

Infectious Cholecystitis and Concurrent Endocarditis in a Dog: Rare but Important Association

Joohyun Jung and Mincheol Choi*¹

Ilsan animal medical center, Daehwa-dong 2030, Ilsanseo-gu, Gyeonggi-do 411-803, South Korea
*Veterinary Radiology Department, College of Veterinary Medicine and Research Institute for Veterinary Science,
Seoul National University, Seoul 151-742, South Korea

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Abstract : A 12-year-old castrated male miniature Schnauzer had anorexia, vomiting, lethargy, and fever for four days. The dog had leukocytosis, thrombocytopenia, hypoglycemia, hypoalbuminemia, hyperbilirubinemia, increased hepatic enzymes on hematologic and biochemical examinations. On abdominal ultrasonographs, there was an enlarged gallbladder with hyperechoic irregular wall thickening. Echocardiography showed vegetative change and regurgitation of aortic and mitral valves. *E.coli* was identified through ultrasound guided percutaneous cholecystocentesis and bile culture. Bacterial cholecystitis and concurrent endocarditis were diagnosed. The dog was recovered from sepsis with antibacterial and aggressive supportive therapy.

Key words : cholecystitis, dog, echocardiography, endocarditis.

Introduction

Infectious cholecystitis and endocarditis are uncommon but well-known diseases in human and veterinary medicine. Infectious cholecystitis is infectious inflammation of the gallbladder, mainly infected by *E. coli*, Streptococci, staphylococci, or clostridia spp. Bile flow obstruction, mucocele, cholelithiasis, tumor, ascending infection of the common bile duct from the duodenum or hematogenous infection may be underlying causes of infectious cholecystitis (1,14,24). Infectious endocarditis is vegetative valvular inflammation from any infection of the body. Discospondylitis, prostatitis, pneumonia, urinary tract infections, pyoderma, periodontal disease, dental scaling, corticosteroid use, long-term indwelling central venous catheters, and congenital cardiac diseases were associated with infectious endocarditis (9,11,12,13,17,18,21,25). However, intercurrent infectious cholecystitis and endocarditis has not reported in the veterinary medicine. This case report describes rare but important association between infectious cholecystitis and concurrent endocarditis in a dog.

Case

A 12-year-old castrated male Miniature Schnauzer (7.7 kg) was presented with a four-day history of anorexia, vomiting, fever and lethargy. The clinical conditions were gradually worsened in spite of antibiotic treatment in the referred hospital for four days. Physical examination revealed tachypnea (48 breaths per minute), cardiac murmur (holosystolic mur-

mur in the left cardiac apex), fever (40.2°C) and right cranial abdominal tenderness. Hematologic tests revealed leukocytosis (38.5×10^9 L; normal range $6\sim 17 \times 10^9$ L) and thrombocytopenia (92×10^9 L; normal range $200\sim 500 \times 10^9$ L per dl). Blood chemistry tests revealed hyperbilirubinemia (Total bilirubin 0.61 mg/dl; normal range 0~0.4 mg/dl), hypoglycemia (glucose 67.4 mg/dl; normal range 70~118 mg/dl), hypoalbuminemia (2.58 g/dl; normal range 2.9~4.2 g/dl), and mildly increased liver enzymes (ALP 550 U/L; normal range 15~127 U/L, AST 60.9 U/L; normal range 15~43 U/L, GGT 14.5 U/L; normal range 0~12 U/L, and total cholesterol 353.9 mg/dl; normal range 353.9 mg/dl). Routine urinalysis was normal. Coagulation test was normal. The dog was considered to have systemic sepsis.

Thoracic radiographs presented mild cardiomegaly without remarkable pulmonary congestion and edema. Abdominal ultrasonographs showed an enlarged gallbladder with hyperechoic irregular wall thickening (4 mm) and loss of normal oval shape. There were no ultrasonographic signs of gallstones, gallbladder rupture or extrahepatic biliary obstruction (Fig 1). Rod-shaped bacteria were identified through ultrasound guided percutaneous cholecystocentesis (Fig 2). Therefore, infectious cholecystitis was diagnosed and ultrasound guided percutaneous bile drainage was performed. As an empiric antimicrobial therapy, cephadrine (Panzedin inj[®], Hankook korus pharm) 30 mg/kg iv tid, metronidazole (Metrynal inj[®], Daehan pharm) 15 mg/kg iv bid, and enrofloxacin (Baytril[®], Bayer animal health) 5 mg/kg sc bid were used. And the intravenous fluid therapy including fresh frozen plasma and analgesic therapy with fentanyl patch (Fentanyl patch 25 µg/hr[®], Myungmoon pharm) 25 µg/hr were performed. On the following day, echocardiography showed remarkable (4.5 mm in aortic valves and 7 mm in mitral

¹Corresponding author.
E-mail : Mcchoi@snu.ac.kr

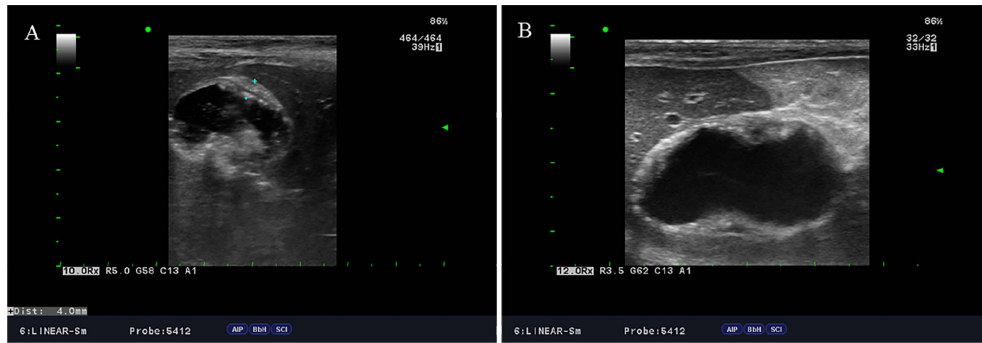


Fig 1. Abdominal ultrasonographs show that the gallbladder has irregular thickened hyperechoic wall and hyperechoic internal sludge. There are no ultrasonographic signs of the gallbladder rupture or extrahepatic duct obstruction.

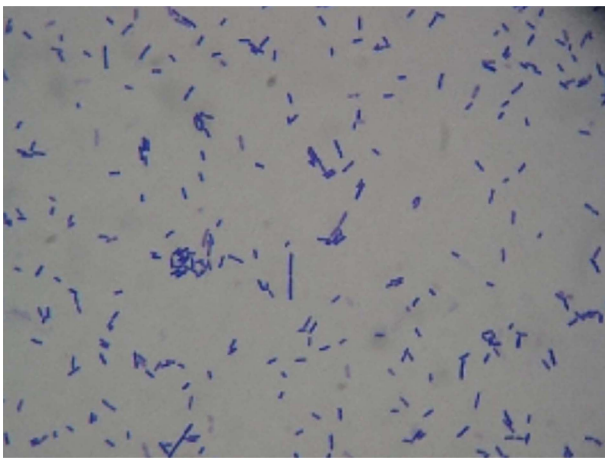


Fig 2. Percutaneous ultrasound guided cholecystocentesis reveals rod-shaped bacteria. Infectious cholecystitis by *Escherichia coli* is confirmed through bile culture.

valves) hyperechoic vegetative changes in the mitral (both anterior and posterior leaflets) and aortic valves. Doppler test showed aortic regurgitation (Vmax 3.86 m/s and pressure half time 271 ms) and mitral regurgitation (Vmax 5.6 m/s). Left ventricle and atrium were dilated (Fig 3). According to the modified Duke criteria (3), these echocardiographic findings were consistent with infectious vegetative endocarditis. Blood culture for bacteremia was negative. Urine culture was also negative. The result of bile culture was *Escherichia coli* and has sensitivity to imipenem, amoxicillin/clavulanic acid and amikacin. According to the bile culture and sensitivity results, antimicrobial therapy was replaced to imipenem (Tipem[®] inj, Myungmoon pharm) 10 mg/kg iv tid and metronidazole (Flasinyl[®], CJ Healthcare) 15 mg/kg iv bid. Bile leakage, hyperechoic surrounding fat and hypoechoic small fluid around the irregular gallbladder on ultrasonography, was found on the following day after percutaneous cholecystocentesis and bile drainage. Fortunately, the hematologic and blood chemistry results were not worsened and the dog was afebrile and eating with aggressive medical care. Ultrasonographic signs of bile leakage were resolved in few days without surgery. The dog was discharged from hospital with resolution of all clinical signs and abnormal hematologic and blood chemistry results after 12-day-hospitalization. Antimicrobial therapy was replaced to oral drug with amoxicillin/clavulanic acid

(clavamox[®], Zoetis) 12.5 mg/kg bid. With this antibiotic, the dog has been treated with cardiac medication with benazepril (Cibacen[®], Novartis) 0.25 mg/kg bid, furosemide (Lasix[®], Handok pharm) 1 mg/kg, spironolactone (Spironolactone guju tab[®], Guju pharm) 1 mg/kg bid, pimobendan (Vetmedin[®], Boehringer Ingelheim) 0.25 mg/kg for another eight months. The dog is alert and active without any clinical signs. However, irregular hyperechoic wall thickening of the gallbladder on abdominal ultrasonography and vegetation and regurgitation of aortic and mitral valves on echocardiography are still static, to date.

Discussion

Infectious cholecystitis is infectious inflammation of the gallbladder. The pathogenesis of cholecystitis is unclear (1,14). Bile flow obstruction, mucocele, cholelithiasis, and tumor may be underlying diseases (1,14). Ascending infection of the common bile duct from the duodenum or hematogenous infection may also be possible. In the patients with ascending infection from duodenum, *Escherichia coli* is often cultured. *Streptococci*, *staphylococci*, or *clostridia spp.* are also found (1,14,24). In this dog, *E. coli* was identified through the cholecystocentesis and bile culture, and ascending infection from duodenum might be mostly suspected. The common clinical signs of cholecystitis are cranial abdominal pain, depression, vomiting, and fever (1,14,24). In the case of gallbladder rupture or extrahepatic biliary obstruction, severe peritonitis, ascites or jaundice can be seen (1,10,14,24). This dog showed remarkable right cranial abdominal tenderness and fever on physical examination. These two clinical signs are specific and highly suggestive of cranial abdominal inflammation such as infectious cholecystitis, pancreatitis, or hepatic abscess. The diagnosis of infectious cholecystitis was based on the abdominal ultrasonographs and cytologic or bacteriological evaluation of the bile. The representative ultrasonographic findings of cholecystitis are diffuse irregular hyperechoic wall thickening of the gallbladder (15,20). Irregular or pinpoint sized hyperechoic spots producing reverberation artifacts within the gallbladder lumen can be associated with gas producing bacterial infection such as *E coli* or *clostridium perfringens* (2). This dog had typical irregular hyperechoic wall thickening of the enlarged gallbladder on ultrasonographs. Reverberation artifacts were not

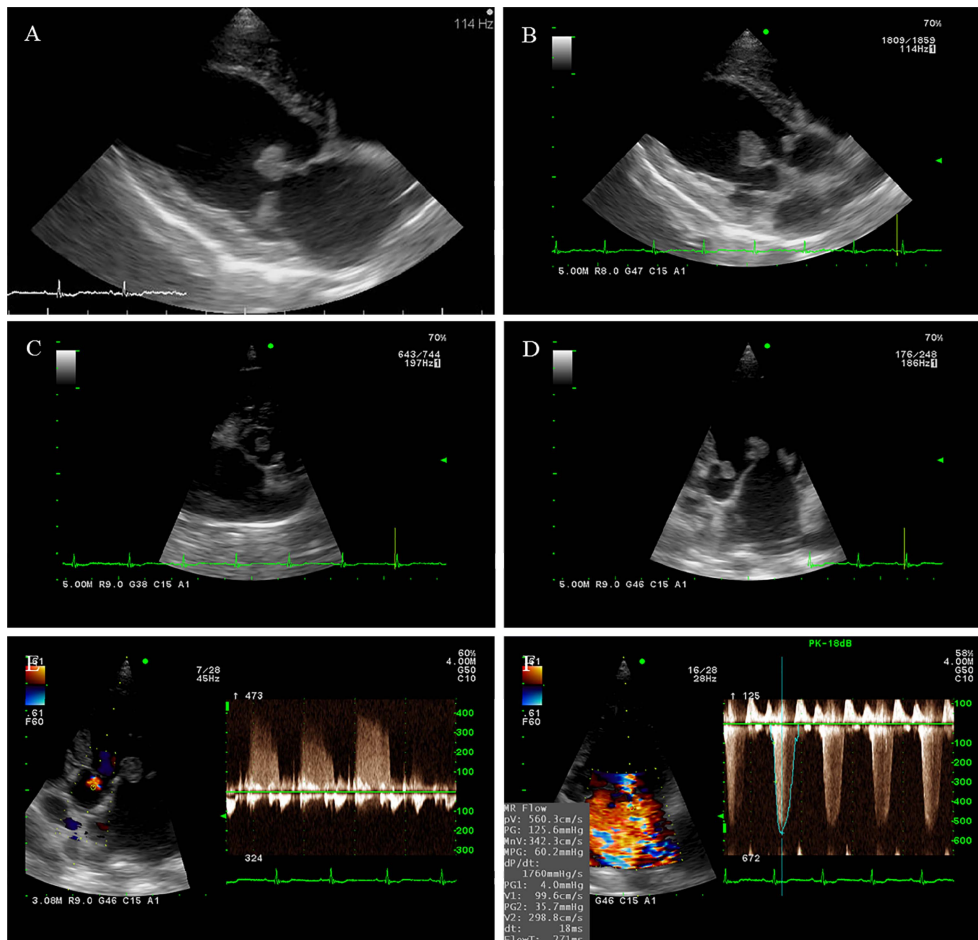


Fig 3. Echocardiographs shows remarkable hyperechoic vegetation in the aortic and mitral valves (A, B, C, D). With vegetation, remarkable aortic (E) and mitral regurgitation (F) are consistent with endocarditis.

identified. There were loss of normal gallbladder oval shape; however discontinuous wall of the gallbladder, hyperechoic surrounding fat, focal ascites, and common bile duct dilation were not identified. Ultrasonographs are very useful to find and differentiate not only cholecystitis, but also gallbladder rupture, focal peritonitis, extrahepatic biliary obstruction, pancreatitis, and any abdominal abscess (10,11,22). The treatment is antibiotics based on the bile culture and sensitivity test through ultrasound guided cholecystocentesis. Cholecystocentesis is contraindicated in the mucocele and biliary obstruction. Percutaneous bile drainage helps treatment actively in the infectious cholecystitis without surgery (20,23). In this dog, percutaneous ultrasound guided cholecystocentesis and bile drainage was helpful for accurate diagnosis and treatment, although there were focal bile leakage. Fortunately, focal bile leakage was resolved spontaneously without worsening of symptoms. Main complication of cholecystocentesis is bile leakage. However, complications are uncommon, cholecystocentesis and bile drainage should be needed for timely diagnosis and medical treatments of infectious cholecystitis without surgery (20,23). In the cases of infectious cholecystitis with biliary calculi, gallbladder bleeding, mucocele, gallbladder rupture, and extrahepatic biliary duct obstruction, cholecystectomy should be needed (10,22).

Infectious endocarditis is common in the middle age, male, and middle-sized or large breed dog. Infectious endocarditis

is vegetative valvular inflammation, resulting in valvular insufficiency. Infectious routes of endocarditis may be from any infection of the body. Discospondylitis, prostatitis, pneumonia, urinary tract infections, pyoderma, periodontal disease, dental scaling, corticosteroid use, and long-term indwelling central venous catheters were reported (9,11,12,17,18,21). Congenital cardiac diseases such as subaortic stenosis and ventricular septal defect can be underlying diseases (13,25). Case of endocarditis with concurrent infectious cholecystitis was not reported in veterinary medicine. Bacteria isolated from endocarditis in dogs are *Staphylococcus spp.*, *Streptococcus spp.*, *Escherichia coli*, *Pseudomonas spp.*, *Erysipelothrix rhusiopathiae*, *Enterobacter spp.*, *Pasteurella spp.*, *Corynebacterium spp.*, *Proteus spp.*, *Bartonella spp.*, *Serratia marcescens* (5-9,16,19,25). Clinical signs of endocarditis are associated with extent of effects on heart and complications, such as congestive heart failure, immune-mediated disease, and thromboembolism. Fever, cough, anorexia, lethargy, weight loss and gastrointestinal disturbance have been reported (9,11,12,17). This dog showed acute anorexia, vomiting, fever, lethargy, tachypnea, and cardiac murmur on history and physical examination. Both infectious cholecystitis and endocarditis might aggravate acute severe systemic sepsis. The diagnosis of endocarditis is based on the echocardiographic findings and blood culture. Representative echocardiographic signs of endocarditis are vegetative aortic or

mitral valves with regurgitant flow. Vegetation is a typically oscillating mass attached to the valvular structures and move independently with valves itself. Vegetation usually results in improper valve coaptation, creating regurgitation (9,11,12, 17). However, differentiation between vegetation and chronic degeneration of mitral valves are difficult. In this dog, obvious vegetation of aortic valves with remarkable aortic regurgitation helped the diagnosis of endocarditis depending on the modified Duke criteria (3). This dog showed remarkable dilation of left atrium (left atrium/aortic root dimension ratio > 2). Left ventricle was also dilated (left ventricular internal dimension on diastole 35.3 mm (normal range of 7.7 kg dog: 19.0–30.8 mm)). Cardiac chamber sizes of infectious endocarditis may be normal to dilated depending on the duration and severity of mitral and aortic regurgitation (4). In this dog, aortic regurgitation was moderate to severe (pressure half time < 300 ms) and mitral regurgitation was severe (dense mitral regurgitation jet, mitral inflow E wave > 1.2 ms, and ratio of mitral regurgitation jet area to left atrium area > 70%). Aortic regurgitation secondary to acute vegetative change may not show left ventricular volume overload (4) whereas severe mitral regurgitation may explain the left atrial dilation. This dog had acute fever and respiratory distress although there were no remarkable signs of left congestive heart failure such as pulmonary congestion and edema on thoracic radiographs. Therefore, this dog was suspected to had mild chronic mitral valve insufficiency with mild dilation of left ventricle and atrium before development of infectious endocarditis. Blood culture needs to confirm echocardiographic findings and helps to determine the most suitable antibiotics. However, previous antibiotic therapy before diagnosis of endocarditis contributes to the reported low prevalence rate of the positive blood culture (9,11,12,17). Unfortunately, blood culture of this case was also negative because prior antibiotic therapy was already given in previous hospital for four days and in this hospital for one day. Urine culture was also normal. On the other hand, *E. coli* was easily identified from cholecystocentesis because the gallbladder might become confined space for micro-organisms and be similar to intra-abdominal abscess. The goal of treatment of endocarditis is to control infection and complications such as congestive heart failure or thromboembolism. Long term antibiotic therapy with broad-spectrum antibiotics recommends. No definitive treatment for valve destruction such as prosthetic valve replacement exists in veterinary medicine. The prognosis depends on the severity of infection and the valves involved. If the aortic valve is affected, the prognosis tends to be poor. Heart failure, embolic complications, and sepsis are highly risky for death (9,11,12,17). This dog was survived with antibiotics treatment from bile culture, bile drainage, antibiotics sensitivity test and aggressive supportive care. Antibiotics were administered for eight months from diagnosis. This report describes intercurrent infections at different sites in the body: infectious cholecystitis and endocarditis. In the case of systemic sepsis, multiple infectious metastasis should be considered. Infectious cholecystitis can be important predisposing or concurrent disease for infectious endocarditis or to the contrary.

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개에서 감염성 담낭염과 동시 발병한 감염성 심내막염 1례

정주현 · 최민철*¹

경기도 고양시 일산동불메디칼센터, *서울대 수의과대학 및 수의과학연구소

요 약 : 12살 중성화 수컷 Miniature Schnauzer 견이 4일 동안 식욕부진, 구토, 기면과 고열로 내원하였다. 혈액 및 혈청검사에서는 백혈구 증가증, 혈소판감소증, 저혈당증, 저알부민혈증, 고빌리루빈혈증, 간효소치의 증가를 보였다. 복부초음파 검사에서 담낭의 고에코성의 불규칙한 벽의 비후 소견이 두드러지고, 심초음파 검사에서 대동맥 및 승모판의 증식성 변화와 역류를 보였다. 초음파유도하에 경피적담낭침자술을 통하여 담즙을 흡인하고 배양하여 *E.coli* 감염을 확인하였다. 따라서 세균성 담낭염과 병발한 심내막염을 진단하였다. 항생제 감수성 검사를 통한 적절한 항생 요법과 적극적인 입원 치료를 통하여 패혈증에서 회복이 되었다.

주요어 : 담낭염, 개, 심초음파, 심내막염