

Treatment strategies of biliary stones through multiple liver lobectomy and cholecystectomy in a dog

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Abstract

A 12-year-old spayed female Maltese dog weighing 3 kg was referred to our Veterinary Medical Teaching Hospital for the evaluation of gallstones. The dog had a history of splenectomy and underlying Cushing's syndrome and had received ursodeoxycholic acid for 2 months. The dog presented with clinical symptoms, including icterus, vomiting, anorexia, lethargy, and abdominal pain. Radiography, ultrasonography, and computed tomography revealed choleliths in the gallbladder, cystic duct, common bile duct, and the hepatic ducts of the quadrate, left medial, and left lateral lobes. In addition, we identified atrophy and cirrhosis of the corresponding lobes of the liver. The choleliths were surgically managed via multiple liver lobectomy and cholecystectomy, including cystic duct and proximal common bile duct resection. The patency of the common bile duct was confirmed by normograde saline flushing using a Tom-cat catheter driven through the cut edge of the common bile duct, followed by ligation. The surgery was completed successfully, and no specific postoperative complications such as bile leakage, massive hemorrhage, shock, sepsis, or systemic peritonitis were observed during the 12-month monitoring period.

Keywords: Canine, multiple cholelithiasis, liver cirrhosis, normograde catheterization

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Introduction

A cholelith is a calculus or stone-like mass formed from bile that precipitates in the biliary system (Ward *et al.*, 2020). Cholelithiasis is rare, accounting for <1% of all hepatobiliary diseases in dogs and cats (Neer, 1992). Moreover, few reports describe gallstones in the intrahepatic or extrahepatic ducts, excluding the gallbladder and common bile ducts (CBDs), which are the most frequently affected areas (Mori *et al.*, 2006; Folk and Lux, 2019; Ward *et al.*, 2020).

Generally, there are no clinical signs, although biliary colic, vomiting, diarrhea, anorexia, lethargy, icterus, and abdominal distension can be present (Folk and Lux, 2019). Biliary duct obstruction, gallbladder perforation, cholecystitis, cholangitis, acute pancreatitis, or gallstone ileus may occur concurrently with cholelithiasis (Ward *et al.*, 2020). Emergency surgery is recommended if cholelithiasis causes complete biliary tract obstruction (Folk and Lux, 2019).

A cholelithiasis diagnosis is typically made via radiographic and abdominal ultrasound examinations (Ward *et al.*, 2020). Ursodeoxycholic acid (UDCA) is generally prescribed to dissolve cholesterol-containing gallstones. However, its effectiveness remains unclear; thus, surgery is mainly recommended (Ward *et al.*, 2020). If gallstones exist in the gallbladder, cholecystectomy should be performed; if stones are present in the CBD, choledochotomy or cholecystoenterostomy can be performed (Folk and Lux, 2019). Rarely, if hepatolithiasis accompanies liver atrophy, liver lobectomy is additionally indicated (Miyazaki *et al.*, 2020).

When multiple choleliths occur in the hepatobiliary system, the clinical symptoms may worsen rapidly; however, since there are only a few reported cases, treatment protocols are not well established. Here, we describe the status, diagnosis, and successful surgical management of cholelithiasis in the gallbladder, CBD, and hepatic ducts in a clinically symptomatic dog. To our knowledge, this is the first report of the successful implementation of multiple surgical management strategies, ranging from multiple liver lobectomy to cholecystectomy, including the cystic duct and

proximal CBD, in a dog with clinical signs of hepatobiliary disease.

Case history

A 12-year-old spayed female Maltese dog (3 kg) was referred to our Veterinary Medical Teaching Hospital for the evaluation of gallstones. The dog had a history of splenectomy and underlying Cushing's syndrome and had received UDCA (10 mg/kg, orally, BID; Daewoong Pharm, Korea) for 2 months.

Physical examination revealed icterus, abdominal pain and enlargement, vomiting, anorexia, and lethargy. Complete blood count revealed mild leukocytopenia (4.89×10^9 white blood cells/l [reference range: 5.05×10^9 – 16.76×10^9 cells/l]) and thrombocytosis (799 K/ μ l [148–484 K/ μ l]). Serum biochemical abnormalities included elevated levels of alanine aminotransferase (176 U/l [10–125 U/l]), aspartate aminotransferase (73 U/l [0–50 U/l]), gamma-glutamyl transferase (47.3 U/l [0–11 U/l]), C-reactive protein (2.0 mg/dl [0.1–1.0 mg/dl]), and total bilirubin (2.4 mg/dl [0–0.9 mg/dl]) and mild hyperkalemia (5.9 mM [3.5–5.8 mM]). Fasting ammonia and serum bile acid concentrations were within normal ranges.

Radiographic examination showed radiopaque materials in the gallbladder and biliary tree region (Figure 1). Ultrasound examination using the Aloka Prosound F75 ultrasound system (Hitachi-Aloka Medical, Tokyo, Japan) with a 1.8–2.5 MHz probe revealed gallbladder wall thickening and hyperechoic materials with distal acoustic shadowing in the gallbladder (approximately 3.2 mm) (Figure 2A). The CBD was dilated (approximately 4.1 mm) and homogeneously contiguous from the porta hepatis to the thickened major duodenal papilla (MDP; approximately 3.5×3.4 mm). Several hyperechoic structures (<1.0 mm) were present in the distal bile duct region before entering the MDP (Figure 2B). Distal acoustic shadowing was also observed in the intrahepatic ducts close to the porta hepatis region (Figure 2C).

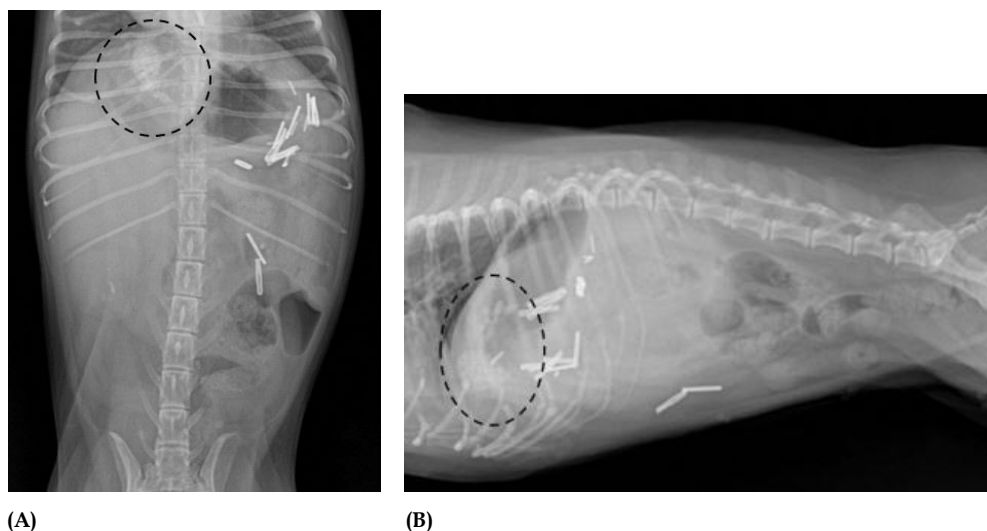


Figure 1 Abdominal radiographic images. (A), (B) Radiopaque materials fill the gallbladder and are visible in the biliary tree region.

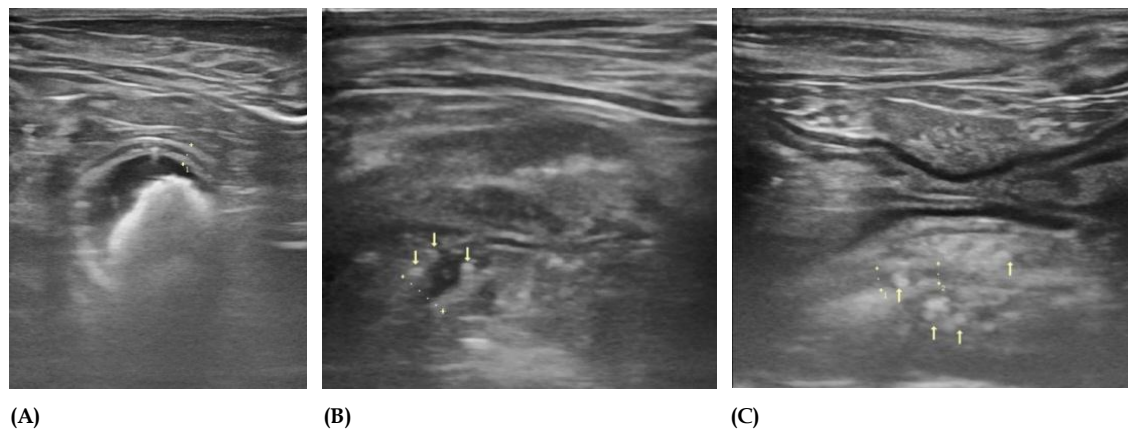


Figure 2 Ultrasonographic images of the (A) gallbladder, (B) common bile duct, and (C) hepatic ducts. (A) In the gallbladder, hyperechoic materials with distal acoustic shadowing are visible, as is double-layer thickening of the gallbladder wall. (B) Several hyperechoic spots (arrows) are visible in the common bile duct, which has expanded to a maximum diameter of 4.1 mm. (C) Hyperechoic materials (arrows) are visible in the intrahepatic ducts close to the porta hepatis region.

Computed tomography (CT) scans using an 80-slice helical scanner (Aquilion Lightning TSX-036A; Canon Medical Systems, Otawara, Japan) were performed to evaluate the exact location of the gallstones in the hepatic duct and determine the anatomical structure (Figure 3). Around the gallbladder, the left medial (LML), left lateral (LLL), and quadrate (QL) liver lobes were markedly reduced in size, with irregular shapes and contours, and had more contrast-enhancement than other liver lobes. The right medial (RML), right lateral (RLL), and caudate (CL) liver lobes were markedly displaced in the right caudolateral direction, with enlarged contours and blunted liver margins (Figure 3A). Hyperattenuating materials were observed in moderate to large amounts

in the gallbladder lumen and the cystic duct (approximately 3.1×2.0 mm). Several materials were observed in the extrahepatic duct emerging from the QL, LML, and LLL and were present within the intrahepatic ducts close to the porta hepatis regions of the QL and LML (Figure 3B). The intrahepatic duct of the LLL was dilated, and those of the RLL, RML, and QL were mildly dilated. The region where the extrahepatic duct with hyperattenuating materials entered the CBD had a tortuous appearance. Small hyperattenuating materials were observed near the MDP extending from the CBD to the duodenum, followed by a dilated CBD (approximately 4.9 mm) with contrast enhancement of the thickened wall layers.

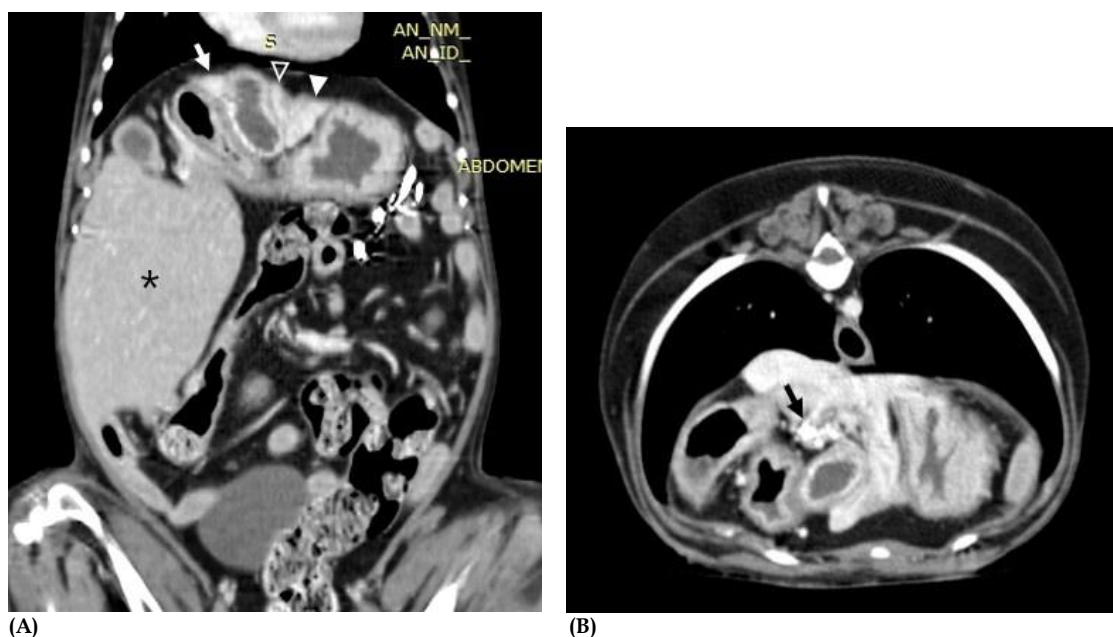


Figure 3 Post-contrast computed tomography images. (A) A dorsal plane, soft tissue window, post-contrast image. The left lateral lobe (arrowhead), left medial lobe (open arrowhead), and quadrate lobe (arrow) are considerably smaller and irregularly shaped with contours and enhanced contrast compared to the other liver lobes. The right medial lobe, right lateral lobe, and caudate lobe (asterisk) are enlarged and considerably displaced in the right caudal direction. (B) A transverse plane, soft tissue window, post-contrast image. Hyperattenuating materials (arrow) are visible in the extrahepatic duct emerging from the quadrate lobe, left medial lobe, and left lateral lobe and in the intrahepatic ducts at the porta hepatis region of the quadrate lobe and left medial lobe.

The dog was premedicated with atropine sulfate (0.04 mg/kg, subcutaneous; Jeil Pharm, Korea), butorphanol (0.1 mg/kg, intravenous [i.v.]; Myungmoon Pharm, Korea), and cefazolin (30 mg/kg, i.v.; Hankook Korus Pharm, Korea). General anesthesia was induced with propofol (4 mg/kg, i.v.; Hana Pharm, Seoul, Korea) and maintained with isoflurane (Terrell, Piramal Critical Care, Bethlehem, PA, USA) and oxygen. Following positioning in dorsal recumbency, a ventral midline incision was made from the xiphoid process to the umbilicus, and a celiotomy was performed. The gallbladder was immediately visible, and the left liver lobes had adhered to the

gallbladder. The adhered liver lobes were yellow-brown, showed atrophic sclerotic degeneration, and were very small and quite hard when palpated. The gallbladder was surrounded by the LML, LLL, and QL and had adhesions. The cystic duct attached to the QL ran tortuously in an abnormal direction. Viewed from the right side, the QL adhered to the right side of the gallbladder and showed the same findings as those of the left lobe. The remaining RML, RLL, and CL had edematous surfaces, enlargement, and blunt margins. Moreover, we found that the main branch of the hepatic duct from these three lobes led to the CBD (Figure 4A).

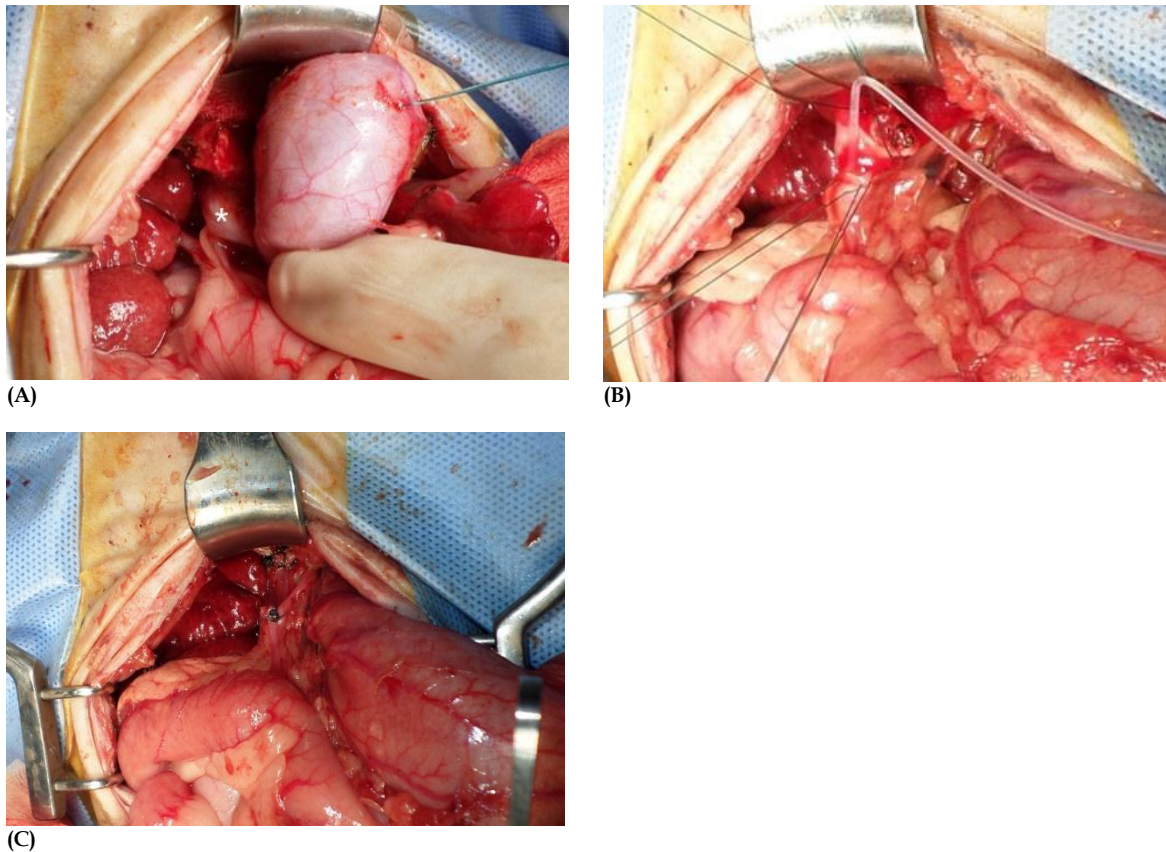


Figure 4 Intraoperative photographs. (A) A tortuous cystic duct (asterisk) is attached to the quadrate lobe, peripheral hepatic ducts, and a portion of the common bile duct. (B) The patency of the common bile duct is confirmed by inserting a Tom-cat catheter and performing saline flushing after making an incision proximal to the point where the main hepatic ducts of the right medial lobe, right lateral lobe, and caudate lobe join the common bile duct. (C) Complete excision of the CBD allows the bile ducts from the remaining right lobe to lead to the duodenum without obstruction.

The LML and LLL were dissected from the gallbladder using electrocautery, tenotomy scissors, and cotton tips. Hemorrhage occurred during dissection from the gallbladder, but hemostasis was achieved with oxidized regenerated cellulose (Surgicel®). Near the hilar, the LML and LLL were double-ligated, followed by lobectomy; each lobe was excised. Similarly, the QL was dissected from the gallbladder. To determine the patency of the CBD by catheterization from the gallbladder, we performed a cholecystostomy and removed the gallstones. Then, a Tom-cat catheter was inserted into the cystic duct; however, CBD entry was impossible because of its tortuous shape. After cholecystectomy, including proximal cystic duct resection, the attached QL, remaining cystic duct, and proximal portion of the CBD were resected. Next, stay suturing was performed

in the CBD at the proximal portion to the main hepatic duct of the RML, RLL, and CL. A 3–4 mm incision was made on that part of the stay suture, a Tom-cat catheter was inserted, and CBD flushing was performed with normal saline (Figure 4B), which confirmed sufficient patency of the CBD by penetrating the MDP. The CBD was completely excised at the incision site after double ligation on the distal side rather than at the incision site for Tom-cat insertion, leading the bile ducts from the remaining right lobe to the duodenum without obstruction (Figure 4C). The abdominal cavity was lavaged several times with warm saline, and the abdominal wall, subcutaneous tissues, and skin were closed routinely.

Postoperative management included analgesia with carprofen (4.4 mg/kg, s.c., once daily; Zoetis, USA), cefotaxime (30 mg/kg, i.v., three times per day;

Pharmgen Science, Korea), famotidine (0.5 mg/kg, i.v., BID; Dong-A ST, Korea), and UDCA (10 mg/kg, orally, BID; Daewoong Pharm, Korea). Supplemental oxygen and fluid therapy (sodium chloride 0.45% solution including vitamin B, arginine, ornithine, and potassium chloride 20 mEq/L) were also administered. On postoperative day 1, a complete blood count revealed mild leukocytosis and anemia. Serum biochemical analysis revealed a normal total bilirubin level with mildly elevated alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transferase levels. On radiography, there were no visible radiopaque materials in the gallbladder region. Ultrasound examination revealed a decreased diameter of the CBD (approximately 2.4 mm) and the MDP (approximately 2.0 × 2.0 mm) (Figure 5). We

found no evidence of recurrence or complications of gallstones, and confirmed that the dog was doing well during the 12-month postoperative monitoring period.

Histologically, the resected liver lobe led to a cirrhosis diagnosis, and the thickened wall of the gallbladder led to a cholecystitis diagnosis. There is severe chronic permanent remodeling of the hepatic lobular atrophy with biliary hyperplasia, portal fibrosis, and mixed inflammation. The gallstones removed from the gallbladder and hepatic duct did not form large lumps but were clustered in small grains. The color of the gallstones was mainly yellow-brown; some were black. Composition analysis revealed mixed-type choleliths made of various substances such as cholesterol, calcium bile acid, and calcite.

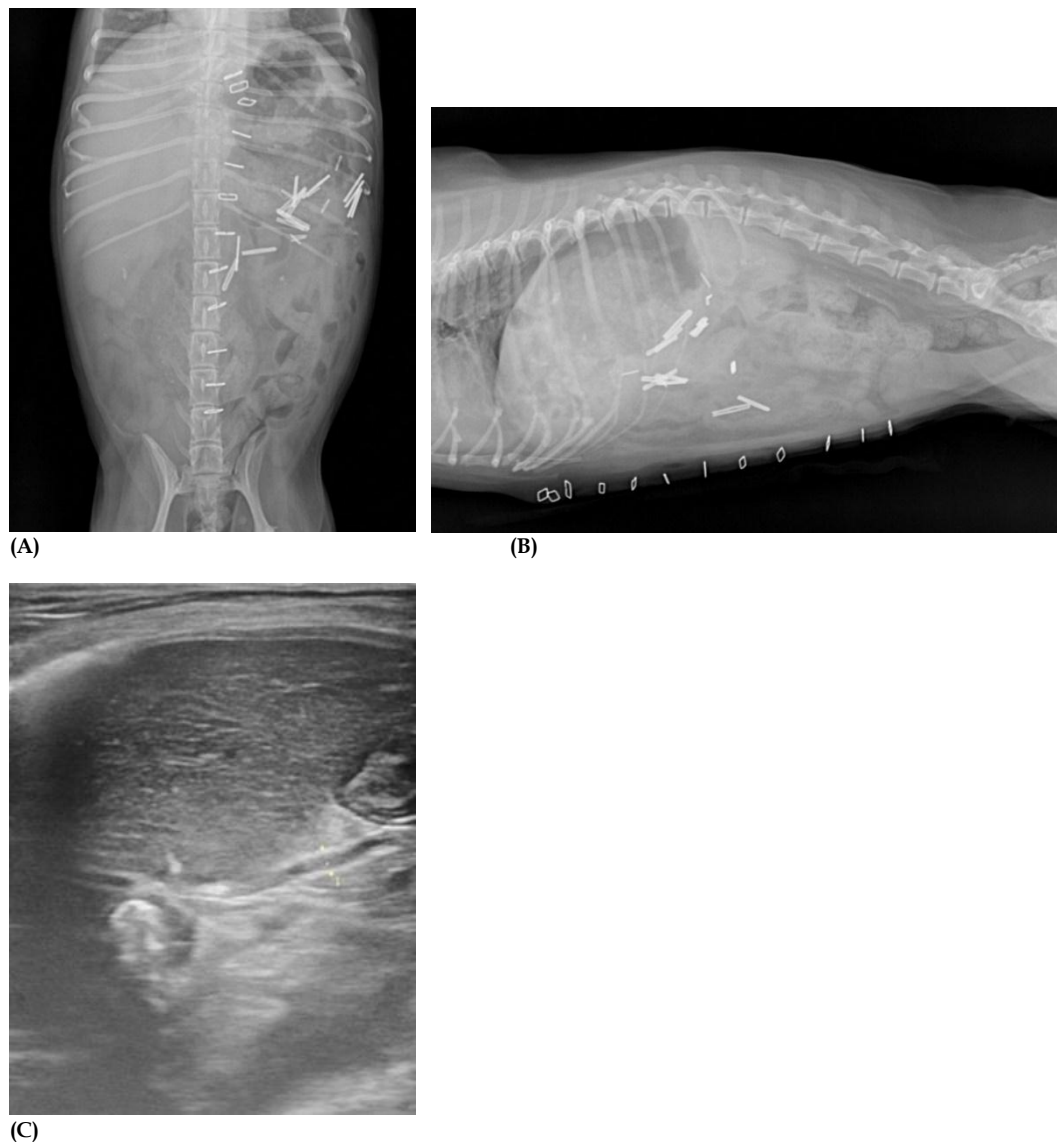


Figure 5 Postoperative photographs. (A), (B) There were no visible radiopaque materials in the gallbladder and biliary tree region on radiography. (C) A reduction of CBD diameter (approximately 2.4 mm) was confirmed by ultrasonography.

Results and Discussion

Oversaturation of cholesterol in the bile, reduced bile excretion, and biliary infection are the main causes of cholelithiasis in humans (Tazuma, 2006). In dogs, the causes have not yet been well established, but the

pathogenesis of choleliths is thought to include cholestasis, biliary infections, and dietary alterations (Johnston and Tobias, 2017).

Gallstones have been classified into three main types: pure cholesterol, mixed, and pigment gallstones (Neer, 1992; Ward, 2006). Here, the cholesterol levels

were normal, and the composition of gallstones was also identified as containing various cholesterol mixtures, calcium bilirubinate, and calcite. Similar to findings from previous studies, gallstone formation in this dog was not accompanied by high cholesterol levels (Ward, 2006; Ward *et al.*, 2020).

Radiographic and ultrasound examinations are commonly used to diagnose cholelithiasis in human and veterinary medicine. Gallstones generally contain mixtures of calcium, appearing radiopaque on radiography and as focal hyperechoic structures with acoustic shadowing on ultrasonography (Neer, 1992). Here, we confirmed the presence of gallstones in the hepatic ducts using radiography and ultrasound, but the location of the gallstones in the hepatic ducts was accurately determined via CT. Therefore, we suggest that CT examinations are more useful than ultrasound examinations, commonly used in dogs, for diagnosing intrahepatic gallstones.

Surgical treatment is required in cases where bile has leaked into the abdominal cavity because of extrahepatic biliary tract rupture or extrahepatic biliary tract obstruction or when necrotizing cholecystitis has occurred (Thompson, 1981; Thompson and Sherman, 2021). Biliary system rupture is caused by severe trauma, avulsion from the normal duct insertion site, or bile outflow obstruction (Thompson, 1981; Thompson and Sherman, 2021). Additionally, gallstones in the bile ducts, inflammation in the biliary tract owing to bacterial or parasitic infection, and biliary tissue neoplasia or cystic hyperplasia can cause biliary system obstruction or cholecystitis (Thompson, 1981; Thompson and Sherman, 2021). Here, no intraperitoneal outflow of bile owing to biliary system rupture was confirmed, but multiple choleliths were found in the gallbladder, cystic duct, CBD, and hepatic ducts that can cause blockage and rupture of the hepatobiliary system. Cholecystitis was confirmed, and liver cirrhosis of the LML, LLL, and QL caused by biliary duct obstruction was also observed. Since 2 months of medical treatment did not yield any therapeutic effects and we observed clinical symptoms of hepatobiliary disease, including icterus, vomiting, anorexia, lethargy, and abdominal pain, we performed emergency surgery.

When performing cholecystectomy, an important consideration is the extrahepatic biliary tract patency, which can be determined by normograde or retrograde flushing using catheterization (Mayhew and Weisse, 2008). In this case, catheterization via a cholecystostomy was attempted to prevent complications from duodenotomy and shorten the operation time, but entry was not possible owing to the tortuous shape of the cystic duct. Such a dilated and tortuous shape is known to be caused by biliary obstruction (Turner and Fulcher, 2001). After cholecystectomy, including the proximal cystic duct, catheterization was facilitated as the tortuous portion was removed in the process of removing the adhered portion of the QL, the remaining cystic duct, and the proximal portion of the CBD together. The CBD was incised to avoid the general complications of normograde flushing via an open cystic duct stump, and a Tom-cat catheter was inserted. Normograde saline flushing was attempted, and CBD patency was

confirmed. To prevent dehiscence, leakage, and stricture of the incision site, which may occur after choledochotomy, the incision site was resected after double ligation at the distal end without suturing (Baker *et al.*, 2011). Complications, such as pancreatitis, decreased gastrointestinal motility, duodenal dehiscence or perforation, gallbladder necrosis, and liver abscess, have been reported with retrograde catheterization (Putterman *et al.*, 2021).

Liver cirrhosis is the end stage of chronic hepatitis and is defined as a diffuse distribution characterized by liver fibrosis and the conversion of normal liver architecture into structurally abnormal nodules and micro- or macro-nodules (Favier, 2009). There are currently no clinically available anti-fibrotic treatments for dogs, and liver transplantation is the only treatment for hepatic dysfunction caused by liver cirrhosis in humans (Favier, 2009).

Several treatment methods have been reported for hepatic duct gallstones in humans. If the gallstones are confined to one lobe and stenosis of the bile duct and destruction of the hepatic parenchyma have progressed, the liver lobe is surgically resected (Mori *et al.*, 2006). Hepaticocutaneous jejunostomy is used to facilitate endoscopic access to the biliary tree for the removal of intrahepatic stones and is generally performed when stones and strictures recur after surgery or are predicted to recur during the first laparotomy (Liu *et al.*, 1998; Watanabe *et al.*, 2020). Moreover, the treatment methods include an endoscopic approach using a basket catheter, percutaneous transhepatic cholangioscopy lithotomy, extracorporeal shock wave lithotripsy, electrohydraulic shock wave lithotripsy, and Nd-YAG laser lithotripsy (Mori *et al.*, 2006). In contrast to human medical research, studies on hepatolithiasis treatment have not been performed in veterinary medicine. Although a few cases of hepatolithiasis in dogs have been reported, to our knowledge, case reports on the surgical management of hepatolithiasis in dogs have not been published.

Although no specific complications occurred after surgery in this case, complications may occur after hepatobiliary surgery. For example, shock, sepsis, systemic peritonitis, hypoproteinemia, hypoglycemia, and hypokalemia may occur after cholecystectomy. Furthermore, after choledochotomy, dehiscence, bile leakage, strictures, and adhesions may occur as complications (Folk and Lux, 2019).

In conclusion, our results indicate that safe and accurate surgical correction via multiple liver lobectomy and cholecystectomy is an effective treatment method for multiple choleliths in the biliary system causing atrophic liver cirrhosis in dogs. To our knowledge, surgical treatment for gallstones in the hepatic duct in dogs has not been reported. Moreover, this is the first clinical report of multiple surgical management strategies ranging from multiple liver lobectomy to cholecystectomy, including the cystic duct and proximal CBD.

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