**Nonsurgical resolution of gallbladder mucocele in two dogs**

Romanie Walter, DVM; Marilyn E. Dunn, DVM; Marc-André d’Anjou, DVM; Manon Lécuyer, DVM

**Case Description**—A gallbladder mucocele was diagnosed in 2 dogs. In both dogs, the mucocele resolved with medical treatment but without the need for surgical intervention.

**Clinical Findings**—A 12-year-old spayed female Miniature Schnauzer had a history of signs of gastrointestinal tract disease and high serum liver enzyme activities. Gallbladder mucocele and hypothyroidism were diagnosed. A 6-year-old neutered mixed-breed dog had chronic intermittent diarrhea and recurrent otitis; gallbladder mucocele and hypothyroidism were diagnosed.

**Treatment and Outcome**—The first dog was treated with S-adenosyl-methionine, omega-3 fatty acids, famotidine, ursodiol, and levothyroxine. Substantial improvement in the gastrointestinal tract condition and complete resolution of the gallbladder mucocele within 3 months were evident, but the dog was not available for further follow-up monitoring. The second dog was treated with fenbendazole, ursodiol, and levothyroxine and fed a hypoallergenic diet. One month after evaluation, abdominal ultrasonography revealed that the gallbladder mucocele was resolving, and treatment was continued. Ultrasonographic evaluation 2 and 4 months later revealed complete resolution of the mucocele.

**Clinical Relevance**—Review of the clinical course of 2 dogs in which there was nonsurgical resolution of gallbladder mucocele revealed that surgery is not necessary in all dogs with gallbladder mucocele. Hypothyroidism may have resulted in delayed gallbladder emptying, and its role in the pathogenesis of gallbladder mucocele merits investigation. Despite this information, until further prospective trials with a control group and standardized treatments and follow-up monitoring can be performed, the authors recommend surgical intervention for treatment of dogs with gallbladder mucocele. (J Am Vet Med Assoc 2008;232;1688–1693)

---

**Abbreviations**

| ALP  | Alkaline phosphatase |
| ALT  | Alanine aminotransferase |
| GGT  | γ-Glutamyltransferase |
| TSH  | Thyroid-stimulating hormone |
| T4   | Thyroxine |

A 12-year-old spayed female Miniature Schnauzer (dog 1) was initially examined by a veterinarian because of intermittent inappetence, vomiting, and diarrhea of 2 months’ duration. During the last 10 days of that 2-month period, clinical signs had increased in frequency, and the owner noticed weight loss. Serum biochemical analyses at the time of initial examination revealed high liver enzyme activities (ALP, 3,320 U/L; reference range, 0 to 200 U/L; ALT, 4,395 U/L; reference range, 0 to 130 U/L; and GGT, 122 U/L; reference range, 0 to 6 U/L) and a high BUN concentration (12.6 mmol/L; reference range, 2.1 to 9.7 mmol/L). The dog was transferred to a referral hospital for abdominal ultrasonography. The ultrasonographic report and review of the digital images of the gallbladder revealed a mucocele that filled approximately 70% of the gallbladder lumen and delineated a smaller amount of immobile and non–gravity-dependent, echogenic, biliary sludge (Figure 1). The mucocele appeared as an interrupted rim of hypoechoic and mildly heterogeneous material that confined the biliary sludge to the central portion of the body of the gallbladder. The gallbladder wall appeared normal, and there was no evidence of common bile duct dilatation or biliary tract rupture. Cytologic analysis of a liver sample obtained via ultrasound-guided fine-needle aspiration was consistent with a vacuolar hepatopathy. Medical treatment was initiated and consisted of administration of S-adenosyl-methionine (20 mg/kg [0.23 mg/lb], PO, q 24 h), omega-3 fatty acids from fish oil (600 mg, PO, q 24 h), and famotidine (0.5 mg/kg [0.23 mg/lb], PO, q 24 h).

After 2 months of treatment, the dog was evaluated at our university veterinary hospital for follow-up consultation. The owner reported that the vomiting and diarrhea had resolved and that the dog had a good appetite. During physical examination, bradycardia and a left-sided grade II/VI systolic heart murmur were detected. Serum biochemical analysis revealed high activities of ALP (1,441 U/L; reference range, 6 to 80 U/L) and ALT (726 U/L; reference range, 4 to 62 U/L). Thyroid hormone and TSH concentrations were indicative of hypothyroidism, with a serum total T4 concentration of 8.1 nmol/L (reference range, 10 to 20 nmol/L) and a TSH concentration of 1.05 ng/mL (reference range, 0 to 0.6 ng/mL). Serum albumin concentration was slightly low at 27 g/L (refer-
ence range, 29.1 to 39.1 g/L), cholesterol concentration was high at 11.18 mmol/L (reference range, 2.85 to 7.76 mmol/L), and triglyceride concentration was high at 3.80 mmol/L (reference range, 0.57 to 1.14 mmol/L).

Abdominal ultrasonography performed by a board-certified veterinary radiologist revealed a diffusely enlarged and heterogeneous liver with ill-defined, faint, hyperechoic and hypoechoic foci. The gallbladder was distended, with a moderate volume of immobile echogenic sludge occupying approximately 40% of the lumen. A hypoechoic, irregular, and interrupted rim was observed at the periphery of the sludge, particularly in the region of the gallbladder neck, consistent with the stellate pattern of a mucocele (Figure 1). The mucocele appeared smaller than during the initial examinations, and fissures between mucus fragments were wider. The gallbladder wall had a normal appearance, and there was no evidence of common bile duct dilatation or biliary edema.

The owners were advised to continue administration of the S-adenosyl methionine and omega-3 fatty acids. In addition, ursodiol (13 mg/kg [5.91 mg/lb], PO, q 24 h), amoxicillin (22 mg/kg [10 mg/lb], PO, q 12 h for 7 days), levothyroxine (0.02 mg/kg [0.01 mg/lb], PO, q 12 h), and a low-fat, low-protein diet were prescribed.

Three months later, the dog was returned to the university hospital because of partial inappetence of 1 week’s duration. The dog was still receiving levothyroxine, ursodiol, S-adenosyl methionine, and omega-3 fatty acids and was consuming a prescription diet. Serum biochemical analysis revealed ALP activity to be high (419 U/L) and ALT activity to be slightly high (127 U/L). Blood urea nitrogen concentration was also slightly high (13.35 mmol/L; reference range, 2.10 to 7.91 mmol/L). Ultrasonography revealed that the liver parenchyma remained heterogeneous in appearance and contained several small hyperechoic nodules; mild accumulation of biliary sludge in the gallbladder neck was also seen, but there was no sign of the mucocele. In fact, the sludge was mobile and gravity dependent and filled the lumen of the gallbladder neck by the end of the exami-
nation (Figure 1). The gallbladder wall was thicker (0.35 cm) than it had been during previous examinations, and the structure had a double-layered pattern, which could have indicated edema, cholecystitis, or both. Hepatic biopsy, bacterial culture of the bile duct, and antimicrobial treatment were recommended. The owner elected not to pursue further treatment or diagnostic testing, and the dog was discharged with recommendations for the owner to continue the same medications. The dog was subsequently unavailable for follow-up monitoring.

A 2-year-old castrated male mixed-breed dog (dog 2) was evaluated at our university veterinary hospital because of vomiting and diarrhea of 3 months’ duration. Treatment with intestinal mucosal protectants, antimicrobials, and a gastrointestinal prokinetic agent had been prescribed by the referring veterinarian but had yielded little improvement. At admission to our facility, no abnormalities were detected. Abdominal ultrasonography revealed an obstructive foreign body in the pylorus. The remainder of the results of the ultrasonographic examination, including assessment of the gallbladder, was unremarkable. Exploratory celiotomy was performed, and a foreign body was removed via gastrotomy. The gallbladder was not mentioned in the surgical report.

Four years later, dog 2 was evaluated again at our university hospital because of intermittent chronic diarrhea, a recent episode of which had been associated with hematochezia. For the preceding 2 years, the cause of the diarrhea had been investigated by the referring veterinarian, who had also treated the dog. Results of coprologic examinations performed by the referring veterinarian had been negative for parasites, whereas bacterial culture of feces had yielded a strong growth of hemolytic Escherichia coli and overgrowth of Clostridium perfringens. Treatments included several courses of sucralfate (0.5 g, PO, q 8 to 12 h), metronidazole [10 mg/kg ([4.5 mg/lb], PO, q 24 h), fenbendazole [50 mg/kg ([22.73 mg/lb], PO, q 24 h for 5 days), and amoxicillin-clavulanic acid [19 mg/kg ([8.64 mg/lb], PO, q 12 h for 3 weeks). Diarrhea recurred within a few weeks after discontinuation of each treatment.

At the time of evaluation at our university veterinary hospital, results of physical examination were unremarkable. Serum biochemical analyses revealed hypercholesterolemia (10.55 µmol/L; reference range, 2.85 to 7.76 µmol/L). A CBC revealed eosinophilia (1.10 ng/mL). Abdominal ultrasonography was unremarkable. Serum total T4 concentration was determined (62.8 nmol/L), and iatrogenic hyperthyroidism was diagnosed. On follow-up abdominal ultrasonography by the same examiner, the gallbladder was smaller and contained less echogenic sludge and a resolving mucocele (Figure 2). Mucus was evident only at the level of the gallbladder neck. The hepatic cyst-like lesion had increased in size. Results of serum biochemical analysis were within respective reference ranges. It was recommended to continue feeding the hypoallergenic diet and treatment with ursodiol but to decrease the dosage of levothyroxine to 0.01 mg/kg (0.0045 mg/lb), PO, every 12 hours.

The dog was reevaluated 2 months later. At that time, serum total T4 concentration was within the reference range (22.7 nmol/L), and abdominal ultrasonography revealed biliary sludge but no gallbladder mucocele. The hepatic cyst-like lesion was unchanged in appearance. Continued treatment with ursodiol and levothyroxine was recommended.

Another evaluation was performed 2 months later. Abdominal ultrasonography of the liver revealed a small volume of biliary sludge, no recurrence of gallbladder mucocele, and a stable hepatic cyst-like lesion. Continued administration of ursodiol and levothyroxine was recommended.

Three months later, the dog was examined at our university veterinary hospital because of dysorexia, vomiting, and polyuria and polydipsia of 2 weeks’ duration. At that time, levothyroxine was being administered, but the owner had stopped administration of the ursodiol 3 months earlier. During that hospital visit, fresh blood was noticed in the dog’s feces, but the remainder of the results of the examination was unremarkable. Urine specific gravity was 1.024, and serum total T4 concentration (17 nmol/L) was within the reference range. Abdominal ultrasonography revealed an irregular band of hyperechoic material in the gallbladder that delineated a hypoechoic area in the region of the gallbladder neck. However, lack of patient cooperation and the presence of gastric gas limited visibility of the gallbladder, which could be only partially assessed via a right-sided intercostal approach. Therefore, recurrence of the mucocele could not be excluded. The dog was discharged, and the owners were instructed to continue administration of levothyroxine. One and a half months later, the dog was returned for abdominal ultrasonography. At that evaluation, the gallbladder appeared normal but...
distended with anechoic bile and a small volume of biliary sludge, but there was no evidence of mucocele (Figure 2).

Discussion

A mucocele is defined as distention of a cavity secondary to abnormal accumulation of mucus. Many terms have been used to describe gallbladder mucocles, including inspissated bile, cystic hyperplasia, mucinous hyperplasia, mucinous cysts, mucosal cysts, cystic mucinous hypertrophy, mucinous cholecystitis, and cystic glandular cholecystitis. Gallbladder mucocles result from dysfunction and proliferation of mucus-secreting cells in the mucosal epithelium of the gallbladder. The underlying cause of this cystic hyperplasia is unknown, and the cause is probably multifactorial. It is probable that deposition of biliary sludge precedes the formation of gallbladder mucocele. Biliary sludge is formed by precipitation of cholesterol crystals, mucin, bile pigments, and bile salts within the gallbladder lumen. This accumulation results from decreased gallbladder motility and increased water reabsorption from the lumen. In approximately 10% of affected dogs, mucocele formation appears to be caused by an impacted stone or mucus, creating an outlet obstruction at the neck of the gallbladder or in the cystic duct. Studies during which cystic duct ligations were experimentally performed failed to induce formation of gallbladder mucocles, although the gallbladders were examined no later than 10 weeks and 3 days after ligation, respectively. Some mucocles have been associated with bacterial infection, usually with a mixed population of E.coli, Staphylococcus spp, Streptococcus spp, Enterobacter spp, Enterococcus spp, or Micrococcus spp. Finally, in 4 studies of gallbladder mucocele in dogs, Cocker Spaniels and Shetland Sheepdogs were overrepresented, which suggests a possible genetic role.
Dogs with gallbladder mucoceles are usually older (10 years of age) and of medium size,\(^1,4\) and both sexes are equally represented. Primary clinical concerns expressed by owners of affected dogs include inappetence (63% to 78.5%), vomiting (72% to 87%), lethargy (41% to 87%), polyuria and polydipsia (0.05% to 36%), and diarrhea (14% to 26.1%).\(^1,5,6\) Approximately 20% of gallbladder mucoceles reported in dogs appear to be incidental ultrasonographic findings.\(^1,5\) Physical examination often reveals signs of abdominal pain (19% to 87%), icterus (18% to 56.5%), fever (23% to 26.1%), and tachycardia (26.1%).\(^2,7,8\) Results of CBCs are usually within reference ranges, although stress leukograms and nonregenerative anemia have been reported.\(^1,4\) Serum biochemical analysis can reveal high activities of ALP, ALT, aspartate aminotransferase, and GGT and high concentrations of BUN, total bilirubin, protein, and total \(T_4\).\(^1,4\) In 1 study, high venous lactate concentrations were always correlated with a ruptured gallbladder.

For many years, gallbladder mucoceles were not considered to be an important cause of extrahepatic biliary obstruction. However, investigators in more recent studies\(^5,8\) suggested that more than half of extrahepatic biliary obstructions are caused by gallbladder mucoceles. This discrepancy may be a result of improvements in ultrasonographic imaging techniques and better recognition of the condition by clinicians.

Ultrasonography is the most useful and sensitive tool for diagnosing gallbladder mucoceles in dogs.\(^1,2\) Gallbladder mucoceles appear ultrasonographically as an immobile accumulation of anechoic-to-hypoechoic material.\(^3\) Immature mucoceles initially have a stellate pattern caused by fracture lines between mucus collections. This pattern can become more evident when delineated by more echogenic, non–gravity-dependent biliary sludge. As a mucocele matures and occupies progressively more of the gallbladder lumen, these fracture lines elongate to form radiating hyperechoic striations that have been described as a kiwi fruit–like appearance.\(^1\) Care must be used so that irregular distributions of anechoic bile and echogenic sludge are not confused with mucocele formation. Sufficient time must be allowed during the ultrasonographic examination to confirm the non–gravity-dependent character of the sludge.

Additional ultrasonographic findings include thickening, hyperechogenicity, or irregularity of the gallbladder wall, although these signs are not good predictors of mucosal hyperplasia.\(^1\) A large gallbladder mucocele may lead to gallbladder rupture, which should be suspected when the wall appears discontinuous and there is evidence of hyperechoic tissue at its periphery. Such ruptures usually are found in the fundic region. In other studies,\(^4,12\) the incidence of rupture ranged from 50% to 60%. The sensitivity, specificity, and positive predictive value of ultrasonography for gallbladder rupture were 85.7%, 100%, and 100%, respectively, in 1 study.\(^1\)

The treatment of choice for dogs with gallbladder mucocele is surgery via cholecystectomy, cholecystotomy, or cholecystoduodenoscopy.\(^1,4,9,11,12\) The perioperative prognosis for dogs that have undergone surgery is guarded, with the mortality rate ranging from 21% to 32%.\(^4,12\) A long-term (2 years) mortality rate of 44% has been reported.\(^8\) Preoperative risk factors for death include increased age; high preanesthetic heart rate; high GGT activity; and high BUN, phosphorus, and bilirubin concentrations.\(^8\) Common surgical complications are pneumonia, pancreatitis, pulmonary thromboembolism, and bile–induced peritonitis.\(^3,8,11\) Postoperative risk factors for death include hypotension, dyspnea possibly secondary to aspiration pneumonia, pulmonary thromboembolism, overhydration or acute respiratory distress syndrome, low serum albumin concentration, high percentage of band cells, and pancreatitis.\(^4,8\) Medical treatment, such as administration of antimicrobials and choleretics, has been attempted, but published results are scarce and do not seem to be favorable.\(^4\)

Both dogs in the present study had hypercholesterolemia. This was similar to findings in another study\(^1\) in which 70% to 72% of dogs with gallbladder mucocele had hypercholesterolemia and 14% had a previous diagnosis of hypothyroidism. In a retrospective study,\(^1\) 23% of dogs with gallbladder mucocele also had hyperadrenocorticism, and 7% were receiving long-term corticosteroid treatment, which suggested that those dogs also may have had hypercholesterolemia.\(^4\) Dogs with gallbladder mucocele and hypercholesterolemia should be evaluated to detect underlying disease (eg, hypothyroidism and hyperadrenocorticism). Finally, it has also been reported that patients with diabetes mellitus and hypothyroidism have delayed gallbladder emptying and may have a tendency to form gallbladder mucoceles.\(^1,13–16\) In humans, rats, and pigs, \(T_4\) has a relaxing effect on the sphincter of Oddi.\(^16,11\) Loss of this relaxing effect in hypothyroid animals may contribute to delayed gallbladder emptying and a higher risk of developing a mucocele.\(^14–17\)

Studies in prairie dogs\(^13\) and humans\(^13\) have revealed a positive correlation between the cholesterol and mucin content of bile and bile viscosity. In addition, prairie dogs fed a diet high in cholesterol had greater cholesterol accumulation in the bile.\(^18\) High bile cholesterol concentration in the gallbladder in turn increases mucin production by the gallbladder mucosa,\(^18\) which leads to a positive reinforcing cycle. Poiseuille’s law states that flow rate is inversely proportional to the viscosity of a given fluid. As the concentration of mucin and cholesterol increases in the gallbladder, these 2 components hydrophobically bind together to form cholesterol monohydrate crystals.\(^18\) The bile becomes more viscous, and evacuation from the gallbladder is delayed.\(^1,18\) This enables more reabsorption of water by the gallbladder mucosa, causing additional concentration of bile acids.\(^1\) Increases in the bile acid concentration in the gallbladder lead to mucosal hyperplasia.\(^4,7\) Mucosal cells release more mucin and increase bile viscosity, so bile evacuation is slowed even more.\(^1,18\) This cycle repeats until the cholesterol crystals and mucin and the increase in viscosity lead to formation of a mucocele.\(^13,19\) All gallbladder tissue submitted for histologic assessment in 2 studies\(^1,13\) had cystic hyperplasia of the gallbladder mucosa. In addition, a study\(^10\) during which the cystic duct was ligated in 18 dogs and a necropsy was performed 3 days later revealed sludge-filled gallbladders and mucus that covered the gallbladder...
mucosa, which contained 1- to 4-mm solid particles. This same finding was reported at days 5, 8, and 14 in prairie dogs fed a high-cholesterol diet, but no signs of obstruction of the cystic or common bile duct were evident. These findings may be suggestive of early mucocele formation.

Information for the dogs reported here has several limitations. Although ultrasonographic imaging is useful and sensitive, histologic analysis of a tissue specimen remains the criterion-referenced standard for diagnosis of a mucocele. Because of the retrospective nature of the report, treatments and evaluations were not standardized and thus were inconsistent between the dogs. Therefore, it is impossible to determine whether correction of the hypothyroidism or other medical management in these 2 dogs had any effect on resolution of gallbladder mucocele. It has been suggested that bacterial culture of bile be performed in all animals with suspected gallbladder mucocele to gain information about potential infectious agents involved in mucocele formation. This was not performed in the dogs reported here because of the potential complications associated with ultrasound-guided aspiration of gallbladder contents. Finally, liver biopsy was not performed in either dog, and underlying liver disease (or the lack thereof) cannot be confirmed.

Medical treatment of dogs with gallbladder mucocele, although apparently successful in the 2 dogs of the present report, can be associated with complications. Regular examinations are recommended, including ultrasonographic examination of the gallbladder and serum biochemical analyses, and frequent communication with clients is important. Detection of clinical signs of gallbladder rupture warrants immediate surgical intervention.

To the authors’ knowledge, the information reported here is the first description of resolution of gallbladder mucocele in dogs in which there was no surgical intervention. This suggests that surgery may not be necessary in all dogs with gallbladder mucocele. This concept opens the door for future studies to evaluate the effect of treatment of underlying endocrine diseases, such as hypothyroidism, hyperadrenocorticism, and diabetes mellitus, on gallbladder mucocele progression. However, at the present time, the authors recommend surgical intervention for dogs with gallbladder mucocele.

References

b. Pepcid A-C, Merck Frosst Canada Ltd, Guelph, ON, Canada.
c. HDI 5000, C8-5 transducer, Philips, Andover, Mass.
d. URSO, AXCAN Pharma Inc, Mont-Saint-Hilaire, QC, Canada.
e. Amoxil, Pfizer Canada Inc, Kirkland, QC, Canada.
f. Thor-tab, Novopharm Ltd, Toronto, ON, Canada.