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CASE REPORT

Clinical, Ultrasonographic and Pathologic Evaluation of Cystic Mucinous Gallbladder in a Dog

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ABSTRACT

An 11 years old male Spaniel Cocker was handled to Animal Hospital with lethargy, polypnea and abdominal distension. At physical examination; abdominal sensitivity was detected. The body temperature and heart rate were measured in physiological levels. On ultrasonographic examination; hepatomegaly, thickened and enlarged gallbladder were detected. Hyperechoic content in the lumen was observed also mild free liquid was seen in the abdomen. Gall bladder wall thickness was measured as 3,5 mm. At biochemical examination; AST, ALP, GGT and total cholesterol levels were significantly increased and AST, glucose and phosphorus levels were slightly increased when compared with the reference values. Due to treatment, the patient died after a week and necropsy was performed. At the pathologic examination; cystic mucinous gallbladder was detected. In this case presentation, clinical, ultrasonographic and pathologic evaluation of cystic mucinous gallbladder in a dog was described.

Key Words: Cystic mucinous gallbladder, Dog, Ultrasonography

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Bir Köpekte Kistik Müsinöz Safra Kesesinin Klinik, Ultrasonografik ve Patolojik Değerlendirilmesi

ÖZ

Bu olgunun materyalini, uyuşukluk, polipne ve abdominal distensiyon şikayetiyle hayvan hastanesine getirilen 11 yaşlı erkek bir Spaniel Cocker oluşturdu. Fiziksel muayenede; karında hassasiyet tespit edildi. Vücut ısısı ve nabız sayısı fizyolojik seviyelerde ölçüldü. Ultrasonografik muayenede; hepatomegali, kalınlaşmış ve genişlemiş safra kesesi tespit edildi. Safra kesesi lümeninde hiperekoik içerik, ayrıca batında az miktarda serbest sıvı görüldü. Safra kesesi duvar kalınlığı 3,5 mm olarak ölçüldü. Biyokimyasal incelemede; AST, ALP, GGT ve toplam kolesterol seviyeleri referans değerlere kıyasla önemli ölçüde artmış olarak tespit edildi. AST, glikoz ve fosfor seviyeleri ise referans değerlerin biraz üzerindeydi. Yapılan sağaltıma karşın hasta bir hafta sonra öldü ve nekropsi uygulandı. Patolojik muayenede, kistik müsinöz karakterde safra kesesi belirlendi. Bu olgu sunumunda bir köpekte rastlanılan kistik müsinöz safra kesesinin klinik, ultrasonografik ve patolojik değerlendirilmesi amaçlanmıştır.

Anahtar Kelimeler: Kistik müsinöz safra kesesi, Köpek, Ultrasonografi.

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INTRODUCTION

Cystic hyperplasia of the gallbladder is excessive enlargement of various sized cystic structures within the thickened hyperplastic mucosa of gallbladder. Most of the cysts substances are abundant amount of mucus (Cullen 2007, Stark et al. 2010). Characteristic appearance of hyperplastic mucosa impart that the various 1 to 3 mm cysts are being exist (Cullen 2007). Cystic mucinous hyperplasia in dogs is an idiopathic tumour-like lesion of the gallbladder, can cause gallbladder mucocele and entire mucosa may be affected (Cullen 2007, Secchi et al. 2012). The cause is not known (Cullen 2007). Mild cystic mucinous hyperplasia which the wall thickness of the gallbladder is 2-3 mm without inflammation and non-papillary mucosa is not cause mucocele. Intermediate hyperplasia, that thickness of the wall of the gallbladder is approximately 5-6 mm without inflammation, and was non-papillary mucosa can cause mucocele. Excessive cystic mucinous hyperplasia that the thickness of the wall of the gallbladder is approximately 10 mm with cholecystitis, the surface of mucosa is papillary, and the lesion caused mucocele (Secchi et al. 2012).

During abdominal ultrasonography, biliary ingredients especially sludge is frequently detected in gallbladder (Brömel et al. 1998, Bandyopadhyay et al. 2007). The structure of the biliary sludge was described as mucin, cell debris, glycoproteins, proteins, and precipitated crystals (Ko et al. 1999, Jüngst et al. 2006). Sludge appears as low-level echoes without acoustic shading (Jüngst et al. 2006) and gravitational motility (Besso et al. 2000). In dogs, formation for improvement the role of diet is not known however due to low cholesterol and free calcium contents in dog bile can limit the gall stone formation (Radlinsky 2013).

The aim of the case report was emphasized to determine the clinical, ultrasonographic and pathologic evaluation of cystic mucinous gallbladder in a dog.

CASE HISTORY

An 11 years old male Spaniel Cocker was handled to Animal Hospital with lethargy, polypnea and abdominal distension. At the anamnesis; as being informed that the case was handled to another clinic with the same symptoms and although the supportive treatment was applied for a week, but despite the supportive therapy the case became worsen. At the physical examination; abdominal sensitivity was detected, nevertheless body temperature and heart beat were measured in normal ranges. On ultrasonographic examination, hepatomegaly, thickened and enlarged gallbladder were detected. Hyperechoic content in the lumen was observed concurrently (Figure 1). And also mild free liquid was seen in the abdomen. Gall bladder wall thickness was measured as 3,5 mm. At the whole blood count examination (Mindray Bc 2800) (Table 1); all parameters were been detected normally. At the biochemical examination (Roche Cobas C111) (Table 2); AST, ALP, GGT and total cholesterol levels were significantly increased. AST, glucose and phosphorus levels were slightly increased when compare with reference values. On the other hand, other biochemical parameters among reference values. A prescription was arranged to patient which contains ursodeoxycholic acid, amoxicillin clavulanic acid, enrofloxacin, nifuroxazide and hepatic diet. Due to treatment the patient died after a week and necropsy was performed.

During necropsy, on macroscopic examination; liver volume was increased and all the lobes surfaces were observed rough and dark brown-black colored. When lumen was opened, gallbladder's wall thickened, in lumen bright blackish colored, intensive consistency sludge was detected. This intergradient cumulated through the bile duct. Entire intestine parts was fuelled with hemorrhagic content and organ walls were thickened. Approximately 300 ml liquid was exist in the abdomen. Lung lobes were collapsed and heart was enlarged almost filled the thorax. Approximately 50 ml fluid was observed within the pericardial sac concurrently.

For microscopic examination, tissues were fixated in neutral buffered formaldehyde solution and they were embedded in paraffin. Paraffin blocks of gallbladder and duct of bladder were cut at 5 micrometer and mounted on slides. And then stained with Hematoxilene and eosin (HE) and Periodic acid Schiff (PAS). Also tissues are taken to adhesive slides for immunohistochemical analysis from paraffin blocks. After deparaffinization and hydration, a commercial streptavidin-biotin-peroxidase complex (Standard VECTASTAIN Elite ABC Kit, PK-6200, Vector Laboratories Inc, CA, USA) was used. All sections were preincubated in 1% non-immune serum at room temperature for 15 minutes to block nonspecific binding of second-step antibody. Further, tissue sections were incubated with MUC5AC (Lsbio, mouse, clone 1-13M1, 1/100 dilution) Cytokeratin (Thermo, mouse, ab1, 1/100) and ki-67 (Thermo, rabbit, sp6, 1/100 dilution) primary antibodies for 1 hour and then rinsed with PBS with a pH of 7.4 at room temperature. The sections were allowed to react according to the ABC kit procedure at room temperature. After that they were incubated with 3-amino-9-ethyl carbazole (ImmPACT AMEC Red Peroxidase Substrate, SK-4285, Vector Laboratories Inc, CA, USA) for 15 minutes and then counterstained with Gill's (III) hematoxylin solution. Gallbladder and bile duct lumens were observed that greenish brown in colour and filled with bile. These organs lamina proprias filled with mucinous fluid and bases of them are fitted with thinned prismatic epithelium occasionally and also coated with enlargements into the lumen and

heterogen sized crystals were exist. At immuno-histochemical evaluation it was observed that luminal structures were stained with mucin antibody and cyst cells were occasionally stained with sitokeratin positively and with ki-67 negatively.

Figure 1. Ultrasonography appearance of hyperechoic sludge in the lumen.

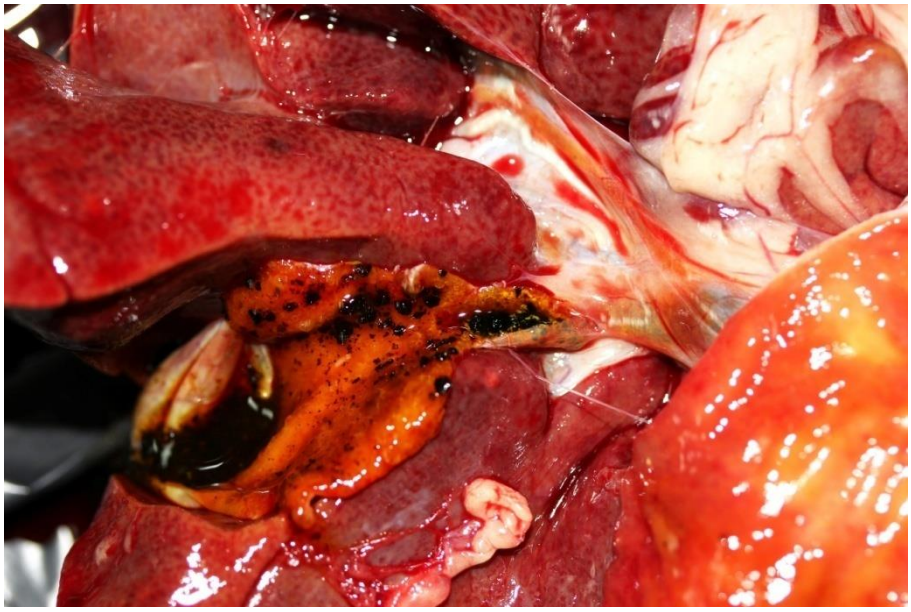

Figure 2: Macroscopic appearance of gallbladder fuelled with sludge.

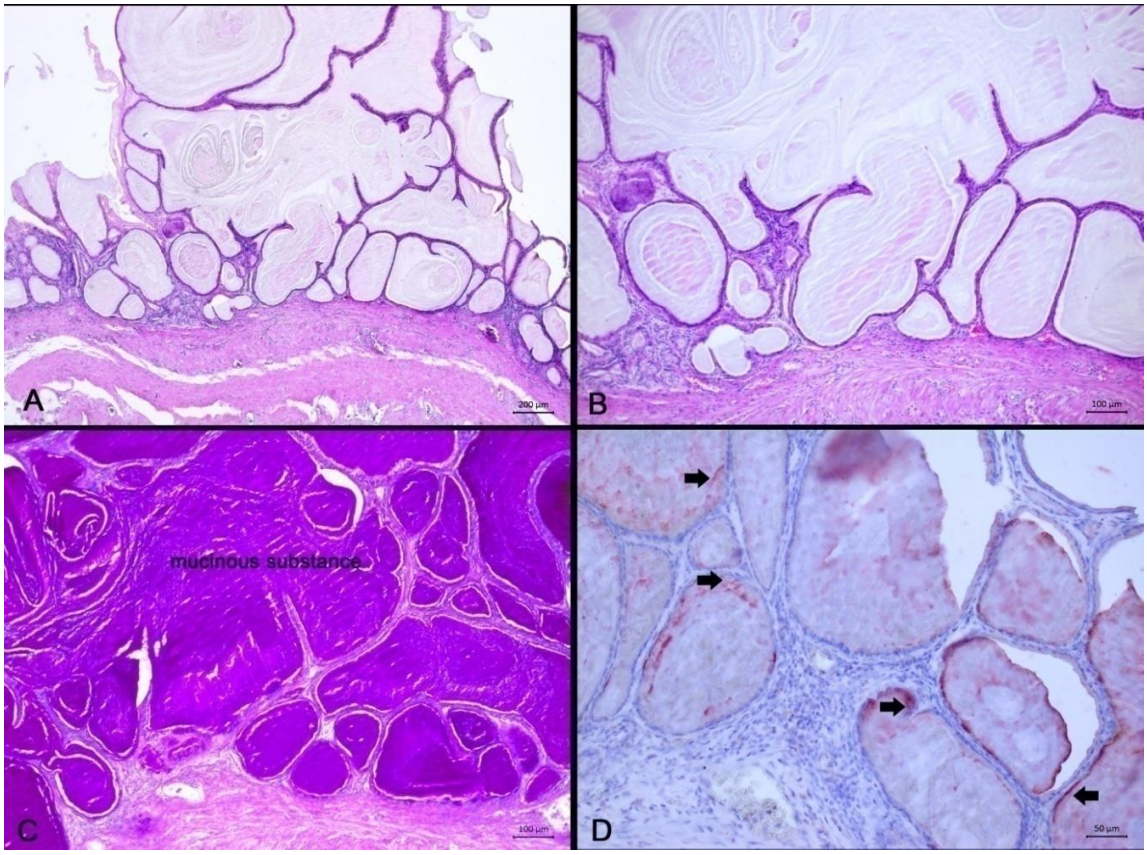

Figure 3: Microscobic appearance of cystic mucinous gallbladder. A-B: low and high power view of the lesion, HE. C: mucinous substance in the cyst lumen, PAS. D: MUC5AC positive mucinous substance (arrows), ABC method.

Table 1: Haematologic parameters

Parameter	**Value**	**Normal Range** (Tvedten 1994)	**Unit**
WBC	14.5	6.02-16.02	$10^3/\mu L$
Lymphocyte	2.5	0.53-3.44	$10^3/\mu L$
Monocyte	0.5	0-0.43	$10^3/\mu L$
Granulocyte	11.5	3.23-10.85	$10^3/\mu L$
RBC	5.38	6.15-8.70	$10^6/\mu L$
HGB	12.1	14.1-20	g/dL
HCT	43.8	43.3-59.3	%
MCV	81.5	63-77.1	FL
MCH	22.4	21.1-24.8	Pg
MCHC	27.6	29.9-35.6	g/dL
RDW	17.1	11.9-14.9	%
PLT	718	166-575	$10^3/\mu L$
MPV	7.8	3.9-6.1	FL

Table 2: Serum biochemical parameters

Parameter	Value	Normal Renge (Tvedten 1994)	Unit
ALT	375	10-94	U/L
AST	62	10-62	U/L
ALP	934	0-90	U/L
Urea	54,5	14.98-68.48	mg/dL
Total Bilirubin	0,4	0.1-0.6	mg/dL
Direct Bilirubin	0,12	-	mg/dL
Ca	9,1	9-11.9	mg/dL
P	6,52	1.9-7.9	mg/dL
TP	5,91	5.3-7.6	g/dL
Albumin	3,01	3.2-4.7	g/dL
Creatinin Kinase	100,4	51-529	U/L
LDH	58,1	42-130	U/L
Glucose	130	53-117	mg/dL
GGT	152	1-6	U/l
Total Triglyceride	48,29	10-500	mg/dL
Total Cholesterol	443,74	116-317	mg/dL

DISCUSSION

ALP production is markedly increase while bile retention (Watson 2010). For cholestasis marker, ALP levels are higher in affected dogs despite no important difference when compare with the other tissues (Hoffmann and Solter 2008). Although ALP levels can elevate with the use of dogs such as some drugs (Gonzalez and Silva 2006). There were no evidences of usage of these drugs in the dog. In this study, it was suggested that ALP elevations exist due to formation of biliary sludge.

In a study which was performed in 18 healthy dogs after cystic duct ligation; black and viscous material microscopically identical to sludge was observed in 72 hours (Bernhoft et al. 1983), although high frequency of thickened bile without proof of hepatobiliary disorders and can be detected by USG and serum biochemistry (Brömel et al. 1998). Normally during abdominal examination biliary sludge can be detected hyperechogenic in ultrasonographic examination and usually acoustic shadowing cannot be seen and position of the gallbladder content is not changed to gravity and dog's lying position (Brömel et al. 1998, Besso et al. 2000, Pazzi et al. 2003, Uno et al. 2009). While cholecystitis, thickening of gallbladder wall generally increase (Nyland and Mattoon 2002). 24 symptomatic and 19 asymptomatic gallbladder mucocele patients were evaluated in a study and in four dogs wall thickness were determined over 3 mm. (Choi et al. 2014). In the present case, gallbladder wall thickness was measured 3,5 mm, hyperechoic and stable lumen content was seen concurrently. Also cystic mucinous hyperplasia was confirmed with histopathology findings as well. It was thought that aforementined patient who has cystic mucinous hyperplasia reflects gallbladder mucocele and wall thickness under 5-6 mm and lumen appearance is a good indicator for evaluating the condition of gallbladder.

Clinical, ultrasonographic and pathologic evaluation of cystic mucinous gallbladder in a dog was described and high serum ALP and GGT levels should be considered for getting suspicious about gallbladder diseases.

Conflict of Interest

The authors declare that there is no conflict of interest.

Ethical Approval: This study is not subject to the permission of HADYEK in accordance with 8 (k) of the "Regulation on Working Procedures and Principles of Animal Experiments Ethics Committees".

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