FULL ARTICLE

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Ultrasonographic aspects of the gallbladder mucocele in 30 dogs: retrospective study

Aspectos ultrassonográficos da mucocele biliar em 30 cães: estudo retrospectivo

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ABSTRACT
Gallbladder mucocele is characterized by hyperplasia of the gallbladder epithelium, increased mucus production, accumulation, and densification of the bile content, which can lead to biliary obstruction, necrosis, and rupture of the gallbladder wall. Its finding may be accidental or related to symptoms. A retrospective study (2016-2019) was carried out based on abdominal ultrasound examinations in dogs, correlating aspects of the gallbladder and biliary system in the mucocele with existing comorbidities. Thirty dogs diagnosed with biliary mucocele were evaluated, of which 46.66% had the disease at an early stage, and 53.33% showed a more advanced stage. Of these, 66.66% were related to endocrinopathies and hyperadrenocorticism. Signs of extrahepatic bile duct obstruction and biliary peritonitis were observed in two animals. Due to their potential risk of complications, follow-up ultrasound assessments are indicated in cases that opt for clinical treatment, not excluding the need for surgical intervention.
Keywords: Gallbladder. Ultrasound. Endocrinopathies. Canine.

RESUMO
A mucocele biliar caracteriza-se pela hiperplasia do epitélio da vesícula biliar, aumento da produção de muco, acúmulo e densificação do conteúdo biliar, podendo levar à obstrução, necrose e ruptura da parede da vesícula biliar. Seu achado pode ser acidental ou estar relacionado à sintomatologia. Foi realizado um estudo retrospectivo (2016-2019) a partir de exames ultrassonográficos abdominais em cães, correlacionando os aspectos da vesícula biliar na mucocele, com comorbidades existentes. Foram avaliados 30 cães com diagnóstico de mucocele biliar, dos quais 46,66% apresentaram a doença em estágio inicial e 53,33% demonstraram estágio mais avançado. Destes, 66,66% tinham endocrinopatias, principalmente hiperadrenocorticismo. Sinais de obstrução de vias biliares extra-hepáticas e peritonite biliar foram observados em dois animais. Por seu potencial risco de complicação, avaliações ultrassonográficas de seguimento são indicadas nos casos de tratamento clínico, não se descartando a necessidade de intervenção cirúrgica.
Palavras-chave: Vesícula biliar. Ultrassom. Endocrinopatias. Canino.

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Introduction

Gallbladder mucocele is characterized by hyperplasia of the gallbladder epithelium and increased mucus production, which leads to excessive mucus accumulation, which can lead to densification of the biliary content, progressive distention of the gallbladder and wall necrosis (Figure 1) (Pike et al., 2004).

The clinical importance of mucocele is mainly related to the risks of infection/inflammation, extrahepatic biliary obstruction, and rupture of the gallbladder wall (Baker et al., 2011; Jaffey et al., 2018).

Gallbladder mucocele (GBM) has been an increasingly frequent finding in routine abdominal ultrasound examinations in dogs (Choi et al., 2014). It occurs more frequently in elderly animals aged 10 years old on average (Besso et al., 2000; Malek et al., 2013; Pike et al., 2004). Several breeds have been reported to be predisposed to GBM formation, including Cocker Spaniel, Shetland Shepherd, Miniature Schnauzer, Pomeranian, and Chihuahuas (Aguirre et al., 2007; Besso et al., 2000; Cook et al., 2016; Jaffey et al., 2019; Malek et al., 2013).

Affected animals may show nonspecific clinical signs of systemic disease, such as vomiting, lethargy, and anorexia (Besso et al., 2000; Malek et al., 2013; Pike et al., 2004). However, in some cases, the detection of mucocele is incidental during the ultrasound examination to look for other conditions (Jaffey et al., 2019).

Although its etiopathogenesis remains unknown, a multifactorial cause is postulated, and several studies have suggested dyslipidemia and endocrine disorders, including hyperadrenocorticism and hypothyroidism, as risk factors (Kutsunai et al., 2014; Lee et al., 2019; Mesich et al., 2009). Other factors that may be related to mucocele formation include the change in bile acid concentration, leading to reduced fluid secretion into the lumen (Kakimoto et al., 2017); alteration of gallbladder motility, increasing bile retention (Tsukagoshi et al., 2012).

An abdominal ultrasound is a sensitive diagnostic tool for the identification of GBM (Worley et al., 2004), characterized by the presence of dense bile content and greater echogenicity, which is immobile regardless of severity or patient positioning (Besso et al., 2000; Choi et al., 2014). The sonographic aspect of mucocele was described in two studies, according to its evolution (Besso et al., 2000; Choi et al., 2014).

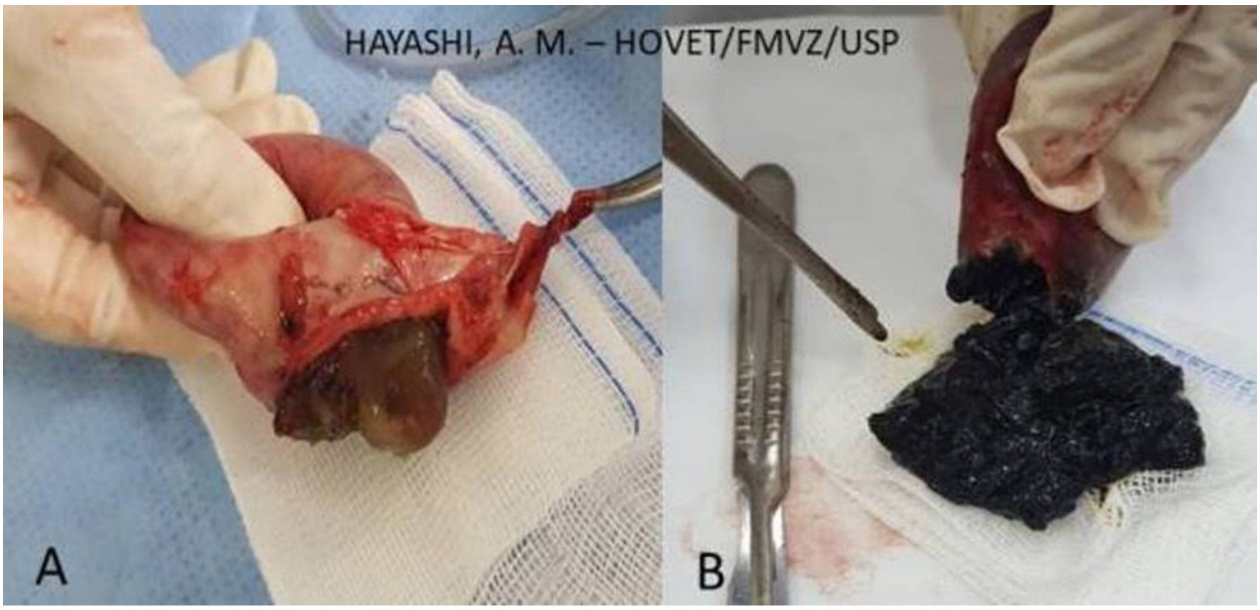


Figure 1 – Macroscopic appearance of gallbladders with mucocele. **A**, the thickened gallbladder wall and more mucous bile content are observed. **B**, Changed wall color and appearance of denser and more organized biliary content. File provided by: Dr. Ayne Hayashi. Source: HOVET Surgery Service at FMVZ-USP (2019).

One of them described five stages, taking into account the appearance of the biliary content and the distention of the organ: type I, echogenic immobile bile wholly occupying the gallbladder; type II, hypoechoic bile surrounding the wall and central echogenic content; type III, stellate pattern with a more significant amount of hypoechoic bile contiguous to the wall and central echogenic bile; type IV, kiwi fruit-like pattern combined with the stellate pattern with presence of finer echogenic striations in the hypoechoic bile surrounding the wall; type V, kiwi fruit-like pattern with a large amount of echogenic, centralized, amorphous bile associated with large gallbladder distention; type VI, kiwi fruit-like pattern, without the presence of residual central bile (Choi et al., 2014).

Ultrasonographic signs of GB rupture may include wall discontinuity, focal free fluid, and increased echogenicity of adjacent tissue. However, ultrasonographic changes may not occur when small or recent ruptures occur (Besso et al., 2000; Jaffey et al., 2018). Some studies tried to correlate the staging of mucocele based on ultrasonographic aspects with the patient's clinical status and the increased risk of gallbladder rupture. However, no correlation was found (Besso et al., 2000; Choi et al., 2014). GB rupture and biliary peritonitis during surgery are related to high mortality in dogs with mucocele (Jaffey et al., 2018; Mehler et al., 2004; Parkanzky et al., 2019). Cholecystectomy and cholecystoduodenostomy are the two surgical techniques indicated in the treatment of complicated GBM with evidence of biliary obstruction or rupture of the gallbladder wall (Ludwig et al., 1997; Mehler et al., 2004; Worley et al., 2004).

The present study aimed to evaluate the different sonographic aspects of bilair mucocele, associating it with the clinical history of the affected dogs.

Material and Methods

A retrospective study was carried out from January 2016 to January 2019 based on the ultrasound reports of abdominal examinations in dogs performed at the diagnostic imaging service of a veterinary teaching hospital.

Data were collected from the Microsoft Office Access system, using a field intended for ultrasound alterations with the keyword "gallbladder." The ultrasound images were retrieved from the medical image storage system, Picture Archiving Communication System (PACS).

After selecting the exams of dogs with GBM, the medical records were analyzed to obtain data regarding symptoms, physical and laboratory exams (complete blood count, serum levels of the ALT, AST, GGT, and FA enzymes, suppression with dexamethasone, stimulation test with ACTH, free T4 and TSH).

Regarding the ultrasonographic aspect of the gallbladder content, it was considered GBM in its initial stage when dense echogenic material was observed with hypoechogenic areas of permeate (mucus) occupying the gallbladder (Figure 2A). It was considered GBM in a more advanced stage when central echogenic material (Figure 2B) and echogenic striations adhered to the wall, stellated aspect, or kiwi fruit-like were observed (Figure 1C and 1D), adapted from (Choi et al., 2014). From type IV, according to Choi, similar to the kiwi fruit, the ultrasonographic aspect becomes quite similar, and this differentiation is often difficult.

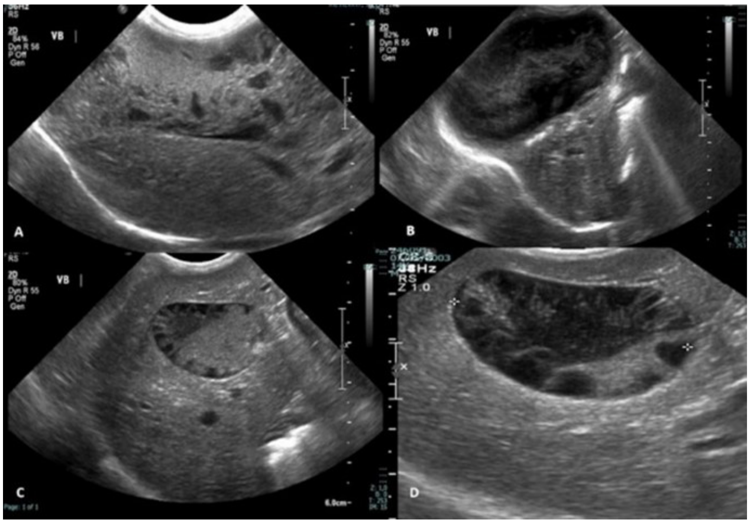


Figure 2 – Ultrasonographic images illustrating patterns I to IV and the progression of stages of biliary mucocele. **A**, Type I: dense echogenic bile with intervening hypoechoic areas (mucus) wholly occupying the GB. **B**, Type II: incomplete stellate pattern, with hypoechoic bile surrounding the wall and central echogenic bile. **C**, Type III: typical stellate pattern with more hypoechoic bile associated with the wall and central echogenic bile. **D**, Type IV: Kiwi fruit-like pattern associated with stellate pattern with finer echogenic striations in the hypoechoic bile surrounding the wall. Source: FMVZ-USP HOVET Diagnostic Imaging Service (2019).

ALT Philips, model HDI 5000 Sono-CT, was used for the ultrasound exams. It carries two multifrequency convex transducers from 2 to 5 MHz and 4 to 7 MHz and a linear transducer from 7 to 12 MHz. Philips, model Affiniti 70, with transducers linear (5 to 18 MHz), microconvex (5 to 8 MHz), and convex (1 to 5 MHz) multifrequency was also used.

Results

In 3 years, 2695 abdominal ultrasound examinations were performed in dogs, of which 290 dogs (10.76%) showed some changes in the gallbladder. Of these, 30 dogs (10.34%) had sonographic changes compatible with GBM.

Of the dogs with mucocele, 20/30 (66.66%) were female, and 10/30 (33.33%) were male.

The age of the animals ranged from 8 to 16 years old, with 12 years being the mean and median.

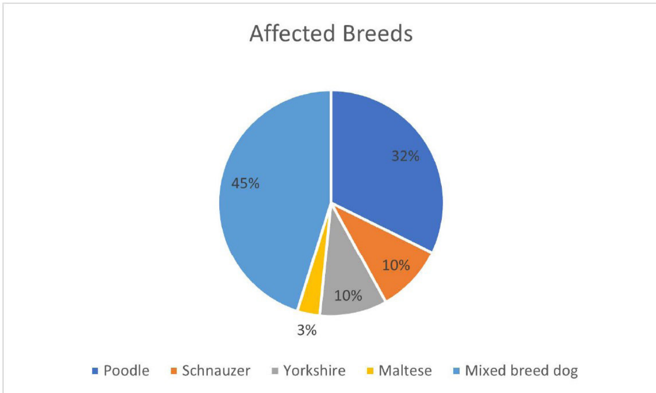
The affected breeds were Poodle 10/30 (33.33%), Schnauzer 3/30 (10.00%), Yorkshire 3/30 (10.00%), Maltese 1/30 (3.33%), and Mixed Breed Dogs 5/30 (16.66%) (Graphic 1).

Of the animals studied, 14/30 (46.66%) showed an early stage of GBM, and 16/30 (53.33%) showed a more advanced stage.

Wall alterations, gallbladder distention, presence of cystic duct and intra and extrahepatic bile duct dilatation, and pericholecystic alterations were correlated with the stage of the mucocele. Of the early-stage GBM, 2/14 (14.28%) showed gallbladder wall thickening, and 3/14 (21.42%) showed accentuated gallbladder repletion. In the advanced stage, 2/16 (12.50%) showed wall thickening, 6/16 (37.50%) showed accentuated gallbladder repletion, 2/16 (12.50%) showed cystic duct distention, 1/16 (6.25%) showed dilated of the common bile duct (> 0.3cm) and 1/16 (6.25%) increase in echogenicity and free fluid in the pericholecystic region (Table 1).

Of the 30 GBM, 20 (66.66%) were related to pre-existing endocrinopathies; 18 animals had hyperadrenocorticism (HAC), one had hypothyroidism (HT), and one had diabetes mellitus (DM). In 9 (32.14%), there was clinical suspicion of endocrinopathy, however, without laboratory confirmation, and in one case (0.03%) with multicentric lymphoma.

Animals confirmed with hyperadrenocorticism showed the following hepatic changes observed on ultrasound: hyperechogenic parenchyma, 10/18 (55.55%), coarse echotexture, 6/18 (33.33%) and hepatomegaly, 15/18 (83.33%). The only animal confirmed hypothyroidism showed decreased liver echogenicity and hepatomegaly (Table 2). The patient with diabetes mellitus presented hepatomegaly and increased echogenicity.



Graphic 1 – Affected breeds.

Table 1 – Absolute and relative frequency of the gallbladder mucocele stage and correlation with other ultrasonographic aspects related to the gallbladder and bile ducts

Ultrasonographic aspects of the gallbladder	Absolute Frequency	Relative Frequency	Absolute Frequency	Relative Frequency
	Early stage mucocele		Advanced stage mucocele	
TOTAL	14	46.66%	16	53.33%
Wall thickening	2	14.28%	2	12.50%
Pronounced gallbladder repletion	3	21.42%	6	37.50%
Cystic duct dilatation	-	-	2	12.50%
Dilation of the common bile duct	-	-	1	6.25%
Increased echogenicity/pericollect free liquid	-	-	1	6.25%

Table 2 – Absolute and relative frequency of ultrasound changes in the liver of animals with a confirmed diagnosis of hyperadrenocorticism, hypothyroidism, and diabetes mellitus

Liver changes on the ultrasound examination.	Hyperadrenocorticism		Hypothyroidism		Diabetes Mellitus	
	Absolute Frequency	Relative Frequency	Absolute Frequency	Relative Frequency	Absolute Frequency	Relative Frequency
Hyperechogenicity	10/17	58.82%			1/1	100%
Hypogenicity			1/1	100%		
Coarse echotexture	6/17	35.29%	-	-		
Hepatomegalia	14/17	82.35%	1/1	100%	1/1	100%

Discussion

Among the animals with GBM, most were females (66.66%), corroborating with other studies that showed 60% (219 animals) (Jaffey et al., 2018) of cases occurring in females. However, another multicenter study with 1194 cases of mucocele showed no gender predisposition (Jaffey et al., 2019).

As the animals age, GBM is more frequent, as observed in the present study and described in the literature (Besso et al., 2000; Jaffey et al., 2019; Lee et al., 2019; Parkanzky et al., 2019). Among the breeds affected by GBM, most dogs were poodles. The assessment of the most affected breed varies according to the most frequent breed reproduction in the region, with a wide variation between different studies (Aguirre et al., 2007; Besso et al., 2000; Cook et al., 2016; Jaffey et al., 2019; Malek et al., 2013). In the study with 1194 dogs, the most affected breeds in descending order were Shetland Shepherd, Cocker Spaniel, and Miniature Schnauzer (Jaffey et al., 2019).

In this study, we chose to classify mucoceles in early and advanced stages based on the ultrasonographic aspect, adapting what was proposed by some authors who describe six types (Choi et al., 2014). From type IV on, the ultrasonographic appearance becomes quite similar. Thus, this differentiation is often difficult. Most animals had a more advanced GBM stage, directly correlating with gallbladder dilation (Besso et al., 2000). Only four animals showed wall thickening, two at an early stage and two at an advanced stage. In the present study, there is no difference in the thickness of the biliary wall about the grades of classification since the thickness of the wall varies according to its distention (Feeney et al., 2008; Hittmair et al., 2001). Obstruction of the extrahepatic bile ducts was evidenced in an animal with a more advanced stage of the disease. In the only dog in which gallbladder rupture was detected, the ultrasonographic aspect of the mucocele was consistent with an early stage. Similarly, in a study that classifies the staging of mucocele, gallbladder rupture was statistically more common in type II (early stage), showing no relation with staging and the probability of rupture.

The incidence of GB wall rupture associated with mucocele in dogs has yet to be discovered due to the limited data in the literature (Jaffey et al., 2018). However, its prevalence ranged from 21.4% to 60.9% in previous studies (Jaffey et al., 2018; Pike et al., 2004). The sensitivity of B-mode ultrasound in detecting necrosis and small ruptures of the gallbladder wall reported was 56%. In a more recent study, ultrasound exams using contrast showed 100% sensitivity and specificity in the identification of necrosis and rupture of the gallbladder wall in dogs, proving to be a complementary tool to the conventional method in cases of suspected gallbladder diseases, including edema, necrosis, and rupture (Bargellini et al., 2018).

The diagnosis of rupture is usually made indirectly from other ultrasonographic evidence, such as increased echogenicity of pericholecystic fat and adjacent free fluid accumulation (Figure 3) (Besso et al., 2000; Choi et al., 2014; Malek et al., 2013).

The endocrinopathies confirmed and correlated with GBM were hyperadrenocorticism, diabetes mellitus, and hypothyroidism, representing a much larger number of patients with hyperadrenocorticism, corroborating the literature (Cook et al., 2016; Jaffey et al., 2019; Lee et al., 2019; Mesich et al., 2009).

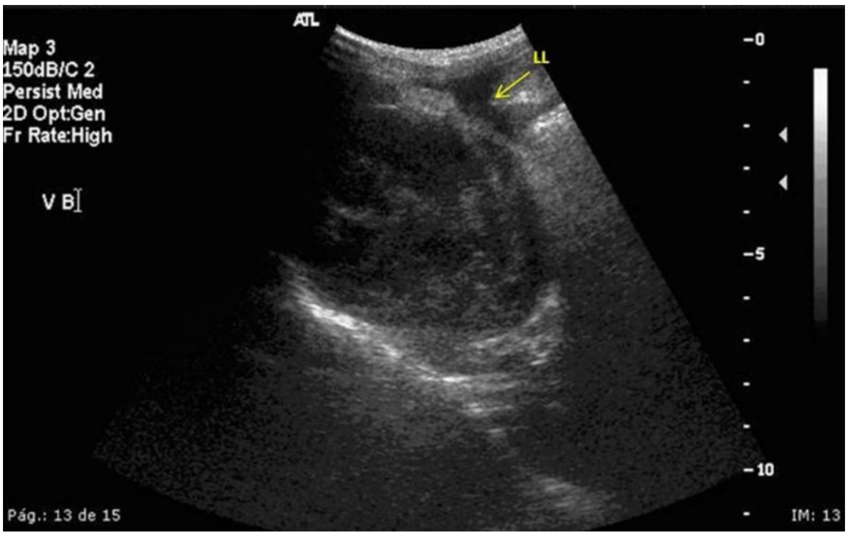


Figure 3 – Ultrasonographic image of a dog's gallbladder with signs of rupture. Pronounced repletion by more echogenic content, occupying the entire gallbladder lumen, increased echogenicity, and free fluid (LL) in the pericholecystic region (yellow arrow). Source: FMVZ-USP HOVET Diagnostic Imaging Service (2017).

Several studies suggest a relationship between pituitary-dependent hyperadrenocorticism (PDH) and mucocele (Aicher et al., 2019; Lee et al., 2019, 2017; Mesich et al., 2009). A retrospective study showed that a considerable number of dogs with mucocele had endocrinopathies and that the probability of a dog with HAC having a mucocele is 29 times higher than that of a healthy dog (Lee et al., 2019; Mesich et al., 2009). Another study demonstrated that dogs with PDH and cholestatic disease, including mucocele, have higher cortisol levels after ACTH stimulation and more severe clinical signs than dogs without mucocele. These findings indicate that cholestatic diseases, including mucocele, are complications related to PDH, and it is essential to carefully monitor these animals due to the higher risk of this disease (Lee et al., 2019, 2017). In contrast, dogs diagnosed with mucocele without obvious clinical signs or physical examination findings consistent with hyperadrenocorticism have elevated cortisol levels post-stimulation by ACTH only in 10% of cases. That indicates that routine tests for hyperadrenocorticism are not justified in dogs with mucocele not presenting clinical signs of hypercortisolemia (Aicher et al., 2019).

In a study conducted with 39 dogs diagnosed with mucocele and without clinical signs compatible with hypothyroidism, approximately 26% presented abnormal results of thyroid hormones, with low serum levels of total T4 and free T4 and elevation of TSH. No changes in anti-thyroglobulin hormone levels and histopathological evidence compatible with autoimmune primary thyroiditis were found. However, it was impossible to determine whether other concomitant non-thyroid diseases influenced the dysregulation of thyroid metabolism or whether the animals presented other causes of thyroid disorder (Aicher et al., 2019). The relaxing effect of the hormone T4 on the sphincter of Oddi is known in humans and pigs (Inkinen et al., 2001; Laukkarinen et al., 2003). The loss of this relaxation in hypothyroid animals may delay the emptying of the GB and increase the risk of mucocele development (Inkinen et al., 2001; Laukkarinen et al., 2003). The only animal with a confirmed diagnosis of hypothyroidism in this study had a primary cause of thyroid dysfunction due to carcinoma in the right thyroid lobe.

Among the 30 animals in this study, only one was diagnosed with diabetes mellitus, corroborating literature findings showing a low association between GBM and diabetes mellitus (Mesich et al., 2009). One study presents the hypothesis that this endocrinopathy can directly induce the development of mucocele or have an indirect effect by inducing hyperlipidemia and dysmotility of the gallbladder. However, it is suggested that further studies are needed to verify whether the metabolic and functional effects on the gallbladder and biliary composition induced by this endocrinopathy are significant enough to result in the development of mucocele (Saunders et al., 2017).

In dogs with GBM, data showed hepatomegaly and increased liver echogenicity. It is known that these abnormalities are compatible with fat infiltration (hepatic steatosis), vacuolar hepatopathy, and chronic cholangiohepatitis, whereby animals with diabetes mellitus also have a hyperechogenic liver secondary to fat infiltration (Nyland et al., 2015). Hepatic steatosis is a common alteration in dogs with hyperadrenocorticism and correlated in this study in which most animals presented hyperechogenic and enlarged liver (Penninck & D'Anjou, 2015). Therefore, sonographic alterations such as biliary mucocele, increased echogenicity, and hepatic size may be indicative of endocrinopathies, especially hyperadrenocorticism

In a multicenter study with 1194 dogs with mucocele, 82% had at least one clinical sign related to biliary tract disease, including vomiting, lethargy, anorexia, diarrhea, abdominal pain, and jaundice (Jaffey et al., 2019). In this study, despite the reduced number of evaluated animals, except dogs with gallbladder rupture, clinical signs were more associated with their underlying diseases found in ultrasound examinations. This superposition of diseases can camouflage the symptomatology related to the biliary system. However, dogs with either GBM type V or type VI were more likely to be clinical than dogs with types I or III (Jaffey et al., 2022).

Few studies compare standardized approaches for dogs with biliary mucoceles that were surgically and clinically treated (Parkanzky et al., 2019; Walter et al., 2008). Cholecystectomy is considered the standard treatment. However, it has been associated with high mortality rates (20% to 40%) in patients presenting with emergency or advanced biliary tract disease (Besso et al., 2000; Parkanzky et al., 2019; Youn et al., 2018). Surgical indication after incidental or early diagnosis of biliary mucocele through ultrasonography is still controversial. However, a recent study demonstrated a low mortality rate (2%) of dogs undergoing elective cholecystectomy compared to the nonelective procedure (20%) (Youn et al., 2018). Another retrospective study compared the long-term survival of dogs treated with cholecystectomy, drug treatment with ursodeoxycholic acid or S-adenosyl methionine, and both. Surgical treatment resulted in a more prolonged survival of approximately 1802 days compared to dogs that received drug treatment, with a shorter survival of about 1034 days.

Dogs initially treated with medications before cholecystectomy had worse survival results, of approximately 203 days, with a 14 times more chance of death when compared to the surgical group (Parkanzky et al., 2019).

The dog with gallbladder rupture was admitted to emergency care with hypovolemic shock. The same animal presented ultrasound signs compatible with biliary peritonitis, and free fluid was collected for confirmation. However, due to the poor general condition and severe clinical picture, the owners chose to perform euthanasia on the animal. The constituents of the bile are toxic to tissues, causing necrosis and vascular permeability changes, leading to bacterial translocation to other organs, including the liver, intestine, and peritoneum. In addition, the presence of bile in the peritoneal cavity increases systemic inflammatory response and susceptibility to sepsis and multiple organ dysfunction (Mehler, 2011). In a recent study, dogs with mucocele and gallbladder rupture that showed signs of peritonitis at the time of surgery had a high risk of death by 2.7 times compared to animals that did not present rupture of the gallbladder and biliary peritonitis (Jaffey et al., 2018).

Conclusion

Mucocele is an alteration in the gallbladder, often associated with endocrine dogs. It may be an incidental finding during an ultrasound examination and may not necessarily be related to the clinical manifestations at the time of diagnosis. However, it is recommended that patients who do not opt for the surgical procedure perform ultrasound controls to monitor this condition.

Conflict of Interest

Authors have no conflict os interest to declare.

Ethics Statement

We certify that the Research "Gall bladder mucocele in dogs: ultrassonography retrospective study", protocol number CEUAx 1170070119 (ID 001078), under the responsibility Carla Aparecida Batista Lorigados, agree with Ethical Principles in Animal Research adopted by Ethic Committee in the Use of Animals of School of Veterinary Medicine and Animal Science (University of São Paulo), and was approved in the meeting of day March 07, 2019.

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