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Renal Ultrasonography Findings in Cats with Feline Infectious Peritonitis

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ABSTRACT Feline infectious peritonitis (FIP) is a fatal disease caused by a mutated feline enteric coronavirus (FECV) that causes a wide diversity of clinical findings. Antemortem diagnosis may be challenging as the non-effusive form causes pyogranulomatous inflammation in various organs including the eye, brain, omentum, liver and kidney compared to the effusive form. Since it has been discussed that the kidney is the organ most susceptible to FIP-related lesion development, this study aimed to evaluate the renal ultrasonography findings in cats with naturally developed non-effusive FIP. Clinical and renal ultrasonographic examinations of 17 cats with compatible clinical findings that would suggest the presence of non-effusive FIP were performed with the appropriate protocol. Both cats' kidneys were evaluated for echogenicity, size (longitudinal length), shape, presence of free fluid, if any, and echogenicity of this fluid. As a result of renal ultrasonography, it was observed that the most prominent abnormal ultrasonographic findings were cortical hyperechogenicity (11 out of 17 cats), medullary rim sign (11 out of 17 cats), renomegaly (10 out of 17 cats), pyelectasis (5 out of 17 cats), loss of corticomedullary differentiation (4 out of 17 cats) and distortion of internal architecture (4 out of 17 cats). In conclusion, it was observed that morphological and parenchymal alterations occur in the renal ultrasonographic evaluation in cats with non-effusive FIP, and renal ultrasonography could provide useful clinical information in evaluating the clinical reflection of vasculitis due to FIP. Although these abnormal renal ultrasonography findings were not specific for FIP, it was concluded that the combination of the observed ultrasonographic findings and other compatible clinical findings and their evaluation together can be used to increase the index of suspicion for antemortem FIP infection.

Keywords: *Cat, Diagnosis, FIPV, Renal cortex, Vasculitis.*

ÖZ

Felin Enfeksiyöz Peritonitisli Kedilerde Renal Ultrasonografi Bulguları

Felin enfeksiyöz peritonitis (FIP), mutasyona uğramış felin enterik koronavirüs (FECV) tarafından oluşturulan, çok çeşitli klinik bulgulara sebep olan ölümcül, viral bir hastalıktır. Effüziv forma kıyasla non-effüziv form göz, beyin, omentum, karaciğer ve böbrek gibi çeşitli organlarda piyogranülamatöz yangıya sebep olduğundan antemortem tanı zorlaşabilir. FIP ile ilişkili lezyon gelişimine en duyarlı organın böbrek olduğu tartışılmış olduğundan, bu çalışmada doğal gelişmiş non-effüziv FIP'li kedilerde renal ultrasonografi bulgularını değerlendirmek amaçlandı. Non-effüziv FIP varlığından şüphelendirecek uyumlu klinik bulgulara sahip 17 adet kedinin klinik muayeneleri ve uygun protokol ile renal ultrasonografik muayeneleri gerçekleştirildi. Tüm kedilerin her iki böbreği ekojenite, boyut (longitidunal uzunluk), şekil, varsa serbest sıvı varlığı ve bu sıvının ekojenitesi yönünden değerlendirildi. Yapılan renal ultrasonografi sonucu en belirgin anormal ultrasonografik bulguların kortikal hiperekojenite (17 kedinin 11'i), medullar rim sign (17 kedinin 11'i), renomegali (17 kedinin 10'u), piyelektazi (17 kedinin 5'i), kortikomedullar ayrımın azalması (17 kedinin 4'ü) ve internal yapıda bozulma (17 kedinin 4'ü) olduğu belirlendi. Sonuç olarak, çalışmamızda non-effüziv FIP'li kedilerde renal ultrasonografik değerlendirmede morfolojik ve parankimal değişimler oluştuğu ve renal ultrasonografinin FIP'e bağlı oluşan vaskülitisin klinik yansımasını değerlendirmede faydalı klinik bilgiler sağladığı gözlendi. Her ne kadar tespit edilen bu anormal renal ultrasonografi bulguları FIP için spesifik olmasa da tespit edilen ultrasonografik bulgular ile diğer uyumlu klinik bulguların kombinasyonu ve hepsinin birlikte değerlendirilmesi, antemortem FIP enfeksiyonu şüphesi indeksini arttırmada kullanılabileceği kanısına varıldı.

Anahtar Kelimeler: *FIPV, Kedi, Renal korteks, Tanı, Vaskülit.*

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INTRODUCTION

Feline infectious peritonitis (FIP) is a progressive and fatal disease caused by virulent feline coronavirus (FCoV), especially in cats younger than 2 years of age with an immature immune system (Pedersen 2009). There are 2 pathotypes of FCoVs: feline enteric coronavirus (FECV), which is the enteric biotype and feline infectious peritonitis virus (FIPV), which is the virulent one (Kipar and Meli 2014; Gülersoy and Maden 2021). FIPV is a mutated form of FECV, and causes a wide variety of clinical manifestations. Although FECV is highly contagious, FIPV is less common than FECV. There are two clinical forms of FIP. The effusive form, is characterized by immune-mediated vasculitis, proteinaceous fluid accumulation in the peritoneal, pleural, pericardial space and subcapsular region of the kidneys. On the other hand, the non-effusive form affects many organs including the eye, brain, kidney, omentum and liver with pyogranulomatous or granulomatous inflammation (Lappin 2003).

It is thought that 0.3-1.4% of cat deaths observed in veterinary clinics and hospitals all over the world are due to FIP. FIP is challenging to diagnose, especially in the absence of effusion, due to the lack of pathognomonic clinical and laboratory findings. Therefore, the sensitivity, specificity, and predictive value of each diagnostic test should be evaluated separately in order to suspect and diagnose FIP (Lappin 2003; Gülersoy and Maden 2021). The disease is fatal when not treated with novel protocols or when treatment is delayed (Gülersoy and Maden 2021). Thus, accurate diagnosis is very critical. Anamnesis, signalment, comprehensive physical examination should be performed for each case, and accordingly, the appropriate diagnostic method should be selected and the FIP index of suspicion should be established (Riemer et al. 2016). It was reported that the most common organ in which FIP-related lesions develop, especially in cats less than 1 year old, is the kidney (Kipar et al. 2005). In this context, ultrasonography (USG) is a valuable diagnostic tool utilized for the investigation of kidney disorders. It has higher accuracy than radiography and provides excellent imaging for evaluation of renal shape, size and internal structures. Also, it is much superior to radiography in cases of effusive FIP. Moreover, despite more advanced imaging devices such as computed tomography and magnetic resonance imaging, ultrasonography is more accessible and inexpensive, often does not necessitate anesthesia, and allows real-time imaging (Seyrek-Intas and Kramer 2008; Kipar and Meli 2014).

Therefore, the aim of this study is to identify renal abnormalities in naturally developing non-effusive FIP cases and to contribute to the antemortem diagnosis of FIP by detecting renal abnormalities that can be used to increase the index of suspicion for antemortem FIP infection.

MATERIAL AND METHODS

The study protocol was approved by the Faculty of Veterinary Medicine, Selçuk University Local Ethics Committee (Approval number: 2020/43). Informed consent was given to the owners of all the cats enrolled in the study and permissions were obtained.

Animal Material

The animal material of this study consisted of 17 cats with compatible clinical findings to suspect the presence of non-effusive FIP, all were admitted to the Animal Hospital for diagnosis and treatment purposes. All cats were client-owned indoor cats and were fed on commercial dry cat food. All cats were evaluated in terms of anamnestic data including breed, sex, age, symptom duration, physical examinations, rapid diagnostic test kit results and the form of FIP infection.

Physical Examinations

Physical examinations of all cats including heart and lung auscultations, body temperature, pulse and respiratory rate measurements, palpable lymph node and gingival capillary refill time evaluations were performed.

Inclusion and Exclusion Criterias

Presence of clinical findings in all the cats such as anorexia, lethargy, weight loss, jaundice, ocular lesions, upper respiratory signs and incoordination which is generally most intense in posterior non-effusive FIP were accepted as compatible findings (Pedersen et al. 2019). Feline Calicivirus (FCV), Feline Herpesvirus (FHP), Feline Immunodeficiency (FIV), Feline Leukemia Virus (FeLV) and Feline Parvovirus (FPV) together with the presence of Toxoplasma were considered for both differential diagnosis and detection of any co-morbid disease in cats eligible for inclusion in the study. In this context, FCV antigen (Ag) (Asan Pharm®, Korea; sensitivity and specificity, 96% and 98% vs IFA, respectively), FHV Ag (Asan Pharm®, Korea; sensitivity and specificity, 96.5% and 98% vs IFA, respectively), FIV antikor (Ab) / FeLV Ag (Asan Pharm®, Korea; sensitivity and specificity, 98% and 98.7% vs IFA, respectively), FPV (Ag) Asan Pharm®, Korea; sensitivity and specificity, 97.8% and 98.8% vs IFA, respectively) and Toxoplasma Ab (Anigen, China; sensitivity and specificity, 100% and 99% vs IFA, respectively) assays were performed using appropriate biological fluid/material in accordance with the manufacturers' instructions. After all the tests were observed to be negative, for the diagnosis of FIP, Biopanda Feline Coronavirus Antigen Rapid Test (Relative sensitivity: 92.54%, Relative specificity: 97.09%) kit, which detects the presence of FCoV Ag, was used. All tests were performed by experienced research assistants at the central laboratory according to the manufacturers' instructions. Positive results were recorded as weakly positive or positive according to color intensity. As a result, the cats (n=17) with positive FCoV Ag test, with no co-morbid viral or protozoal disease, and with clinical findings compatible with non-effusive FIP (Pedersen 2009; Pedersen et al. 2019) were included in the study.

Ultrasonographic Examinations

Both of the kidneys were evaluated for echogenicity, size (longitudinal length), shape, presence of free fluid, if any, and echogenicity of this fluid. All images were acquired using an ultrasound machine (Mindray z60, China) with a 7.2 to 11 MHz microconvex probe. An 11 MHz microconvex probe was used to image the kidneys at the optimum resolution. To eliminate the air gap between the probe and the skin, acoustic coupling gel was applied to the shaved area and waited for 5 minutes. Pressure was applied slowly with the probe to prevent renal displacement during the ultrasonographic examination. Each kidney was completely scanned in the longitudinal, dorsal and transverse planes. The renal pelvis is discernible at the medial part of the kidney in the long axis in the true dorsal view. The central renal sinus is not apparent in the longitudinal plane, but two hyperechoic lines made up of cross-sectioned renal pelvic diverticula are discernible. In the longitudinal and dorsal planes, the kidney's cranial and caudal poles should be of comparable size. At the level of

the renal hilus, the transverse plane is at a 90° angle to the longitudinal and dorsal planes, and it contains the V- or U-shaped renal crest at the top of the renal medulla. At least 2 planes of still renal images of both kidneys were evaluated for all included non-effusive FIP cases.

RESULTS

Anamnestic Data

The cats included in the present study were those who did not have any previous disease history and did not use any medication/vitamin. The mean age of the cats included in the study was 1.85±0.6 years. The mean body weight was 1.72±0.42 kg. The breeds of the cats were mostly mix breed (n=6), Scottish fold (n=4), Persian (n=3), British longhair (n=2), and Bombay (n=2). Of the cats included in the study, 12 were male and 5 were female, and all were non-neutered. In addition, in the anamnesis, it was learned that the mean duration of symptoms before admission to the hospital was 11.64±6.24 days.

Physical Examination Findings

The mean body temperature of the cats with non-effusive FIP was 39.04±0.41 °C. Respiratory rate was 71.76±14.26 breaths/minute, heart rate was 124±10 beats/minute, and gingival capillary refill time was 3±0.93 seconds. No marked abnormal finding was detected as a result of lung auscultation. Lymphadenopathy was evident in 4 cats. 6 cats had keratic precipitate. There was significant incoordination in 3 cats and it was observed that they could not stand without support.

Renal Ultrasonography Findings

It was observed that the most prominent abnormal ultrasonographic findings were cortical hyperechogenicity (11 out of 17 cats), medullary rim sign (11 out of 17 cats), renomegaly (10 out of 17 cats), pyelectasis (5 out of 17 cats), loss of corticomedullary differentiation (4 out of 17 cats) and distortion of internal architecture (4 out of 17 cats). While renomegaly was bilateral in 6 of the cats, it was unilateral in 4 of them. The mean longitudinal kidney length of the cats was 4.56±1.01 cm for the right kidney and 4.62±0.91 cm for the left kidney. Abnormal renal ultrasound findings of the cats are presented in Table 1, the percent distribution chart is presented in Figure 1, and the ultrasonographic images are presented in figures 2, 3, 4, 5, 6 and 7 respectively.

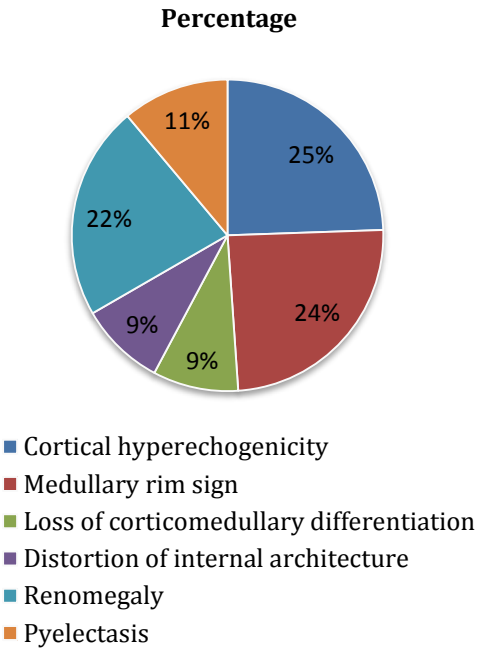

Figure 1. Percentage distribution of the abnormal ultrasonographic findings in cats.

Table 1. Abnormal renal ultrasound findings of the cats.

Abnormal Findings	Cats																	Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	
Cortical hyperechogenicity		x	x		x	x	x	x	x	x	x		x	x				11
Medullary rim sign	x		x	x		x		x			x	x	x		x	x	x	11
Loss of corticomedullary differentiation						x				x	x						x	4
Distortion of internal architecture			x					x					x	x				4
Renomegaly	x	x			x	x	x			x	x				x	x	x	10
Pyelectasis						x	x			x			x	x				5

x: Present.

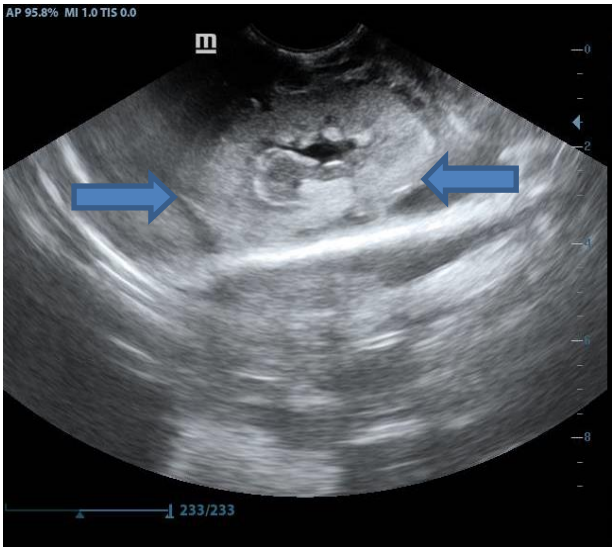

Figure 2. Prominent cortical hyperechogenicity (blue arrows).

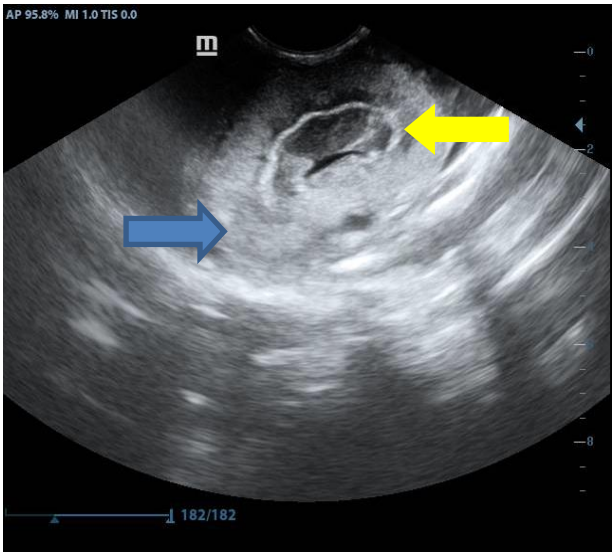

Figure 3. Cortical hyperechogenicity (blue arrow) with irregular and thick medullary rim sign (yellow arrow).

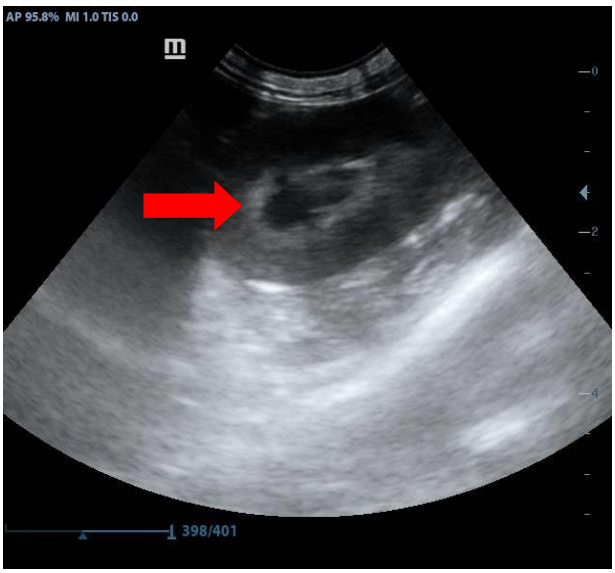

Figure 4. Loss of corticomedullary differentiation (red arrow).

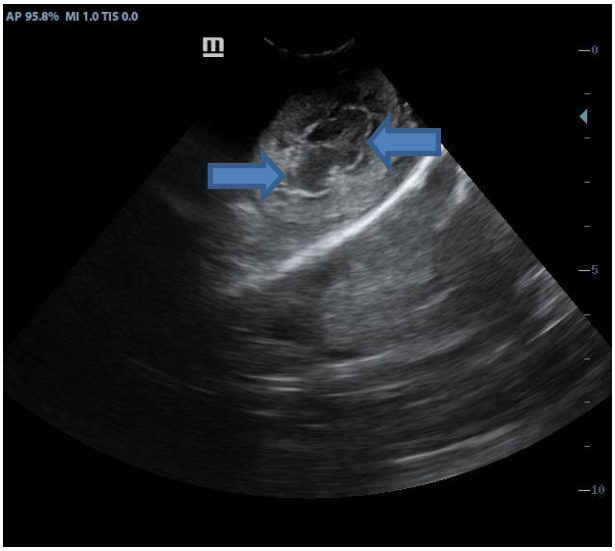

Figure 5. Distortion of internal architecture (blue arrows).

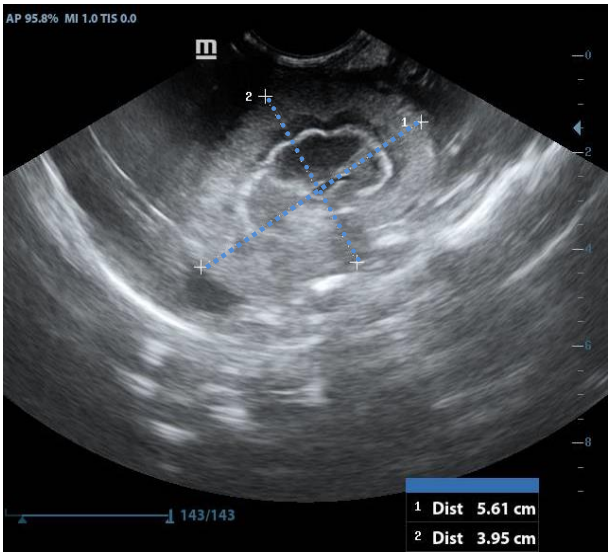

Figure 6. Prominent renomegaly (5.61–3.95 cm).

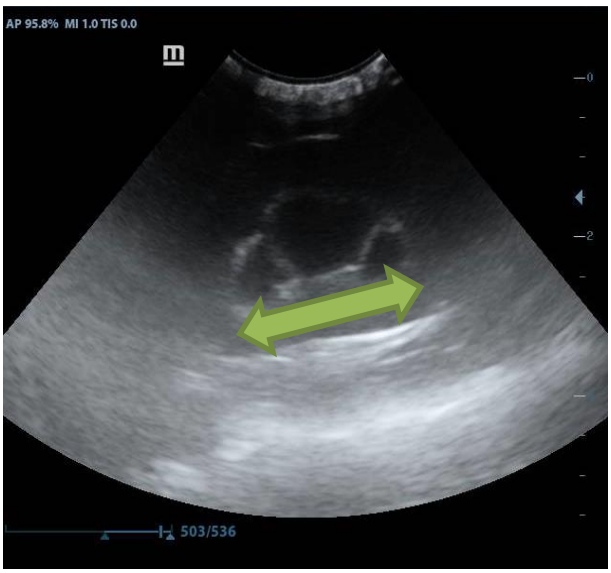

Figure 7. Severe pyelectasis (green arrow).

DISCUSSION AND CONCLUSION

It is still difficult to diagnose feline infectious peritonitis (FIP) in cats in clinical settings. The cornerstone of antemortem diagnosis continues to be a comprehensive history, physical examination, and appropriate choice and interpretation of diagnostic testing (Diaz and Poma 2009). Considering the fact that ultrasound is inexpensive, non-invasive, adequate and effective in demonstrating renal anatomical and parenchymal details, the abnormal ultrasonographic renal findings such as cortical hyperechogenicity, medullary rim sign, and renomegaly, although not specific for FIP, could be used to increase the index of suspicion for antemortem FIP infection in combination with other clinical findings.

Diagnosis of FIP can be easy in the presence of effusion with characteristic signalment. However, in the absence of effusion, diagnosis is challenging due to the diversity and non-specific nature of clinical findings (Hartmann et al. 2003). The clinical presentation of FIP differs according to the systemic findings or the affected organs, even fever may or may not be present. For this reason, many studies have discussed the diagnostic methods required for the antemortem diagnosis of FIP or its use in increasing the index of suspicion (Kipar et al. 2006; Pedersen et al. 2019). Ultrasonography, one of these diagnostic methods, plays an important role in the diagnostic process of many cat diseases. In particular, examination of the kidneys with B-mode ultrasonography provides detailed information about size, shape, contour and internal structures. Investigation of the kidneys and perinephric space also provides useful information about various conditions such as corticomedullary disorders, chronic renal failure, hydronephrosis (Walter et al. 1988). The non-effusive form of FIP is known to cause pyogranulomatous lesions in various tissues and organs including the kidneys (Gülersoy and Maden 2021). Thus, both clinical and ultrasonographic examination are utilized to observe alterations due to FIP infection (Kipar et al. 2006). It was reported that cats younger than 1 year of age are more predisposed to the development of FIP-related lesions, and these lesions are mostly observed in the kidney, and the kidney is the most susceptible organ (Kipar et al. 2005). Although the reasons for the predominance of FIP-related kidney lesions are not fully elucidated, several factors may contribute to the development of these alterations. The kidney has a single circulatory system and receives 20% of the cardiac output, and the kidneys have two different capillary beds, the glomerular and the peritubular capillary network. Also, due to complex afferent arterioles, blood flow is 40 times higher than in other organs (Blantz et al. 2005). Moreover, FIP vasculitis mostly affects the small-to-medium veins, and this type of veins are common in the leptomeninges of the renal cortex. For this reason, in line with these aforementioned factors, abnormal vascular changes are more common in the kidneys and the most frequently affected organ in FIP infection is the kidney (Kipar et al. 2006). In the present study, renal ultrasonographic examination revealed both parenchymal and anatomical significant abnormalities of the cats with naturally developed non-effusive FIP. These findings may be related to the dense vascular structure of the kidney, the characteristics of FIP-related vasculitis and severe infiltration of lymphocytes, plasma cells, and some dead neutrophils, as well as dilation and congestion of the interstitial blood vessels, result in severe degenerative and progressive necrotic alterations within the lining endothel of the convoluted tubules (Sharif et al. 2010).

In healthy cats, the left kidney is just caudal to the fundus of the stomach, lateral to the aorta and caudomedial to the top of the spleen (Larson 2009). The cranial pole of the right kidney can be detected in the renal fossa of the caudal lobe of the liver, which is ventral and occasionally medial to the duedonum, lateral to the caudal vena cava. Ultrasonographic examination of both kidneys can be easily performed caudal to the ribs (Seyrek-Intas and Kramer 2008). A normal shape of the kidney is bean-shaped, oval, and its outline is soft and clearly circumscribed. The renal capsule is hyperechoic, linear and invisible due to the parallel projection of the ultrasound beam at the ends of the kidney. In some cases, shading at the ends has also been reported (Mannion 2006). In the present study, the kidneys of the cats with non-effusive FIP were ultrasonographically imaged in the specified anatomical regions (Larson 2009) and no presence of nephroptosis was detected.

Three different regions have been defined in the healthy kidney. These are the renal cortex, medulla and sinus. The healthy renal cortex is granular and uniformly echoic (d'Anjou and Penninck 2015). The right kidney is usually mildly hypo- or isoechoic compared to the liver parenchyma, and the left kidney is hypoechoic-to-isoechoic compared to the spleen parenchyma. However, in healthy cats, fat deposition in the cytoplasm of the proximal tubular epithelium can result in increased cortical echogenicity (Nyland et al. 1995). Renal echogenicity can be normal, hyperechoic or hypoechoic. A diffuse hyperechoic appearance with precise corticomedullary differentiation was reported in kidney lymphosarcoma, glomerulo-interstitial nephritis and metastatic squamous cell carcinoma and pyogranulomatous nephritis due to FIP (Kipar et al. 2005). Also, increased cortical echogenicity may occur due to acute tubular necrosis resulting from conditions such as glomerular or interstitial nephritis, ethylene glycol toxicity, diffuse renal lymphosarcoma, metastatic squamous cell carcinoma, and FIP. Moreover, increased renal echogenicity, pyelectasis and renomegaly were reported as the most common manifestations in cats with acute kidney injury due to various etiologies (Cole et al. 2019). Previously, it was reported that FIP may cause interstitial nephritis, which is characterized by swelling of the spaces between the kidney tubules (Kipar et al. 2006). Cortical hyperechogenicity, which is one of the most important abnormal renal findings of the present study, can be explained by the fact that vasculitis due to FIPV mostly affects the small-to-medium veins and this type of veins are common in the leptomeninges of the renal cortex (Blantz et al. 2005).

The renal pelvis is encircled by the medulla, which is the kidney's deepest region. When compared to the cortex, the medulla can be practically anechoic in healthy cats, especially in young kittens. It is sectioned by linear echogenicities and interlobar veins can be observed. Short parallel echogenic lines at the corticomedullary junction indicate the walls of curved veins (Nyland and Mattoon 2015). These veins reach out the medulla from the sinus to the cortex and may cause acoustic shadowing (Mannion 2006). There must be a precise differentiation between the cortex and the medulla. In some cats, a parallel hyperechoic band may be observed in the outer area of the medulla at the corticomedullary junction. This appearance is called rim sign and it has been reported that it can be observed both in healthy cats (especially in old cats) and in pathological cases such as acute tubular necrosis, lymphoma, pyegranulomatous vasculitis due to FIP,

portosystemic shunt and chronic interstitial nephritis (Biller et al. 1992). It was reported that the incidence of medullary rim sign was similar between azotemic cats and non azotemic cats. In most cases, this ultrasonographic finding was reported to result from mineral deposition within the lumina of the renal tubules (Mannion 2006; Lamb et al 2017). The outer area of the renal medulla is a metabolically very active and is therefore highly susceptible to ischemia/ischemia-related conditions. It was hypothesized that, following any stimulus/injury, the distorted renal tissue may undergo dystrophic mineralization leading to medullary rim sign formation. It was reported that the medullary rim sign, which is observed in FIP, is associated with increased number and size of the acoustic interface due to perivascular infiltrate (Biller et al. 1992). According to the previous reports, medullary rim sign is a relatively widespread, non-specific finding which can be observed in both normal and diseased kidneys. Although it cannot be considered as an indicator of a kidney disease alone, it may be an indicator of subclinical renal disease or previous renal damage (Mantis and Lamb 2000). Besides cortical hyperechogenicity, one of the most prominent findings of the present study is the medullary rim sign. It has been reported that focal hyperechoic nodules or diffuse cortical echogenicity can be observed in the non-effusive form of FIP (Biller et al. 1992). In addition, the hypoechoic subcapsular rim encircling both kidneys can also be detected. Therefore, the medullary rim sign of the present study may be associated with cellular infiltration due to FIP-related vasculitis (Dennis and McConnell 2007).

The conditions of polycystic kidney disease, renal lymphosarcoma, and FIP are frequently the causes of diffuse or multifocal renomegaly in cats. The characteristic appearance of polycystic kidney disease makes it simple to distinguish from other diseases in the differential diagnosis of renomegaly (Sherding 2006; Larson 2009). Therefore, renomegaly, which is one of the most prominent findings of the present study, may be associated with immune-mediated vasculitis, disseminated perivascular pyogranulomatous inflammation, and exudative fibrinous polyserositis resulting from the introduction of FIPV-infected macrophages to the kidney (Sherding 2006). The pyelectasis detected in the present study may be due to transient polyuria and pyogranulomatous inflammation (Walter et al. 1988).

Detection of diffuse parenchymal abnormalities of the kidney could be challenging to diagnose. In this context, increased or decreased cortical echogenicity, loss of corticomedullary differentiation and distortion of internal architecture can be considered. Although aforementioned findings are non-specific, combination with other existing clinical findings may increase the index of suspicion of the related disease (Larson 2009). Considering the symptom duration of the present study in the cats with naturally developed non-effusive FIP before admission to the hospital (11.64±6.24 days), these findings may be associated with the progression of the disease (Kipar et al. 2006; Larson 2009; Lamb et al. 2017; Gülersoy and Maden 2021).

This study has some limitations. Although certain viral and protozoal diseases were considered in the differential diagnosis of non-effusive FIP, the lack of renal clearance and kidney-related serum biochemistry analyte measurements, and the low number of animals could be counted as limitations.

Ultrasonography is superior to radiography, especially in the presence of effusion (Seyrek-Intas and Kramer 2008). In the present study, it was observed that ultrasonographic evaluation of kidneys provides useful clinical information in cats with non-effusive FIP. Although these observed abnormal renal ultrasonography findings are not specific for FIP, the combination of aforementioned ultrasonographic findings and other compatible clinical findings can be used to increase the index of suspicion for antemortem FIP infection.

CONFLICTS OF INTEREST

The authors report no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Idea / Concept: EG, CB
Supervision / Consultancy: MO
Data Collection and / or Processing: EK, MAG, İG, AŞ
Analysis and / or Interpretation: EG, CB, MO
Writing the Article: EG, MO
Critical Review: EG, CB, EK, MAG, İG, AŞ, MO

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