

# ULTRASONOGRAPHIC CHARACTERISTICS OF CANINE RENAL LYMPHOMA

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There is little published information on the ultrasonographic appearance of canine renal lymphoma. The purpose of this retrospective study was to provide additional information regarding the ultrasonographic characteristics of canine renal lymphoma, suggest ultrasonographic description criteria, and evaluate the role of fine-needle aspirate cytology in the diagnosis of this disease. The ultrasonographic features of confirmed renal lymphoma were reviewed in ten dogs. Pyelectasia was found in all dogs. Other ultrasonographic findings were loss of corticomedullary distinction (9/10 dogs), renomegaly (8/10 dogs), renal deformity (6/10 dogs), hypoechoic lesion(s) (6/10 dogs), and hyperechoic lesion(s) (2/10 dogs). Hypoechoic lesions were described as masses, nodules, and indistinct areas. In 30% of the cases (3/10 dogs) ultrasound revealed only minor abnormalities, including grade 1 pyelectasia, mild renomegaly, and focal loss of corticomedullary definition. Bilateral lesions were seen in nine dogs (90%). Renal fine-needle aspirates were performed in 9/10 dogs, yielding a diagnosis in seven on first attempt (78%). Two dogs had been given a provisional cytological diagnosis of round cell neoplasia; in one dog lymphoma was confirmed by second aspirate and by tissue core biopsy in the other. In 1/10 dogs, lymphoma was found at necropsy. Findings indicated that ultrasonographic signs of canine renal lymphoma may be subtle, canine renal lymphoma should be included in the differential diagnosis when the above ultrasonographic features are observed, and fine-needle aspirate cytology is a useful method for diagnosing this disease. © 2014 American College of Veterinary Radiology.

**Key words:** biopsy, dog, fine-needle aspirate, lymphoma, renal, ultrasound.

## Introduction

RENAL TUMORS ARE UNCOMMON IN DOGS, comprising less than 2% of primary neoplasms. Most are epithelial in origin (adenocarcinoma and carcinoma), with other reported classes being mesenchymal (hemangiosarcoma, fibrosarcoma, anaplastic sarcoma) and mixed type (nephroblastoma).<sup>1,2</sup> Lymphoma is one of the most frequent neoplasms in the dog and is generally easy to diagnose, as cytology is a sensitive method to confirm suspicion.<sup>3,4</sup> Despite these factors, primary renal lymphoma has been rarely reported. Canine lymphoma is typically a multicentric disease, although occasionally the neoplastic infiltrate is limited to one organ as it occurs with extranodal presentations.<sup>5-8</sup> Reaching a definitive diagnosis of primary lymphoma is challenging. To be considered, sampling of multiple tissues should be performed to rule out other organ infiltration. In humans, commonly agreed criteria for defining most primary renal or extranodal lymphomas are a histologic diagnosis and absence of other nodal or extranodal involvement.

At the time of this report, little published information could be found on the ultrasonographic characteristics of canine renal lymphoma. In the 11 dogs reported, ultrasonographic findings included renomegaly ( $n = 7$ ), loss of corticomedullary distinction ( $n = 2$ ), loss of architecture ( $n = 4$ ), solitary mass ( $n = 1$ ), multiple masses/nodules ( $n = 4$ ), multiple poorly defined areas within the parenchyma ( $n = 1$ ), multifocal hypoechoic areas ( $n = 1$ ), diffuse hypoechogenicity ( $n = 1$ ), hydronephrosis ( $n = 1$ ), and thickened cortices ( $n = 1$ ). However, in most publications, the description of the ultrasonographic features is not detailed. Eight dogs had bilateral involvement, two had unilateral disease, and one was not reported.<sup>9-18</sup> Only one high resolution and few low resolution ultrasound illustrations of renal lymphoma were available in three reports.<sup>11, 14, 15</sup>

The purpose of this retrospective study was to provide additional information regarding the ultrasonographic appearance of canine renal lymphoma, suggest ultrasonographic description criteria, and evaluate the role of fine-needle aspirate cytology in diagnosis of this disease.

## Materials and Methods

Electronic medical records at the Royal Veterinary College (RVC) UK were searched for confirmed cases of

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canine renal lymphoma from August 2007 to December 2012. Criteria for inclusion were a definitive histological and/or cytological diagnosis of renal lymphoma, and dogs were required to have evidence of renal function impairment at presentation (polyuria/polydipsia, or clinicopathologic findings such as elevated creatinine or isosthenuria), or in which the largest tumor burden was determined to be renal by imaging or at necropsy. Dogs were required to have at least one abdominal ultrasound examination performed at the referral hospital at the time of presentation, and the images needed to be available for review. Information recorded included signalment, renal values, any administration of fluid therapy prior to imaging, ultrasonographic findings, diagnostic method of lymphoma, and complications of renal sampling.

Ultrasound images of the kidneys were retrospectively reviewed by a board certified veterinary radiologist (LB) and classified based on presence or absence of the following: (1) parenchymal lesions (unilateral or bilateral), (2) renal enlargement (unilateral or bilateral), (3) deformed shape (unilateral or bilateral), (4) pyelectasia (unilateral or bilateral), (5) degree of pyelectasia for each kidney (defined as grade 1, up to 2 mm in width; grade 2, between 2 and 5 mm; and grade 3, more than 5 mm), (6) loss of corticomedullary distinction (unilateral or bilateral), (7) hypoechoic nodules (defined as well defined round hypoechoic lesions less than 2 cm in diameter), (8) hypoechoic masses (defined as well defined lesions greater than 2 cm), (9) hypoechoic areas (defined as nonround, nonwell defined hypoechoic lesions), (10) hyperechoic lesions, and (11) perirenal and/or subcapsular lesions (defined as abnormalities not considered to be retroperitoneal fluid). Renomegaly was assigned when the observer considered kidney length measured in the sagittal view to be enlarged or, if available, when the ratio between renal length and aortic diameter measured at renal level was more than 9.1.<sup>19</sup> The grade of pyelectasia was assigned based to the highest score found in either kidney. Nonrenal ultrasonographic findings were retrieved from the original report and also recorded.

## Results

Ten dogs from August 2007 to December 2012 were identified, and included four Labrador Retrievers, one Rotweiler, one Newfoundland, one Border collie, one Tibetan Terrier, one West Highland White Terrier, and one mixed-breed dog. The ages ranged from 3 to 11 years old with a mean of 6.7  $\pm$  2.7 years. Four dogs were spayed females, three neutered males, two intact males, and one intact female. Seven dogs received fluid therapy prior to imaging and three did not. Nine of 10 dogs were azotemic with creatinine value  $>1.6$  mmol/L at the time of presentation, one was isosthenuric, and five had a history of polyuria/polydipsia.



FIG. 1. Sagittal ultrasound image of the left kidney in a dog with renal lymphoma demonstrating multiple hypoechoic nodules (asterisks), a hypoechoic area (arrows), pyelectasia, and loss of corticomedullary distinction.

Cytologic and histopathologic samples were acquired with ultrasound-guidance by fine-needle aspirate using a 21-gauge or a 23-gauge hypodermic needle or 18-gauge percutaneous tissue-core biopsy. All final diagnoses were made by a board certified veterinary pathologist.

An Acuson Sequoia 512 ultrasound system (Siemens plc, Berkshire, UK) with vector (10V4) and curvilinear (6C2) electronic transducers was used. A 5-8 MHz frequency was selected depending on the size of the patients, and sagittal images of the kidneys were acquired. Abdominal ultrasound revealed bilateral renal lesions in nine dogs, and one dog was affected unilaterally. Parenchymal lesions were seen in nine dogs; abnormalities were bilateral in six and unilateral in three (one in the left kidney and two in the right). Parenchymal lesions were comprised of loss of corticomedullary distinction, parenchymal hypo- and/or hyperechoic lesions, renomegaly, and renal deformity. In eight dogs renomegaly was present; six had bilateral enlargement and two had unilateral enlargement (one left kidney and one right). The kidneys were bilaterally deformed in four dogs and unilaterally deformed in two. Pyelectasia was observed in all dogs, and was bilateral in nine; these were classified as grade 1 ( $n = 4$ ), grade 2 ( $n = 1$ ), and grade 3 ( $n = 5$ ). Loss of corticomedullary distinction was present in nine dogs. In five the abnormality was bilateral and generalized, and in four it was unilateral (of which it was generalized in one dog and focal in three).

Six dogs had hypoechoic lesions. These consisted of hypoechoic nodules, hypoechoic masses, and hypoechoic areas (Fig. 1 and 2). A unilateral lesion (a hypoechoic mass) was present in one dog and bilateral hypoechoic lesions were present in five. Of these five, four had at least one hypoechoic mass (two bilateral, two unilateral), four had at least one hypoechoic nodule (two bilateral, two unilateral), and five had bilateral hypoechoic areas. Only two dogs were found to have hyperechoic lesions; one had a

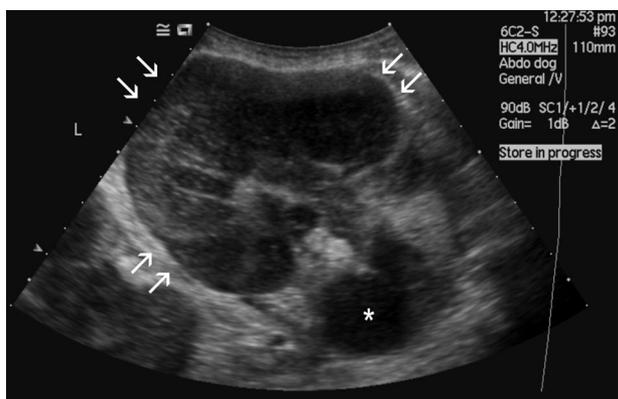


FIG. 2. Sagittal ultrasound image of an enlarged left kidney in a dog with renal lymphoma demonstrating a hypoechoic mass (arrows), hypoechoic nodule (asterisk), and loss of corticomedullary distinction. Note that the hypoechoic mass is causing renal deformity.

focal area of medullary hyperechogenicity and the other a poorly margined area of hyperechogenicity affecting cortex and medulla on the cranial pole, and both were focal and unilateral. Perirenal and/or subcapsular lesions were not observed on initial ultrasound in any dogs.

Other abdominal ultrasound findings included enlarged lymph nodes [ $n = 4$ , consisting of medial iliac, renal, and paraaortic ( $n = 1$ ), medial iliac only ( $n = 1$ ), renal only ( $n = 1$ ) and mesenteric only ( $n = 1$ )], splenic nodules ( $n = 2$ ), hepatic nodules ( $n = 2$ ), thickened gall bladder wall hypoechoic externally and hyperechoic internally ( $n = 2$ ), minimal to mild ascites ( $n = 2$ ), hypoechoic pancreas ( $n = 1$ ), thickened small intestinal wall ( $n = 1$ ), rectal mass ( $n = 1$ ), minimal retroperitoneal fluid ( $n = 1$ ), and hyperechoic perirenal fat ( $n = 1$ ).

In three dogs, ultrasound revealed mild abnormalities: grade 1 pyelectasia, mild renomegaly and focal loss of corticomedullary definition in one dog; grade 1 and grade 2 pyelectasia in another (Fig. 3), and grade 1 pyelectasia, focal loss of corticomedullary definition and hyperechoic areas in the medulla in the last (Fig. 4).

In one dog, initial ultrasound revealed only mild renal enlargement, focal loss of corticomedullary distinction and grade 1 pyelectasia, findings compatible with nonspecific nephropathy. One month later, persistent erythrocytosis and development of azotemia led to further investigations and a second ultrasound. At that time, marked renomegaly, generalized loss of corticomedullary distinction, and grade 3 pyelectasia were found and fine-needle aspirates from the left kidney confirmed lymphoma. A few hours later, this patient's clinical condition deteriorated with marked lethargy and cardiovascular compromise, and acute development of hypoechoic subcapsular or perirenal lesions was demonstrated ultrasonographically and on abdominal CT (Fig. 5). Due to the Hounsfield unit number in pre- and post- contrast CT images, these lesions were in-

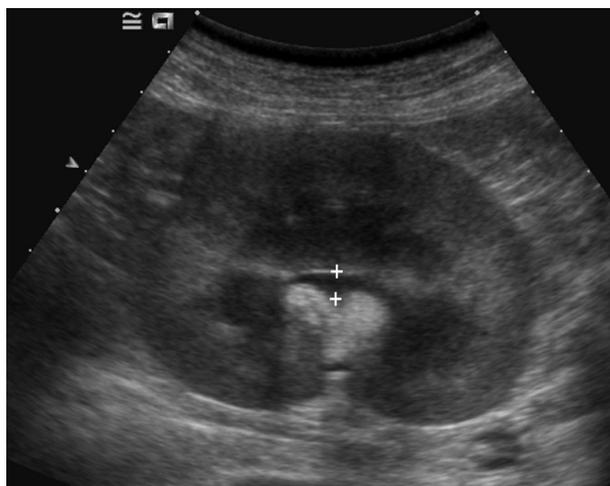


FIG. 3. Sagittal ultrasound image of a left kidney in a dog with renal lymphoma demonstrating grade 2 pyelectasia (measured between the crosses). In this case renal lymphoma was diagnosed at necropsy.



FIG. 4. Sagittal ultrasound image of the right kidney in a dog with renal lymphoma demonstrating focal loss of corticomedullary distinction and hyperechoic areas within the medulla (asterisks). Renal length was considered to be normal (measured between the crosses). In this case renal lymphoma was diagnosed by fine-needle aspiration of the right kidney.

terpreted as renal hemorrhage and this was confirmed at necropsy.

Ultrasound guided fine-needle aspirates of the kidneys were acquired in nine dogs. In seven of nine cases (78%) cytological examination of the samples was diagnostic of lymphoma on first analysis. In one dog renal fine-needle aspiration was repeated after a provisional cytological diagnosis of round cell tumor; and a final diagnosis of lymphoma was reached. In the other dog a provisional cytological diagnosis of plasma cell tumor or lymphoplasmacytic lymphoma was given; ultrasound-guided renal tissue core biopsy confirmed the presence of lymphoma. There were no known complications attributable to fine-needle aspirates or tissue core biopsies. In one dog lymphoma was confirmed at necropsy. In this dog, nonspecific renal lesions

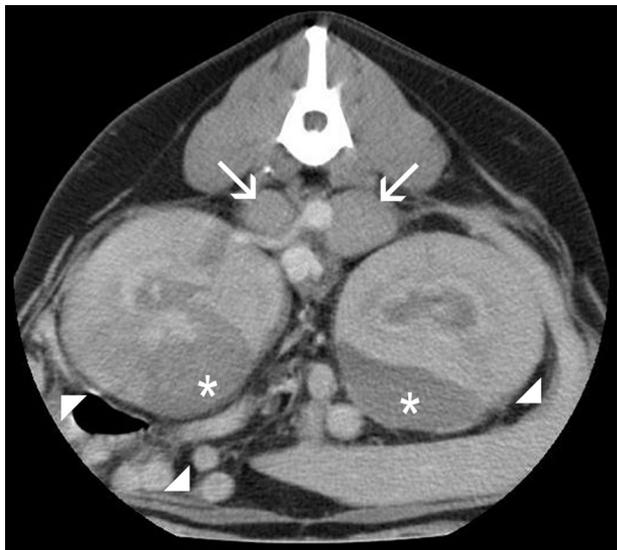


FIG. 5. Post contrast transverse CT image of a dog with renal lymphoma demonstrating marked bilateral renomegaly with parenchymal enhancement, and bilateral nonenhancing regions (asterisks) on the ventral aspect of the kidneys. These lesions were confirmed to be renal hemorrhage at necropsy. Note the regional lymphadenopathy (arrows) and mild ascites (arrowheads).

were found on ultrasound and assigned grade 2 and grade 1 pyelectasia on the left and right kidney, respectively.

### Discussion

All of the dogs in the current study presented with clinical signs compatible with the World Health Organization's criteria for substage b lymphoma: lethargy, vomiting, or diarrhea. Nine dogs were azotemic. With only one exception, this prompted further investigation followed by fine-needle aspirate sampling of the kidneys and often other organs, with the advantage of requiring only mild sedation for patient compliance. Individual ultrasound characteristics of renal lymphoma seen in our dogs could also be seen in dogs with other renal neoplasms such as histiocytic sarcoma, hemangiosarcoma, or carcinoma. Hypoechoic nodules are frequently observed with histiocytic sarcoma, but hyperechoic lesions have also been documented.<sup>20,21</sup> Hemangiosarcoma and carcinoma have been described as hypoechoic renal masses or nodules; however, they are usually unilateral in distribution.<sup>22,23</sup> In this study, bilateral renal lesions were present in nine of ten dogs. In humans as well, renal lymphoma lesions are typically bilateral and this is in contrast with carcinomas that are more frequently unilateral.<sup>24,25</sup> Pyelectasia, renomegaly, hypoechoic parenchymal lesions, and loss of corticomedullary distinction were commonly seen in our study. This combination of ultrasound characteristics is similar to previously reported findings in human and feline forms of renal lymphoma.<sup>26-28</sup> A significant association has been found

between hypoechoic capsular thickening and renal lymphoma in cats.<sup>29</sup> Retroperitoneal extension to the kidneys or perinephric space is a pattern common in humans with widespread disease but was not seen in this subset of dogs.<sup>24</sup> As our selection criteria excluded patients with extensive multicentric disease, the dogs in this series did not commonly have severe sonographic lesions in other organs.

In most instances (7/10 dogs), renal ultrasound demonstrated marked abnormalities. However, in three dogs, the ultrasonographic findings were mild and nonspecific. Mild renomegaly in particular could be misdiagnosed or overlooked in some dogs with renal lymphoma as there is a great interbreed variability of renal size in dogs. A method for measuring renal size with ultrasound has been described, but the degree of accuracy of this method in identifying kidney enlargement remains unknown.<sup>19</sup>

One dog with mild renal changes on initial ultrasound had obvious lesions on the repeated exam performed four weeks later. It is likely that in this instance an early phase of the disease was depicted on initial presentation, with tumor growth being primarily interstitial while preserving parenchymal structures and normal contour of the kidneys. This imaging-pathologic correlation has been seen in humans.<sup>30</sup> Repeat ultrasound scans and fine-needle aspirations may therefore be useful in dogs with mild or nonspecific renal ultrasound findings, especially if presented with signs of renal impairment.

Pyelectasia was reported in all ten dogs. Mild pelvic dilation may be due to a number of causes, including intravenous fluid administration and conditions affecting glomerular filtration rate. Pyelectasia is a nonspecific finding and should be interpreted with caution. Seven of the dogs with pyelectasia in the current study had received fluid therapy prior to abdominal ultrasound. However, of these seven dogs, four had grade 3 pyelectasia and one grade 2. These grades are considered unlikely to be due to fluid therapy alone. Hydronephrosis is commonly documented in humans with renal lymphoma.<sup>30</sup> Our findings suggest that pelvis dilation could also be an indicator of canine renal lymphoma. There is little information available regarding the correlation between the severity of pyelectasia and specific diseases. Furthermore, assessment of renal pelvic dilation is not well standardized in veterinary literature. Consistent guidelines regarding the ultrasound method used to measure renal pelvis size or a scoring system to classify pyelectasia are lacking. The terms mild, moderate, and severe are subjective. We attempted to improve standardization of renal pelvis measurements in our study by introducing a grading system based on pelvic width measured in sagittal plane.

In one dog, the disease progressed to bilateral renal hemorrhages that were evident on repeated ultrasound imaging. This patient had undergone fine-needle aspiration of the left kidney only. Renal hemorrhage was not considered to be

iatrogenic as it was present in both kidneys. Spontaneous renal hemorrhages have not been reported in the veterinary literature for lymphoma, but have been occasionally documented in humans.<sup>31</sup> While CT examinations are not possible for all patients, particularly those that are unstable, this is thought to be a more sensitive and comprehensive method to assess renal abnormalities. Computed tomography can be especially helpful with the addition of contrast to assess early and late phases of renal enhancement. It can also better detect other organ or regional lymph node involvement and evaluate adjacent structures. Computed tomography is the imaging modality of choice in humans with suspected renal lymphoma.<sup>26</sup>

Six of ten dogs in this series presented with hypoechoic focal lesions, consistent with that reported in the human literature. The decreased echogenicity is thought to reflect the predominant lymphocytic component as both lymph nodes and nonlymphoid organs become hypoechoic with infiltration of lymphoma.<sup>30,32,33</sup> Renomegaly without distortion of the contour is most common in humans with Burkitt's lymphoma, either primary or multicentric form, and is due to diffuse infiltration of neoplastic cells.<sup>34</sup> In our study renomegaly was found in eight dogs, but in two it was not associated with renal deformity, suggesting a similar behavior to Burkitt's lymphoma. As healthy renal parenchyma does not contain lymphatic tissue, it has been hypothesized that the source of renal lymphoma is the capsular lymphatics, the perirenal fat, or chronic inflammatory processes in the kidney with recruitment of lymphocytes and subsequent neoplastic transformation. As the cancer progresses, cells proliferate within the interstitium, between nephrons and blood vessels, resulting in expansile masses that replace the parenchyma and stretch the capsule. Asymmetrical growth can be evident in solitary masses, and rapid uniform growth of neoplastic foci results in the multiple masses frequently observed.<sup>26</sup> Alternatively, multiple mass lesions could be a

result of hematogenous dissemination as the smaller interlobular arteries extend into the cortical space.<sup>30</sup>

Labrador Retrievers were overrepresented in our sample population. This may suggest a breed-associated risk of renal lymphoma, however no reliable conclusions can be made in view of the small number of cases and in the absence of statistical power. Future studies may be warranted to further explore this theory.

In our study, fine-needle aspirate cytology sampling of seven of nine dogs (78%) yielded a definitive diagnosis at first attempt. The role of fine-needle aspiration cytology for the evaluation of most neoplasms is well-recognized in the veterinary literature, and commonly used for diagnosis of lymphoma in lymph nodes and most nonlymphoid organs. Findings from the current study also support this sampling technique for dogs with renal lymphoma. Increased sensitivity can be achieved by repeat sampling or immunophenotyping.<sup>35</sup> In one of the dogs in this study, repeated aspiration was effective in confirming lymphoma. Percutaneous biopsy sampling and histopathology provided a more definitive diagnosis in cytologically inconclusive cases. No complications to renal biopsy occurred in these dogs.

In conclusion, the ten dogs with renal lymphoma in the current study had a combination of ultrasonographic characteristics similar to that described for the human form of the disease (renomegaly, hypoechoic lesions, and bilateral involvement). The findings of this study suggest that the pathology of tumor proliferation in dogs and humans may also be similar. A larger study may provide more insight into the similarities. Based on findings in a few dogs, it is also possible that kidneys affected with lymphoma may not have obvious sonographic lesions. For these cases, additional advanced imaging, repeated ultrasound or renal biopsies may then be helpful. Fine-needle aspirate cytology was a high-yield test for the disease in this sample of dogs.

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