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Cholelithiasis Complicated with Biliary Sludge and Urolithiasis in a Dog

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Abstract : A 10-year-old intact female Miniature Schnauzer dog was referred with the primary complaint of persistent anorexia, remittent fever, vomiting and abdominal pain. Hemogram suggested a chronic inflammatory disease. Serum biochemistry showed moderate hepatobiliary cellular damage with severe cholestasis. Abdominal radiography and ultrasonography revealed hepatomegaly, choleliths and sludges in gall bladder and small stones in urinary bladder. Based on diagnostic findings, the case was diagnosed as cholelithiasis complicated with biliary sludge and urolithiais. Using cholecystectomy and cystectomy, choleliths and uroliths were removed from gall bladder and urinary bladder, respectively. The clinical condition was dramatically improved after surgery.

Key words **:** cholelithiasis, biliary sludge, cholestasis, urolithiasis, dog.

Introduction

Bile is formed by hepatocytes and discharged into the canaliculi lying between the hepatocytes. Pancreatitis, neoplasia, cholelith and gallbladder mucocele (biliary sludge) are the common causes of extrahepatic biliary tract obstruction. A gallbladder mucocele is an abnormal accumulation of inspissated mucus that distends the gallbladder and causes some degree of extrahepatic biliary tract obstruction.

Case

A 10-year-old intact female Miniature Schnauzer dog was referred at Veterinary Teaching Hospital of Kangwon National University with the primary complaint of persistent anorexia, fluctuant fever, vomiting and abdominal pain for last 2 weeks. In physical examination, the dog was lethargic with high fever (rectal temperature 39.4°C). Complete blood cell count (CBC) showed severe leukocytosis ($53.4 \times 10^3/\mu L$; reference range: $6\text{-}17 \times 10^3/\mu L$) neutrophilia with left shift ($34.1 \times 10^3/\mu L$; reference range: $3.0\text{-}11.8 \times 10^3/\mu L$), lymphocytosis ($9.1 \times 10^3/\mu L$; reference range: $1.0\text{-}4.8 \times 10^3/\mu L$) and monocytosis ($9.34 \times 10^3/\mu L$; reference range: $0.2\text{-}2.0 \times 10^3/\mu L$), suggesting chronic inflammatory process in a certain part of the body. No abnormalities were observed in red cell index.

Serum biochemistry showed increased hepatic leakage enzymes (alanine aminotransferase; ALT 628 IU/L, reference range: 3-100 IU/L; aspartate aminotransferase; AST 72 IU/L, reference range: 1-50 IU/L) and cholestatic enzymes (alkaline phosphatase; ALP 1048 IU/L, reference range: 20-300 IU/L; γ-glutamyl transpetidase; GGT 19 IU/L, reference range: 1-6 IU/L). Total bilirubin was initially 0.4 mg/dl increased to 0.6 mg/dl at the 2 week of consultation (reference range 0-0.4 mg/dl). However, the dog was not icteric. Cholesterol level was also maintained 344 mg/dl (upper limit of reference range; 126-350 mg/dl) to 400 mg/dl (slight higher than reference range). Biochemical findings strongly suggested moderate hepatic cellular damage with severe cholestasis. Urinalysis showed mild increase in bilirubin, urobilirubin and leukocyte suggesting hepatic disease and urinary tract inflammation.

Abdominal radiography revealed enlargement of hepatic shadow with scallop shaped hepatic margin (Fig 1) and stacks of small stone in urinary bladder (Fig 2). Ultrasonography

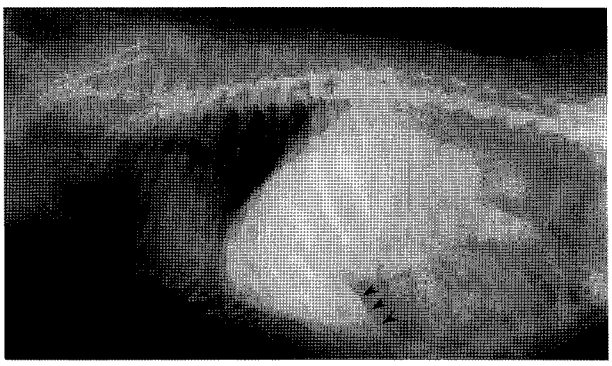

Fig 1. Abdominal radiography of this dog. The hepatic shadow is abnormally enlarged. Due to hepatic enlargement, the hepatic margin looks "scallop-shaped".

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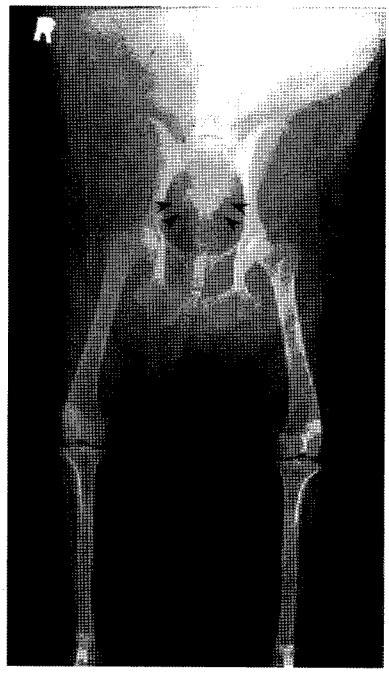

Fig 2. Abdominal radiography of this dog. The urinary bladder contains stack of small stones.

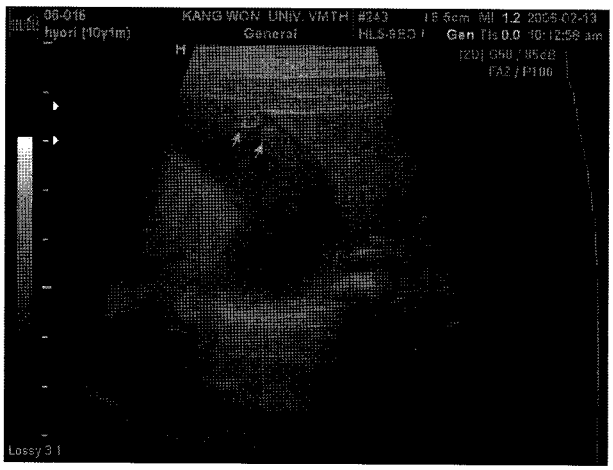

Fig 3. Ultrasonography of the liver and gallbladder taken standing position in this dog. Notice the ill-definednd accumulation of echogenic materials in gallbladder.

confirmed hepatomegaly and enlarged hepatobiliary duct, suggesting extrahepatic obstruction. Interestingly, ill-defineded accumulation of echogenic materials was observed in gallbladder, suggesting choleliths or biliary sludge (Fig 3). Hyperechogenic materials were also observed in urinary bladder indicating urinary stones (Fig 4). Based on results of CBC, serum biochemistry and diagnostic imaging studies, the case was diagnosed as cholelithiasis complicated with biliary sludge and urolithiasis.

The dog was initially treated medically. The medications

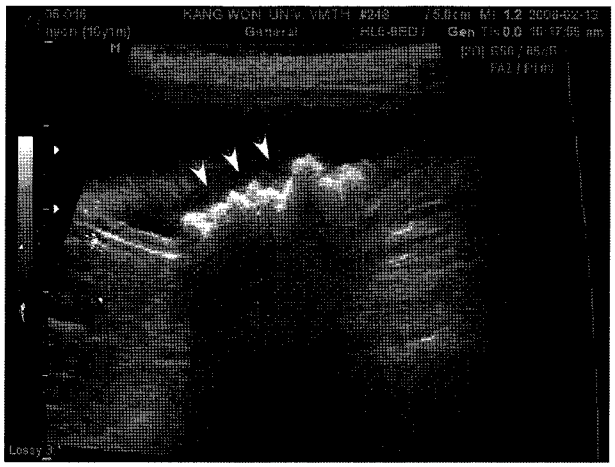

Fig 4. Ultrasonography of the urinary bladder in this dog. Notice hyperechogenic materials in urinary bladder.

prescribed were prednisolone (1 mg/kg BID, IM) for slowing down the progress of hepatic cellular damage, ursodeoxycholic acid (10 mg/kg SID, PO) for improving biliary excretion, sulcralfate (250 mg/kg, SID, PO) and ranitidine (2 mg/kg, BID, IV) for minimizing gastric disturbances, and cefazoline (10 mg/kg, BID, IV) for fighting infection. The fluid (0.45% saline plus 2.5% dextrose) with multi-vitamins and glutachione (1 mg/kg, BID, PO) was administered to restore fluid loss from vomiting. The dog was initially responded to treatment. The hepatic enzymes were significantly reduced (ALT 28 IU/L, AST 16 IU/L, ALP 355 IU/L, GGT 6 IU/L) after 1 week of treatment. However, hemogram still showed persistent leukocytosis ($69.9 \times 10^3/\mu L$). The dog was then released with prescription (prednisolone, sulcralfate, urosodeoxycholic acid, cefazoline and glutachione).

One week later, the dog was re-visited for checking up the progress of treatment. The hepatic enzymes were re-elevated (ALT 310 IU/L, AST 34 IU/L, ALP 812 IU/L, GGT 20 IU/L) and leukocytosis persisted ($57.4 \times 10^3/\mu L$). The same prescription kept for another week, since the clinical condition of dog seemed to be better, according to owner's statement.

The dog was then re-examined after another week. The hepatic enzymes were still elevated (ALT 461 IU/L, AST 69 IU/L, ALP 1500 IU/L, GGT 47 IU/L). However, the leukocytois was significantly improved (total WBC count $37.9° \times 10^3/\mu L$). Since elevation of hepatic enzyme persisted, surgical removal of choleliths and uroliths were applied. On surgery, the liver was enlarged and common bile duct to duodenum was almost completely obstructed. No obstruction and inflammation were found in pancreatic duct to duodenum. Using cholecystectomy, choleliths were removed from the gallbladder (Fig 5A). To achieve the patency from bilary duct to duodenum and remove biliary sludges inside gallbladder, saline irrigation was performed (Fig 5B). The bile juice was taken for microbiological examination. The uroliths were also removed from the urinary bladder, using cystectomy (Fig 5C). CBC

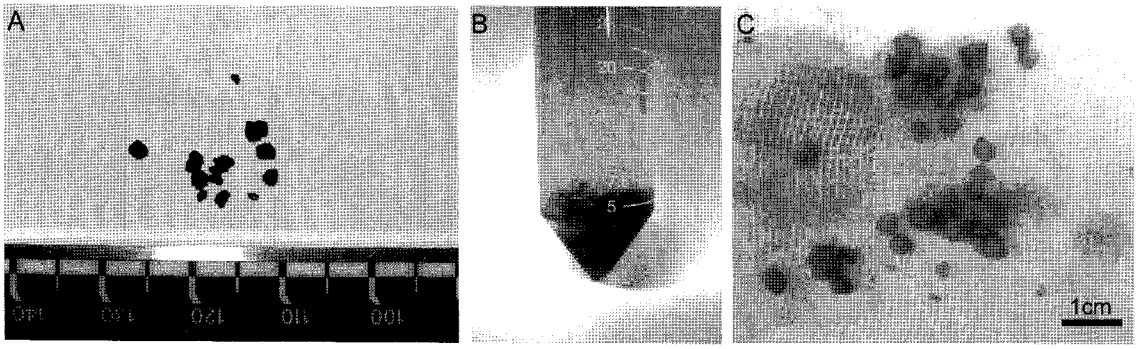

Fig 5. Choleliths (A), biliary sludges (B) and urinary stones (C) taken out from this dog.

and serum biochemical tests revealed marked improvement in hepatic cellular damage after surgery (ALT 138 IU/L, AST 28 IU/L, total WBC $30.2 \times 10^3/\mu L$). However, ALP (1500 IU/L) and GGT (40 IU/L) evaluated at 3 weeks after surgery was persistently high despite surgery. However, the dog had good appetite and much more active than before surgery. The dog was then released. The condition of dog was very stable in the follow-up studies. No bacteria were isolated from bile juice making etiology of this case unidentified. The urinary stone was calcium oxalate revealed by microscopic examination. Low protein and high carbohydrate diets (e.g. Hill's L/D) were recommended for long-term management. No further treatment related to calcium oxalate urolithiasis was performed after removal of stone from urinary bladder.

Discussion

The sludge in the gallbladder seen on ultrasound is consistent with hepatobiliary disease (2). Rule-outs for hepatobiliary disease include cholangitis, cholangiohepatitis, pancreatitis, mucocele, neoplasia, or a cholelith (5). Smaller breeds and older dogs were overrepresented, especially Cocker Spaniels (1). In this case, the ultrasonographic and radiographic patterns of the gallbladder were not thought to be consistent with gallbladder mucoclele found in literature (Kiwi fruit pattern) (1). Furthermore, pancreatitis was thought to be less likely since the amylase and lipase activities were within reference intervals, although panacreatitis is the most common cause of extrahepatobiliary obstruction (EHBO) (3). The increased ALP activity and bilirubin concentration were suggestive of cholestatic disease, and the increased ALT activity was indicative of hepatocellular disease (7). Although both processes are occurring simultaneously, the massive increase in serum ALP activity followed by the increase in serum ALT activity is suggestive of primary biliary disease. Biliary tract disease can cause subsequent hepatocellular damage and an increase in ALT activity. In this dog, the material in the gall bladder was presumed to have caused extra-hepatic cholestasis, which over time resulted in chronic hepatitis. Cholesterol is produced primarily by the liver, and is either excreted in the bile unchanged or converted to bile acids (7). The increase in serum cholesterol in combination with the increase in serum ALT and ALP activities in this dog is most likely due to biliary obstruction causing a reflux of cholesterol into the serum.

EHBO can be caused by cholelithiasis, biliary mucoclele and sludges, neoplasia obstructing biliary tract and pancreatitis (3). Clinical signs of icterus, vomiting, anorexia, or a combination of these signs were commonly exhibited (4). One retrospective study found extraluminal obstruction of the biliary tract by pancreatitis is the most common cause of EHBO (3). However other retrospective study found the biliary obstruction caused by either cholelithiasis or biliary sludges was the common cause of EHBO (8). Not all dogs showed clinical signs of EHBO (6). One retrospective study found 76% of dog having biliary mucocele showed clinical signs associated with EHBO (6). In this study, median values for serum activities of ALT and ALP, serum total bilirubin concentration, and total WBC count were significantly higher than reference range (6). Overall perioperative mortality rate for dogs that underwent cholecystectomy was 21.7% (6). One other study found motality rate was 31.8% after cholecystectomy (9). The causes of post-operative death were bile-induced peritonitis, pancreatitis, cholecystitis, or severe renal failure bile-induced peritonitis (9). However most literature recommended cholecystoduodenostomy or cholecystectomy for removal of gallbladder stones or sludges (2,4,9).

Although severe leukocytosis with left-shift was suggestive finding of bacterial infection, no bacteria has been isolated from the bile juice taken at surgery, suggesting that pre-medicated antibiotics may eliminate potential bacterial pathogens from the bile. Another possible explanation is that leukocytosis may be caused by lower urinary tract infection, since the dog also had urolithiasis, and thus gall bladder itself had only sterile infection.

Conclusion

This case study described the rare case of EBHO caused by gallbladder stones and sludges, including medical and surgical management. Surgical outcome was fair, but long-term prognosis of this case was not sure since the case was complicated with urinary tract disease.

Acknowledgement

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개의 담낭 슬러지와 요 결석증을 동반한 담석증

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요 약 : 10년령의 암컷 Miniature Schnauzer 개가 지속적인 식욕결핍, 이장열, 구토, 복통 등의 증상으로 내원하였다. 혈액검사 상에서 백혈구 수치는 만성 염증 소견을 나타내었고, 혈액 화학검사에서는 심한 담즙정체를 나타내는 중등도의 간담도계 이상 지표를 보여주었다. 복부 방사선과 초음파상에서 간종대, 담낭내 슬러지와 결석, 방광내 결석등이 관찰되었다. 이러한 진단 소견을 바탕으로 본 증례를 방광 결석증이 합병된 담낭내 담석과 슬러지에 의한 간외성 담관 폐색증으로 진단하였다. 담석과 방광결석을 담낭절제술과 방광절제술을 통해 담낭과 방광으로부터 각각 제거하였으며, 수술 후 환축의 임상증상 개선은 매우 빠르게 진행되었다.

주요어 : 담석증, 답즙 슬러지, 담즙 정체, 요로 결석증, 개.