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CASE REPORT
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Biliary Peritonitis in a Dog after Perforation of the Gallbladder during Laparoscopic Cholecystectomy

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ABSTRACT

***Background*:** Iatrogenic gallbladder perforation during laparoscopic cholecystectomy (LC) is a common complication and occurs in at least one third of human patients undergoing LC. This is attributed to the fragility of the gallbladder wall associated with mucocele and cholecystitis, in addition to the need for repetitive gripping and traction of the gallbladder during its manipulation with laparoscopic instruments. As complications from this event are rare in human patients, conversion to laparotomy is not routinely indicated and the adverse consequences of bile spillage are minimized by abundant irrigation of the peritoneal cavity and adequate antimicrobial therapy. On the other hand, there is little information regarding the outcome of laparoscopic management of this complication in laparoscopic cholecystectomies in dogs, particularly since most surgeons indicate conversion in these cases. Thus, we describe a case of biliary peritonitis that developed in a dog after laparoscopic management of iatrogenic perforation of the gallbladder during a laparoscopic cholecystectomy, in a case of gallbladder mucocele. To the best of our knowledge, there are no reports of biliary peritonitis following laparoscopic management of iatrogenic gallbladder perforation during LC in dogs.

***Case*:** A 14-year-old Poodle was referred for clinical evaluation with selective appetite, recurrent episodes of hyporexia, and abdominal discomfort. Ultrasound findings characterized chronic liver disease and gallbladder mucocele. The patient was referred for laparoscopic cholecystectomy, during which the gallbladder was iatrogenically perforated, with extravasation of a large volume of bile content. This complication was managed by copious abdominal irrigation via laparoscopic access and antimicrobial therapy. On the second postoperative day, the patient started to present apathy, hyporexia, emesis, and jaundice. The patient remained hospitalized in the intensive care unit for stabilization and monitoring through hematological examinations and serial abdominal ultrasound. Due to progressive worsening of the clinical picture, an exploratory laparotomy was performed ten days after the initial surgical procedure. This examination showed multiple adhesions and the presence of bile residues adhered to numerous points on the peritoneal surface and pancreas. Despite the intensive treatment instituted, death occurred 10 h after the second surgical procedure.

***Discussion*:** The high risk of gallbladder perforation during laparoscopic cholecystectomies correlates with the dissection step or repetitive grasping and traction of the gallbladder with laparoscopic instruments. Conversion is not routinely indicated and laparoscopic management is considered effective in humans. However, in this case, the presence of a large volume of extravasated semisolid bile content and its adherence to the mesothelial surface made it impossible to remove it in its entirety despite the abundant irrigation of the abdominal cavity, resulting in a picture of biliary peritonitis in the postoperative period. In view of the reported negative outcome, the authors encourage the adoption of measures that minimize the risk of gallbladder perforation when performing LC in dogs. These include the use of atraumatic instruments or aspiration of bile content before surgical manipulation. Cases in which such a complication is recorded should be carefully monitored to enable early diagnosis and treatment of biliary peritonitis. Furthermore, conversion should be considered when there is extravasation of large volumes of bile, particularly in the presence of gallbladder mucocele, until future studies establish the safety and effectiveness of laparoscopic management of this complication.

Keywords: gallbladder mucocele, minimally invasive surgery**,** laparoscopic cholecystectomy, dogs.

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INTRODUCTION

Laparoscopic cholecystectomy (LC) is the standard treatment for benign gallbladder disease [25]. Despite the benefits of this minimally invasive technique, few studies address the results of LC in the canine species [11,15,22,23]. Iatrogenic gallbladder perforation is common and occurs in at least one third of all human patients undergoing LC [1]. Given that complications from this event are rare, conversion to laparotomy is not routinely indicated [20]. In addition, the adverse consequences of bile spillage are minimized by abundant irrigation of the peritoneal cavity and adequate antimicrobial therapy [21]. On the other hand, the veterinary literature shows divergent approaches on the management of this complication. Among the few published case series, some authors indicate conversion at the slightest sign of biliary tract rupture [15,22,23], while others describe satisfactory results for laparoscopic management of both pre-existing ruptures and iatrogenic gallbladder perforations [11]. To the authors' knowledge there are no reports of biliary peritonitis following laparoscopic management of iatrogenic gallbladder perforation during LC in dogs. In cases that described biliary peritonitis as a postoperative complication of LC in this species, surgical reintervention revealed extrahepatic bile duct injury [11,22]. The present report describes a case of biliary peritonitis after laparoscopic management of iatrogenic gallbladder perforation during laparoscopic cholecystectomy in a dog with gallbladder mucocele.

CASE

A 14-year-old Poodle was referred for clinical evaluation, presenting with selective appetite and having had recurrent episodes of hyporexia and abdominal discomfort within the past 3 years. Previous ultrasound findings characterized chronic liver disease and a large volume of biliary sludge. The patient was under therapy with manipulated ursodeoxycholic acid [15 mg/kg/PO] for 3 years, and with manipulated silymarin [30 mg/kg/PO], manipulated S-adenosylmethionine (SAME) [20 mg/kg/PO], and therapeutic diet[1] [Royal Canin Gastrointestinal Low Fat©] for 1 year. Despite clinical treatment, the condition progressed to gallbladder mucocele, as diagnosed in the most recent ultrasound examination. The patient was thus referred for laparoscopic cholecystectomy.

After anesthetic induction and orotracheal intubation, anesthetic maintenance was performed with isoflurane[2] (Isoforine®) vaporized in oxygen. Laparoscopic cholecystectomy with three portals was performed by a surgeon at an early stage of the learning curve. The first portal, measuring 11 mm[3], was positioned in the midline, 1 to 2 cm caudal to the umbilicus, using an open technique. After introducing a 10 mm and 0º endoscope[3] into the abdominal cavity, pneumoperitoneum was established with carbon dioxide (CO_2) at a maximum pressure of 10 mmHg and a speed of 1.5 L/min. Two additional portals were established under laparoscopic guidance, both paramedian and cranial to the first portal. The second portal, also measuring 11 mm[3], was introduced in the left lateral abdominal quadrant, and the third portal, of 6 mm[3], in the right lateral abdominal quadrant. The portal on the right of the midline was used for retraction and exposure of the gallbladder and cystic duct, while the one on the left was used for dissection maneuvers, clipping, and tissue transection.

Gallbladder mobilization from the fundus region was performed with a 5 mm[3] laparoscopic Kelly forceps (Figure 1A). The cystic duct and cystic artery were dissected, isolated, and occluded using a 5 mm[4] right angle laparoscopic forceps and applying four 10 mm titanium hemostatic clips through a laparoscopic clipper[5]. Transection of the cystic duct between the distal and proximal clips was performed with 5 mm[2] laparoscopic Metzenbaum scissors. During the stage of dissection of the gallbladder from the liver bed, leakage of biliary content occurred from a perforation located at the point of gallbladder grasping. Given the impossibility of applying titanium clips to the rupture point (Figure 1B) due to the high degree of gallbladder distension, the site was temporarily occluded using Kelly forceps[3].

After completely released, the gallbladder was removed from the abdominal cavity, pulled together with the 11 mm portal positioned in the midline. Four samples of liver tissue were obtained for histopathological examination, and complete abdominal irrigation was performed with 0.9% sodium chloride solution, at the proportion of 1.2 L/kg of body weight. This procedure was followed by aspiration of the lavage fluid using a laparoscopic irrigation and suction cannula. After verifying the apparent absence of biliary content and hemorrhage, the abdomen was decompressed by releasing CO2 and the surgical accesses were oc-

cluded in 3 planes. The patient was discharged from hospital within 12 h of the surgical procedure with the prescription of sodium dipyrone[6] [Dipirona® - 25 mg/kg, VO, TID for 4 days] and tramadol hydrochloride[7] [Cronidor® - 4 mg/kg, VO, TID for 2 days], meloxicam[8] [Maxicam® - 0.1 mg/kg, VO, SID for 3 days], enrofloxacin[9] [Baytril® - 2.5 mg/kg, VO, BID for 7 days] and metronidazole[6] [Metronidazol® - 15 mg/kg, VO, BID for 7 days], in addition to the aforementioned protocol (ursodeoxycholic acid, silymarin, and SAME). Histopathological report confirmed the presence of mucinous cystic hyperplasia and mucocele for the gallbladder sample, and moderate diffuse cholestasis in the liver samples. The bile content was submitted to bacterial culture, showing no growth after 48 h of incubation.

On the 2nd postoperative day, the patient started to present apathy, hyporexia, vomiting, and jaundice, being thus admitted to a private veterinary clinic for reassessment and monitoring. With the exception of the nonsteroidal anti-inflammatory drug, the same medications mentioned at the time of discharge were prescribed, which should be administered by parenteral route. Maintenance fluid therapy was instituted, with the addition of omeprazole[10] [Omeprazol® - 1 mg/kg, IV, SID for 5 days] and maropitant citrate[11] [Cerenia® - 1 mg/kg, SC, SID for 3 days]. On the 3rd postoperative day, the patient was active, without jaundice or episodes of emesis and with a restored appetite, being discharged from hospital on the 4th postoperative day.

On the 5th postoperative day the patient returned to the referral hospital presenting with neurological signs, characterized by ataxia and a report of a seizure episode. In view of this, the administration of metronidazole[6] was suspended and the patient was referred to the intensive care unit for stabilization. Blood samples were collected and the blood count revealed anemia, hematocrit 23% (reference range 37-55%) and neutrophilic leukocytosis 26,796 μL (reference range 2,700-9,400 μL) with a left shift 308 μL immature neutrophils (reference range 0-100 μL), as well as elevated values for alanine aminotransferase enzyme 1,542 IU/L (reference range 17-95 UI/L) and alkaline phosphatase 1,806 IU/L (reference range 7-115 UI/L). Abdominal ultrasound revealed the presence of moderate mesenteric reactivity in the right cranial epigastric region and findings compatible with acute pancreatitis. No changes were detected in the caliber and course of the hepatic ducts and common bile duct, with the occurrence of free fluid in such a small amount that it was impossible to collect it by abdominocentesis. Ceftriaxone[10] [Ceftriaxona sódica® - 30 mg/kg, IV, BID] was prescribed in addition to dipyrone[12] [Dipirona Ibasa® - 25 mg/kg, IV, TID], cloridrato de tramadol[7] [Cronidor® - 4 mg/kg, IV, TID], enrofloxacin[13] [Chemitril® - 2.5 mg/kg, IV, BID], omeprazole[10] [Omeprazol® - 1 mg/kg, IV, SID for 5 days], maropitant citrate[11] [Cerenia® - 1 mg/kg, SC, SID], ursodeoxycholic acid, silymarin, and SAME at the same doses and frequencies previously mentioned.

The patient remained under monitoring and intensive care, demonstrating resolution of neurological signs on the 7th postoperative day. On the 8th postoperative day a blood transfusion was performed to correct anemia. The patient remained stable until the ninth postoperative day, when it started to experience hyporexia, diarrhea, and marked prostration. Although the findings of serial ultrasound examinations did not show significant changes, subsequent laboratory tests reflected changes consistent with worsening of the clinical picture, whit high neutrophilic leukocytosis (49,810 μL) whit a left shift (2,930 μL) and persistent elevation of liver enzymes. The patient was referred for exploratory celiotomy on the 10th postoperative day, in which biliary content appeared to be adhered to the pancreatic surface and to numerous points on the mesothelial surface (Figure 2A, 2B & 2C). The analyses did not identify extravasations from the cystic duct ligation site or from rupture of other extrahepatic bile ducts. The abdominal cavity was irrigated with 0.9% sodium chloride solution, at a rate of 1 L/kg, followed by aspiration of the lavage fluid. After careful inspection and removal of part of the greater omentum and biliary concrements adhered to the visceral and parietal peritoneum, an abdominal drain was placed and the abdominal cavity was synthesized in three planes.

Hemodynamic parameters were unstable during exploratory celiotomy and during the immediate postoperative period, in which the patient remained under monitoring in the intensive care unit. Despite the care taken, 10 h after the 2nd surgical procedure the patient had a cardiorespiratory arrest and died despite resuscitation maneuvers.

DISCUSSION

Despite the numerous benefits of the laparoscopic approach, it appears to have a higher risk of

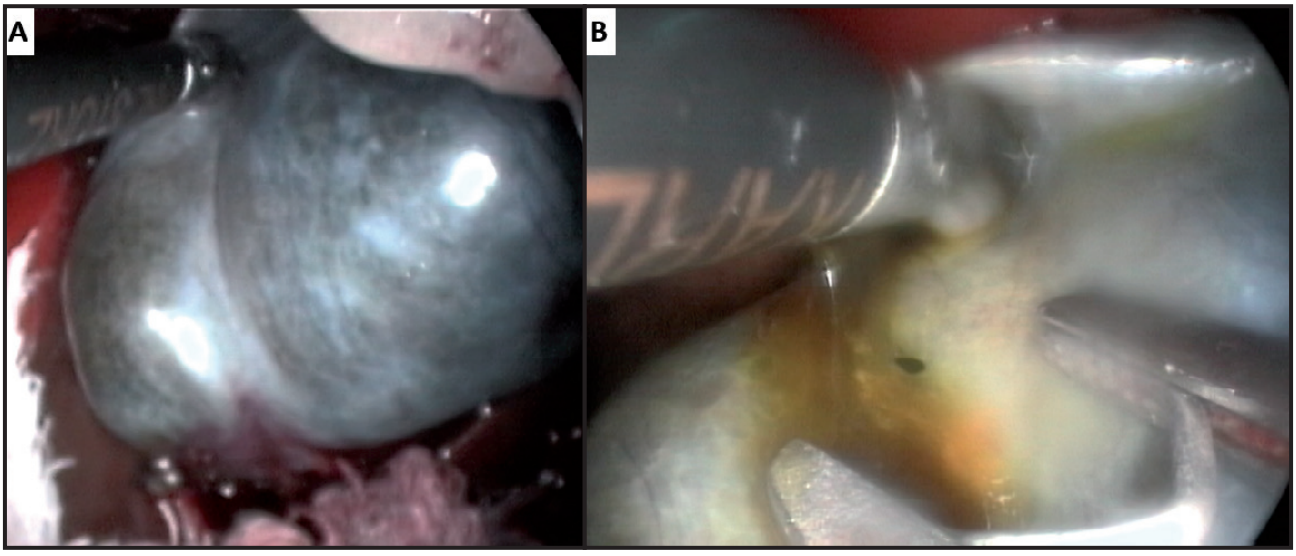

Figure 1. Intraoperative view of the laparoscopic cholecystectomy in a dog with gallbladder mucocele. A- Gallbladder showing a high degree of distension, grasped with laparoscopic forceps before perforation. B- Attempt to occlude the puncture point by applying a titanium clip with a laparoscopic clipper.

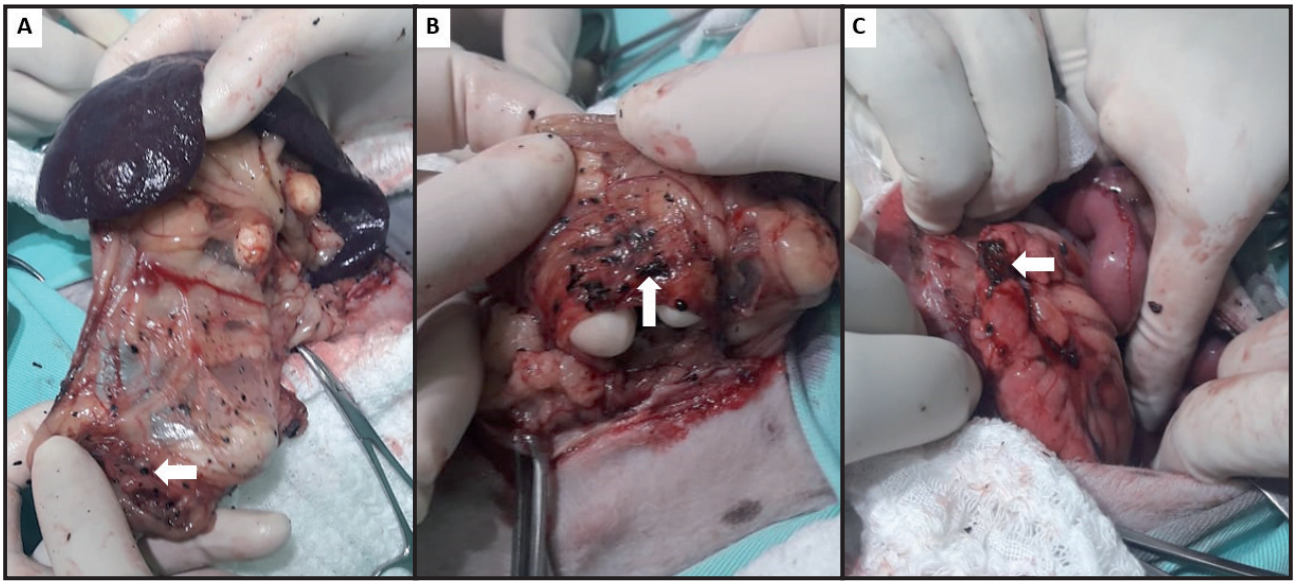

Figure 2. Intraoperative view of the surgical reintervention, showing several residues of biliary content adhered (arrow) to the greater omentum (A & B) and pancreas surface (C).

gallbladder perforation in relation to open cholecystectomy in humans [1]. This is a relatively common intraoperative complication, with prevalences ranging from 13% to 50% of LC procedures [17]. For the canine species, the few published studies recorded this complication in 6% [23] to 21% [11] of LC cases, in contrast to prevalences that range from 3% [18] to 7% [14] in open cholecystectomies. The high percentage of cases thus characterized can be attributed to the need for repetitive grasping and traction of the gallbladder during its manipulation with laparoscopic instruments [12,21,24]. A study evaluating LC in humans described this procedure as the cause of gallbladder rupture in up to 75% of cases [3]. It was also the cause of the perforation in the present case, which can be explained by the recognized fragility of the gallbladder wall in cases of mucocele [2,10], particularly when associated with a high degree of gallbladder distension, as observed in the patient in question.

Notwithstanding, inadvertent penetration of the gallbladder wall during its dissection remains the most frequent cause of iatrogenic gallbladder perforation in LC [1,20,21,24]. Loss of definition of the cleavage plane between the gallbladder and the liver bed in the presence of chronic or acute inflammatory lesions [4], as well as lesions resulting from the use of electric scalpel [12,20], are the main causes of rupture at this surgical stage. In the present case, dissection was

performed without the use of electrosurgical current, which may have minimized the risk of perforation. In any case, such data justify the need for special attention to these stages of the LC procedure, which should be emphasized during the training period of surgeons.

With a view to minimize the risk of gallbladder perforation, the literature proposes technical modifications and new methods of dissection of the gallbladder from the liver bed [24]. In this sense, authors recommend the use of blunt instruments, such as retractors [22], or the use of surgical sponges or gauzes attached to the tips of laparoscopic forceps [11] to manipulate the gallbladder during surgical maneuvers. Other authors also indicate the use of atraumatic instruments and forceps with wider surfaces [3,4]. The use of a laparoscopic Kelly forceps (whose tip is sharp) for grasping and traction of a gallbladder with a high distension degree - and therefore subject to necrosis by intraluminal pressure - was defined as a determining factor for the occurrence of iatrogenic perforation in the procedure reported here.

In the authors' experience, another modification of the standard technique that is routinely used with excellent effectiveness, although not performed in the case described, consists of reducing gallbladder intraluminal pressure before dissection by transparietal aspiration of its contents under laparoscopic guidance. In a prospective randomized study involving human patients with cholelithiasis, this procedure significantly reduced the risk of iatrogenic perforations, as well as operative time and hospital stay, without resulting in complications [6]. Although we can assume that aspiration prior to gallbladder dissection could have avoided gallbladder perforation, it is important to note that the feasibility of this procedure is to some extent conditioned by the consistency of the bile. In the present case it could be ineffective in the face of the semisolid content characteristic of advanced mucoceles.

The indication of conversion to laparotomy in the face of iatrogenic gallbladder perforation remains controversial in the veterinary literature and was not performed in this case. Within the few published case series, most authors indicate conversion to open surgery at the slightest sign of biliary tract rupture [15,22,23], while others report positive results with laparoscopic management of such a condition [11]. Otherwise, given that complications resulting from this event are rare in humans, conversion to laparotomy is not routinely indicated [20], even in the impossibility of removing gallstones from the abdomen [12,17,21].

Several studies involving LC series in humans demonstrate that the adverse consequences of gallbladder perforation can be minimized by occlusion of the perforation point and immediate recovery of the extravasated contents, followed by abundant irrigation of the peritoneal cavity and adequate antimicrobial therapy [1,3,4,12,21,24]. Kanai *et al*. [11] described the aforementioned laparoscopic management, adopted in the present case, as satisfactory in 16 cases of iatrogenic gallbladder perforation during LC in dogs, resulting in no postoperative complications. These results contrast with the outcome of the case reported here and comparisons in this regard are limited, since the authors do not characterize which diseases involved the gallbladder in these events, nor do they detail the magnitude of the bile extravasation that occurred. Likewise, the comparison of data with studies mentioning laparoscopic management of this condition in humans should be interpreted with caution, as these studies predominantly involved cases of cholecystitis and cholelithiasis. In both these diseases, the consistency of the extravasated content does not correspond to the gelatinous or semisolid bile characteristic of gallbladder mucoceles, which could result in greater effectiveness of the procedures for recovering the extravasated content and irrigating the peritoneal cavity in relation to our study case.

Another possible explanation for the differences in the results is the use of abdominal drains [4,11,12,24], which was not adopted in the present case. As pointed out by the aforementioned authors, the placement of drains close to the hepatic fossa and their maintenance during different periods in the postoperative period seems to be an effective measure in reducing postoperative morbidity in the face of leakage of biliary content into the abdominal cavity. Based on this experience, the authors state that in cases of extravasation of large volumes of bile, particularly in cases of mucocele with semisolid content, the possibility of conversion should be considered for adequate removal of the extravasated content, as well as evaluating the need for placement of abdominal drains for postoperative management.

Despite the high frequency of intraoperative gallbladder perforation in LC in humans, the overall risk of complications in the immediate or long-term

postoperative period is low [4,12,20], with reports of prevalences ranging from 0.02% [3] to 2.9% [20]. These studies do not mention biliary peritonitis among the complications attributed to gallbladder perforation, which in turn include intraperitoneal abscess, fistula formation, and small bowel obstruction secondary to adhesions [3,20]. It should also be noted that all the complications mentioned correlate with the presence of gallstones not removed from the abdominal cavity. In the present case, despite the copious irrigation of the abdominal cavity and the apparent effectiveness of the procedure upon laparoscopic inspection, the adherence of semisolid biliary content to the omentum and mesothelial surface made it difficult to remove it in its entirety, which contributed to the evolution of the condition to biliary peritonitis in the postoperative period. Although 2 other studies on LC in dogs have also described biliary peritonitis, these cases were not preceded by intraoperative bile extravasation, and surgical reintervention revealed injury to the remaining cystic duct [11] or hepatic ducts [22]. The present case showed no similar damage to the bile ducts or displacement of cystic duct clips during surgical reintervention.

Bile constituents are cytotoxic, induce tissue inflammation, and alter vascular permeability, which results in fluid transudation and translocation of endogenous anaerobic bacteria from the liver, intestines, and blood to the abdominal cavity and bloodstream [7,16]. This predisposes the organism to systemic inflammatory response, as well as sepsis and multiple organ dysfunction [10]. Despite the recognized severity of biliary peritonitis, its clinical course is often masked by the presence of vague and nonspecific clinical signs [13]. This usually results in prolonged clinical courses and makes diagnosis challenging. In addition to the nonspecific clinical signs presented by the patient and the conviction of the effectiveness of laparoscopic management in resolving the complication, some confounding factors delayed the diagnosis of postoperative biliary peritonitis in the present case. The persistently high activity of serum liver enzymes, as shown in the biochemical analysis of the patient, was already reported for the period after LC in dogs [15]. The authors attributed this finding to factors related to anesthesia, direct or indirect effect of pneumoperitoneum, as well as diffuse cholestasis (identified in liver samples). Moreover, ultrasound examination showed evidence of acute pancreatitis, which is one of the potential complications of cholecystectomy in dogs [14,22,26,27], described as a component of the so-called postcholecystectomy syndrome, which refers to abdominal pain in patients after gallbladder removal [9].

Although abdominal ultrasound is the most used tool for the diagnosis of biliary peritonitis due to gallbladder rupture [5,8,10,19,27], some studies report its questionable sensitivity (56.1%) [10] and low specificity (44.4%) [13]. The presence of a moderate echogenic reaction near the gallbladder fossa, as identified in the postoperative ultrasound examination of the patient, is a finding consistent with biliary peritonitis [8]. However, we initially related this finding to tissue inflammation resulting from recent surgical manipulation of the tissues of this region. Furthermore, sample collection by abdominocentesis was made impossible by the small volume of free fluid identified in the exam. The analysis of bilirubin in this sample is currently the most useful tool in the diagnosis of biliary peritonitis [26]. It is noteworthy that, in the impossibility of performing abdominocentesis, diagnosis can be made by means of peritoneal lavage with a dialysis catheter [13].

Studies have consistently related gallbladder rupture to mortality, so dogs that experience such a complication at the time of surgery are 2.7 times more likely to die [10]. Among the parameters under study, high peripheral leukocyte count was the most consistent marker of worsening of the clinical condition of the patient. This is one of the factors that significantly affect the survival of patients with biliary peritonitis [13]. The presence of septic bile can also significantly affect survival, as bile salts impair local host defense mechanisms and reduce phagocytic activity, aggravating *Escherichia coli* peritonitis [8,13]. Although we did not isolate bacteria from the patient's bile culture, the prophylactic antimicrobial therapy performed may be considered a confounding factor, as suggested by other studies [14,19]. Given that positive bacterial cultures are detected in the bile in up to 66.7% of cases of mucocele in dogs [5], antimicrobial therapy was instituted in the face of gallbladder perforation while awaiting the result of the culture. The established protocol included the combination of antimicrobial agents efficacious against gram-negative aerobes (fluoroquinolones) and anaerobes (metronidazole), as the literature indicates both these organisms in cases of biliary peritonitis [13].

The definitive treatment for biliary peritonitis is laparotomy for decontamination and resolution of the underlying cause [26]. Although the duration of sterile biliary effusion before surgical treatment is not a factor that significantly affects survival [13], we believe that early surgical intervention after initial stabilization of the patient could have a positive impact on survival. In view of the negative outcome described in this report, the authors encourage the adoption of measures that minimize the risk of gallbladder perforation when performing laparoscopic cholecystectomy in dogs. Cases in which such a complication is recorded should be carefully monitored for early diagnosis and surgical treatment of biliary peritonitis. Furthermore, conversion should be considered when there is extravasation of large volumes of bile, particularly in the presence of gallbladder mucocele, until future studies establish the safety and effectiveness of laparoscopic management of this complication.

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