritoneal cavity, where the freely diffusible elements are rapidly returned to the blood and then to the liver for elimination. Those components of bile that are not freely diffusible, such as bile acids, would then gradually accumulate in greater quantities and concentrations in the peritoneal fluid. Considering the markedly discordant values in serum and peritoneal bile acids concentrations in the 1 dog in which both were evaluated, further evaluation of the bile acids gradient seems warranted in the diagnosis of anicteric gallbladder rupture. Given that this comparison is simple to perform on fluids that would have already been collected, clinicians should consider evaluating the bile acids gradient in cases where gallbladder rupture is suspected and results of fluid analysis for bilirubin are confounding or not confirmato y.

Four of the 5 dogs described in the present report had evidence of gallbladder necrosis, and 1 dog had evidence of fibrinolytic, suppurative cholecystitis on histologic evaluation. Although the number of dogs in this study was extremely small, on the basis of histopathologic findings in these cases, pressure necrosis secondary to gallbladder mucocele presence is considered a possible mechanism for gallbladder rupture, and this hypothesis has been described previously.[4,7,8] Because the prevalence of gallbladder mucocele is reportedly increasing in canine patients, further exploration into the pathogenesis of mucoceles and gallbladder rupture without bile duct obstruction is needed in veterinary medicine.[2,4,8,12]

The findings of this case series suggested that hyperbilirubinemia and high concentrations of bilirubin in abdominal fluid contents are not necessarily present in dogs with gallbladder rupture. Furthermore, our results suggested that testing of abdominal fluid for bile acids may be indicated in some cases in which a diagnosis remains challenging or elusive. Additional studies are needed to further evaluate the diagnostic value of abdominal fluid bile acids measurement prospectively in a larger number of patients.

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