

GALLBLADDER MUCOCELE



BASICS

OVERVIEW

- Gallbladder (GB) accumulation of tenacious, thick, mucin-rich, inspissated bile conglomerate (sludge) impairing GB reservoir capacity and GB contraction, thereby thwarting periprandial bile expulsion; often associated with episodic abdominal pain.
- Organized sludge expands GB lumen, flattens/thins GB wall; when severe, provokes necrotizing cholecystitis and occasional GB rupture.
- Canine syndrome, rare in cats.
- Initiated by GB dysmotility.

SIGNALMENT

- Dog.
- Shetland sheepdogs, miniature schnauzers, cocker spaniels, bichon frisé, shih tzu overrepresented in one study of 219 dogs.
- Middle-aged to older adults.
- No sex predilection.
- Associated with endocrinopathies—adrenal hyperplasia (typical or sex hormone atypical form), hypothyroidism, diabetes mellitus, and administration of glucocorticoids; these likely associated with GB dysmotility, hypertriglyceridemia, or hypercholesterolemia that may impart negative influence on GB contraction.
- Notably associated with hypertriglyceridemic syndromes.

SIGNS

General Comments

- Symptomatic or asymptomatic—depending on stage at diagnosis: mature vs. immature gall bladder mucocele (GBM).
- Asymptomatic GBM—often serendipitously discovered on abdominal US.

Historical Findings: Symptomatic

- Episodic periprandial abdominal discomfort.
- Anorexia.
- Vomiting.
- Lethargy.
- $\pm$ Polyuria/polydipsia—reflects underlying endocrinopathy.
- Collapse—vasovagal episode or bile peritonitis.

Physical Examination Findings

- May demonstrate no physical signs if immature GBM.
- $\pm$ Lethargy.
- $\pm$ Cranial abdominal discomfort—GB dysmotility and maturing GBM.
- Jaundice late in syndrome.
- $\pm$ Dehydration.
- $\pm$ Fever—secondary infection.

CAUSES & RISK FACTORS

- Inborn errors of lipid metabolism (hypertriglyceridemia)—miniature schnauzer, Shetland sheepdogs, beagles, others.
- Medical/dietary conditions provoking hypercholesterolemia or dyslipidemia—endocrinopathies, recurrent pancreatitis, feeding high-fat diet to dog with predisposing disorder or dyslipidemia.
- GB dysmotility.
- Cystic mucosal hyperplasia—common in older dogs; may be aggravated by sex hormones (e.g., progestins).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Conditions causing GB bile stasis—GB dysmotility; or other causes of incomplete GB emptying such as cystic duct or GB wall neoplasia, pedunculated adenomatous mucosal lesions, ball-valve cholelith obstructions.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Inflammatory leukogram—variable, depends on GB wall viability and hepatic impact of GBM.
- Stress leukogram—if underlying hyperadrenocorticism.
- Nonregenerative anemia—if chronic inflammation or hypothyroidism.

Biochemistry

- High liver enzymes—may be noted on acute presentation for GBM or serendipitously discovered on routine health assessments; alkaline phosphatase (ALP), γ -glutamyl-transferase (GGT), alanine aminotransferase (ALT), $\pm$ aspartate aminotransferase (AST) variably affected; ALP activity predominant.
- High ALP—often associates with glycogen-type vacuolar hepatopathy (VH), may reflect adrenal endocrinopathy or glucocorticoid therapy.
- Variable hyperbilirubinemia; depends on GBM maturation and common bile duct patency.
- Low albumin—if ruptured biliary tree and bile peritonitis.
- Prerenal azotemia—if ruptured GB, sepsis, or dehydration from vomiting.
- Electrolyte abnormalities with fluid and acid-base disturbances—due to bile peritonitis or persistent vomiting.

Urinalysis

No specific features.

OTHER LABORATORY TESTS

- Triglyceride concentrations.
- Coagulation tests—normal unless chronic extrahepatic bile duct obstruction (EHBD), GB rupture, bile peritonitis, sepsis, or disseminated intravascular coagulation (DIC).

IMAGING

- Abdominal radiography—normal or large liver; loss of detail in cranial abdomen if focal peritonitis with GB rupture or concurrent pancreatitis; rarely intrahepatic gas.
- Abdominal US—liver may be large, with rounded margins, or normal sized; diffuse to multifocal hyperechoic hepatic parenchyma (associated with glycogen-type VH); may have hypoechoic nodular appearance if severe VH; typical GBM US image: lumen filled with amorphous echogenic “organizing” nongravitational debris with stellate or finely striated pattern resembling sliced kiwi fruit (“kiwi sign”); distended GB (>1.2 mL/kg bodyweight) and sometimes distended common bile duct $\pm$ cystic duct if EHBD; pericholecystic edema may enhance

GB wall imaging; pericholecystic or generalized effusion with hyperechogenicity of surrounding tissues may indicate focal peritonitis and bile leakage (even if GB wall not ruptured); diffusely thick GB wall with segmental hyperechogenicity and double-rimmed or laminated appearance associates with necrotizing cholecystitis; GB rupture associated with discontinuous GB wall or difficult-to-image GB; ruptured GBM may have inspissated congealed biliary material released into abdominal cavity where discrete free-floating “mass” may be discovered; intrahepatic bile ducts may be difficult to visualize or appear prominent or distended.

- GB motility study—indicated if suspected developing GBM serendipitously recognized if GB volume ≥ 1.2 mL/kg bodyweight; sequential GB volume measurements determined after meal ingestion (100 g food; may include 0.5 mg/kg erythromycin as motilin agonist provoking GB contraction if no response with food alone). Normal GB contraction results in $\geq 25\%$ decline of initial or baseline GB volume on one or more recorded postprandial images. Procedure: image GB at 0, 15, 30, 45, 60, 90, 120 min relative to feeding.
- GB volume in mL = $[\text{length (cm)} \times \text{width (cm)} \times \text{height (cm)}] \times 0.52$.

DIAGNOSTIC PROCEDURES

- Aspiration sampling—fluid adjacent to biliary structures or free in abdominal cavity; clarifies GB rupture and/or infection; *caution*: do *not* perform cholecystocentesis on suspected GBM as this may cause bile peritonitis.
- Laparotomy—for diagnosis, cholecystectomy, perhaps cholecystenterostomy.
- Laparoscopy—*not* advised as CBD should be flushed to patency.
- Liver biopsy—collect biopsy distant to GB; biopsy from GB area often interpreted as severely fibrotic or as cholangitis.
- Bacterial culture/sensitivity—any effusion; GB wall, mucinous debris clinging to GB wall (scrape GB wall for best sample), liver (single inoculum); request aerobic and anaerobic bacterial culture. Positive ranging from 17% to 33% in different studies; histologic identification of bacteria unreliable.
- Cytology—impression smears of GB wall mucinous debris and liver assist prompt recognition of suppurative septic inflammation or rarely neoplasia.

PATHOLOGIC FINDINGS

- Gross—mature GBM: GB distended, wall may appear normal, erythematous, or hemorrhagic $\pm$ focal areas of necrosis; may be evidence of focal peritonitis with adhesions; liver and extrahepatic biliary structures usually appear normal but EHBD possible; GB contents: dark green-black, tenacious, firm, or organized as solid light green-yellow rubbery conglomerate. Slender long proliferative mucosal projections or cystic mucosal hyperplasia on GB mucosa are common. Immature GBM: normal to distended GB with thick dark black green bile with black particulate calcium bilirubinate debris.

(CONTINUED)

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• Microscopic—mature GBM demonstrates mural thinning with elongate mucosal fronds $\pm$ cystic mucosal hyperplasia and laminated dehydrated mucin; occasional particulate bilirubinate conglomerates in GB sections; mixed inflammatory infiltrates and fibrosis in chronic GBM; focal areas of necrosis usually caused by arterial thrombosis; Gram stain and modified Steiner's stains should be used to detect intraluminal bacteria as not all cultures recover infectious organisms. If GB not sectioned before fixation, mucosa may not fix and will appear necrotic. Liver biopsy collected distant to GB often discloses glycogen-type VH with no evidence of mechanical bile stasis if immature GBM and underlying endocrinopathy; ascending suppurative cholangitis and cholangiohepatitis may be secondary complications.



TREATMENT

• Outpatient management—ursodeoxycholic acid and S-adenosylmethionine (SAME) induce bile acid and non-bile acid mediated cholestasis and provide hepatoprotection—but medical therapy is *not* advised to resolve GBM. While medical management has occasionally resolved immature GBM in some dogs, these patients remain at risk for GBM recurrence. Naïve unmonitored treatment with choleretics may eventuate in ruptured GB. • Inpatient—depends on whether patient presents with severe acute necrotizing cholecystitis, suppurative cholecystitis, intact nonurgent mature GBM, or incidentally discovered immature GBM. • If patient hyperlipidemic, investigate cause, restrict dietary fat, avoid glucocorticoids. • Symptomatic patients require exploratory surgery for cholecystectomy and evaluation/treatment for potential bile peritonitis. • Cholecystotomy and mucocele removal with GB retention *not* advised; high risk for recurrent GBM and potential bile peritonitis. • Fluid therapy—balanced polyionic solutions to correct hydration and electrolyte status. • Be prepared for blood component therapy. • Abdominal lavage—at surgery if bile peritonitis encountered.



MEDICATIONS

DRUG(S) OF CHOICE

Antimicrobials

Initiate combined broad-spectrum antimicrobials *before* surgery; continue treatment 4–8 weeks if

septic complications; adjust drugs based on culture and sensitivity test reports and biochemical appraisals. If no histologic or culture evidence of infection and postoperative recovery unremarkable, discontinue antimicrobials 7–10 days after surgery.

Vitamin K1

0.5–1.5 mg/kg IM/SC q12h for three doses—if *jaundiced*; oral route ineffective if EHBDO.

Antiemetics/Antacids/Gastroprotectants

• Antiemetics—may be needed during preoperative interval. Maropitant citrate (Cerenia®), NK-1 antagonist—2 mg/kg PO or 1 mg SC q24h up to 5 days. Ondansetron—0.1–0.3 mg/kg PO 30 min before feeding, maximum q8h, or 0.1–0.2 mg/kg slow IV push q6–12h if vomiting. • Antacids—preoperative interval, proton pump inhibitors preferred: omeprazole 0.7–1.0 mg/kg PO/IV q24h or pantoprazole 0.7–1.0 mg/kg IV q24h. • Gastric prokinetics—if postoperative gastric atony: metoclopramide 0.2–0.5 mg/kg PO/IV/SC q6–8h or 1–2 mg/kg/day CRI. • Gastroprotectant—if suspected gastritis, esophagitis, or upper gastrointestinal bleeding: sucralfate—0.5–1.0 g PO q8–12h.

Choleretics

• Maintain hydration status to optimize cholestasis. • Ursodeoxycholic acid—choleretic, hepatoprotectant, anti-inflammatory, anti-endotoxic effects: 10–15 mg/kg PO divided BID daily with food for best bioavailability; treat until complete biochemical recovery or chronically if suspect persistent cholangitis. • SAME—choleretic, antioxidant, and metabolic benefits; choleretic dose (40 mg/kg PO q24h on empty stomach) higher than antioxidant dose.

Antioxidants

• Vitamin E— α -tocopherol 10 IU/kg/day PO with food: antioxidant, anti-inflammatory, antifibrotic influence. • SAME—20 mg/kg PO daily 2h before feeding; give until liver enzymes normalize or indefinitely if chronic hepatitis or cholangitis.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

• Repeat sequential hematology, biochemistry, and imaging to monitor surgical recovery; if GBM caused clinicopathologic abnormalities, all changes

should resolve within weeks. • Persistent clinicopathologic abnormalities implicate underlying endocrinopathy, intrahepatic cholangiopathy, or other liver disease.

• At-risk dogs should have US assessment of GB as part of routine health appraisal when middle-aged to geriatric.

POSSIBLE COMPLICATIONS

• Suppurative cholangitis or cholangiohepatitis. • Bile peritonitis. • EHBDO.

EXPECTED COURSE AND PROGNOSIS

• Good with successful surgery, chronic choleretic therapy, correction/management of comorbid conditions, dietary and/or medical management of hypertriglyceridemia. • Anticipate protracted clinical course if ruptured biliary tract or peritonitis—dogs with ruptured GBM 2–3 times more likely to succumb to GBM-related illness. • Recrudescence may occur if mucocele contents removed and GB retained, with or without chronic medical therapy. • Chronic postoperative jaundice may reflect iatrogenic stricture at site of cholecystectomy.



MISCELLANEOUS

SEE ALSO

• Bile Peritonitis.
• Cholecystitis and Choledochitis.
• Cholelithiasis.
• Glycogen-Type Vacuolar Hepatopathy.
• Hepatitis, Chronic.

ABBREVIATIONS

• ALP = alkaline phosphatase.
• ALT = alanine aminotransferase.
• AST = aspartate aminotransferase.
• DIC = disseminated intravascular coagulation.
• EHBDO = extrahepatic bile duct obstruction.
• GB = gallbladder.
• GBM = gallbladder mucocele.
• GGT = γ -glutamyltransferase.
• SAME = S-adenosylmethionine.
• VH = vacuolar hepatopathy.

Suggested Reading

Aguirre AL, Center SA, Randolph JF.

Gallbladder disease in Shetland Sheepdogs: 38 cases (1995–2005). *J Am Vet Med Assoc* 2007, 231:79–88.

Jaffey JA, Graham A, VanEerde E, et al.

Gallbladder mucocele: variables associated with outcome and the utility of ultrasonography to identify gallbladder rupture in 219 dogs (2007–2016). *J Vet Intern Med* 2018, 32:195–200.

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