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Study of the ultrasonography features of renal lymphosarcoma tumor in cats

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Abstract This study aimed to evaluate the ultrasonographic characteristics of lymphosarcoma and also the role of fine needle biopsy in cats. In this study, five domestic short-haired and native cats with renal lymphosarcoma tumors including 3 females and 2 males with an average age of 7-9 years were collected. After each of these cats was referred to the radiology department, an ultrasound was performed by the radiologist of the abdominal cavity, and kidney symptoms were reported. In the evaluation of ultrasonography, pelvis dilatation was observed in all cats. The kidney cortex was not distinct from its central section, enlargement of the kidney in 4 cases, deformed kidneys in 3 cases, decreased echogenicity of the kidneys in 3 cases, and kidney echogenic increase in 2 cats were observed. In 95% of cases, lesions were bilateral. Kidney sampling was performed by fine needle aspiration in 4 cats. In the initial evaluation, the diagnosis was given in 3 cases (86%). The diagnosis of temporary cytology was given from round neoplasia cells in two cats. One of them, lymphosarcoma was confirmed by second aspiration, and the other cat was biopsied of the medulla tissue. In one case, the diagnosis was followed by a necropsy. The findings indicate that the signs of ultrasound of kidney lymphosarcoma in cats may not be significant, and in cases of high ultrasound characteristics, differential diagnoses should be considered. Also, biopsy for cytological tests by fine needle aspiration can be valuable in diagnosing this disease.

Introduction

Lymphosarcoma (lymphoma) is one of the most common cancers diagnosed in most breeds of cats [1]. It is a cancer of the lymphocytes (a type of blood cell) and lymphoid tissues. Lymphoid tissue is normally present in many places in the body including lymph nodes, spleen, liver, gastrointestinal tract, and bone marrow [2]. Lymphosarcoma can be divided into several different forms, which depend upon the primary (predominant) site of the tumor. Some cats have multiple sites of involvement and do not fit well into just one category. These are usually animals with very advanced disease. The kidneys may be the primary site of involvement [3]. Cats that have this type are often seen because of signs related to kidney failure (increased thirst, increased urination, loss of appetite, vomiting). A biopsy (tissue) or cytology sample is required to make a diagnosis of lymphosarcoma. In some cases, it can obtain a diagnosis without surgery. However, in some cases, we may need to perform a surgical biopsy to obtain adequate tissue to confirm the diagnosis. The ease with which a diagnosis can be made depends upon

where the tumor is located [4]. A complete evaluation of a cat suspected of having lymphosarcoma includes a search for tumors in other locations (this is what we call staging). A complete blood count (CBC), a serum chemistry profile, urinalysis, and FeLV/FIV testing are always performed and provide important information regarding the effects of cancer on body functions as well as the ability of the patient to handle chemotherapy [2,5]. An abdominal ultrasound (sonogram) allows us to evaluate the liver, spleen, internal lymph nodes, and intestinal tract for possible tumor involvement. Chest X-rays allow us to look for internal lymph nodes, lung involvement, an enlarged mediastinum, or fluid around the lungs [6,7]. A bone marrow aspirate allows us to look for tumor cells in the bone marrow as well as to evaluate the marrow's ability to produce normal blood cells [8]. At the time of this report, little published information could be found on the ultrasonographic characteristics of feline renal lymphosarcoma.

Thymidine kinase (TK) is known as a cytoplasmic enzyme involved in the phosphorylation of deoxythymidine to deoxythymidine monophosphate as part of the major one-step salvage pathway in the synthesis of pyrimidine. TK is included in both cytosolic (TK1) and mitochondrial forms (TK2). TK1 is related closely to the proliferation of cells, and its activity may be linked with the degree of DNA synthesis and correlated to the rate of proliferation of cells, which especially is high in haematopoietic malignancies. Determination of serum TK1 (sTK) activity possesses various applications in human clinical oncology, such as early detection of malignancy and monitoring of response to treatment. TK activity has also been evaluated in canine and feline oncology where levels have been assigned to reflect the clinical stage of lymphoma and lymphosarcoma, as well as prognosis, and prediction of relapse before the improvement of clinically detectable disease [9,10].

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

Materials and Methods

Animals

Five domestic short hair and native cats with renal lymphosarcoma tumors including 3 females and 2 males with an average age of 7.9 years were investigated.

Experiment procedure

After each of these cats was referred to the radiology department, an ultrasound was performed by the radiologist of the abdominal cavity, and renal symptoms were reported. The ultrasound device that was used for ultrasonography was EUB-8500 XP (Hitachi Medical Corporation, Tokyo, Japan), and a linear probe with a frequency of 8-10 MHz frequency was selected depending on the size of the patients, and sagittal images of the kidneys were acquired. Criteria for inclusion were a definitive histological and/or cytological diagnosis of renal lymphosarcoma, and cats 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. Cats 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. The information recorded included signalment, renal values, any administration of fluid therapy before imaging, ultrasonographic findings, diagnostic method of lymphosarcoma, 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: Parenchymal lesions (unilateral or bilateral), Renal enlargement (unilateral or bilateral), Deformed shape (unilateral or bilateral), Pyelectasis (unilateral or bilateral), Degree of

pyelectasis for each kidney (defined as grade I, up to 0.5mm in width; grade II, between 0.5 and 1.5 mm; and grade III, more than 1.5 mm), Loss of corticomedullary distinction (unilateral or bilateral), Hypoechoic nodules (defined as well defined round hypoechoic lesions less than 0.5 cm in diameter), Hypoechoic masses (defined as well defined lesions greater than 0.5 cm), Hypoechoic areas (defined as nonround, non-well defined hypoechoic lesions), Hyperechoic lesions, and Perirenal and/or subcapsular lesions (defined as abnormalities not considered to be retroperitoneal fluid). To evaluate kidney enlargement, its length can be measured on the sagittal axis, or its size can be obtained based on the ratio between the kidney length and the diameter of the aorta, which in the enlargement of the kidney, its length will be nine times the diameter of the aorta.

Thymidine Kinase 1 and lactate dehydrogenase (LDH) Assay

TK1 and LDH activity was assayed in 10 cats with renal lymphosarcoma tumors and 10 clinically and para-clinically healthy cats. The TK1 activity was measured by OwjAzmaPlast Co. Tehran Kit based on the ELISA technique. Serum LDH activity was detected by the Spectrophotometric method (Spekol, 1500) (Pars Azmoon Co Kit. Tehran. Iran). A p-value of 0.01 was set as statistical significance.

Results

Abdominal ultrasonography determined bilateral renal lesions in four cats, and one cat was affected unilaterally. Parenchymal lesions were seen in four cats; abnormalities were bilateral in three and unilateral in one cat. Parenchymal lesions were comprised of loss of corticomedullary distinction, parenchymal hypo- and/or hyperechoic lesions, renomegaly, and renal deformity. In four cats, renomegaly was present; 3 cats had bilateral enlargement and 2 cats had unilateral enlargement (one left kidney and one right). The kidneys were bilaterally deformed in 2 cats and unilaterally deformed in 2 cases. Pyelectasis was observed in all cats, and was bilateral in four cases; these were classified as grade I (n = 2), grade II (n = 1), and grade III (n = 2). Loss of corticomedullary distinction was present in 4 cats. In five the abnormality was bilateral and generalized, and in 4 cats it was unilateral (of which it was generalized in 1 cat and focal in 3 cats). Three cats had hypoechoic lesions. These consisted of hypoechoic nodules, hypoechoic masses, and hypoechoic areas (Figure 1).

Fig 1. A sagittal sonogram of the left kidney in a cat with renal lymphosarcoma. Several hypoechoic nodules are observed in renal parenchymal tissue (arrows).

A unilateral lesion (a hypoechoic mass) was present in one cat and bilateral hypoechoic lesions were present in 2 cats. Of these 5 cases, 4 cats had at least one hypoechoic mass (two bilateral, two unilateral), 4 cats had at least one hypoechoic nodule (two bilateral, two unilateral), and 5 cats had bilateral hypoechoic areas. Only 2 cats were found to have hyperechoic lesions; one had a focal area of medullary hyperechogenicity and the other a poorly marginated area of hyperechogenicity affecting the cortex and medulla on the cranial pole, and both were focal and unilateral. Perirenal and/or subcapsular lesions were not observed on the initial ultrasound in any cats. Other abdominal ultrasound findings included enlarged lymph nodes, consisting of medial iliac, renal, and paraaortic, medial iliac only, renal only and mesenteric only, splenic nodules, hepatic nodules, thickened gall bladder wall hypoechoic externally and hyperechoic internally, minimal to mild ascites, hypoechoic pancreas, thickened

small intestinal wall, rectal mass, minimal retroperitoneal fluid, and hyperechoic perirenal fat. In 3 cats, the ultrasound revealed mild abnormalities: grade 1 pyelectasis, mild renomegaly, and focal loss of corticomedullary definition in one cat; grade I and grade II pyelectasis in another (Figure 2), and grade I pyelectasis, focal loss of corticomedullary definition and hyperechoic areas in the medulla in the last. In one cat, the initial ultrasound revealed only mild renal enlargement, focal loss of corticomedullary distinction, and grade I pyelectasis, findings compatible with nonspecific nephropathy.

Fig 2. Transverse ultrasound plane of a right kidney in a cat with renal lymphosarcoma. Measured between the crosses illustrating garde II of renal pelvic dilatation (pyelectasis).

One month later, persistent erythrocytosis and the development of azotemia led to further investigations and a second ultrasound. At that time, marked renomegaly, generalized loss of corticomedullary distinction, and grade III pyelectasis were found and fine-needle aspirates from the left kidney confirmed lymphosarcoma. 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 (Figure 3).

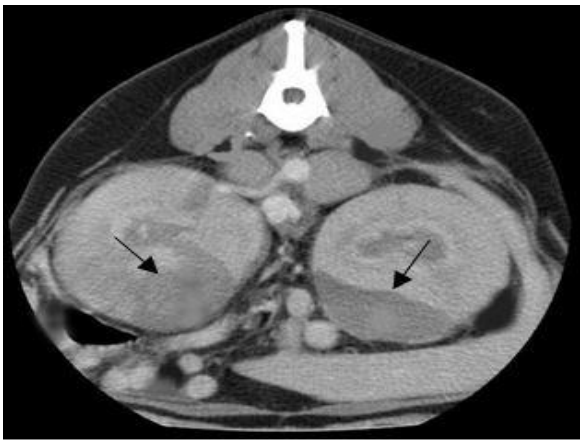

Fig 3. Computed tomography scan of a cat with renal lymphosarcoma. Illustrating marked bilateral renal enlargement with parenchymal enhancement, and bilateral non-enhancing regions (arrows) on the ventral aspect of the kidneys.

Due to the Hounsfield unit number in pre- and post-contrast CT images, these lesions were interpreted as renal hemorrhage and this was confirmed at necropsy. Ultrasound-guided fine-needle aspirates of the kidneys were acquired in 4 cats. In three of four cases (86%) cytological examination of the samples was diagnostic of lymphosarcoma on first analysis. In a cat in primary ultrasound, there was only one partial renal enlargement, focal disappearance between the cortical and medullary parts of the kidney, and pelvic dilatation, which were consistent with nonspecific nephropathy. A month later, persistent erythrocytosis and an increase in azotemia led to later examinations and second sonography. At this time, the enlargement of the kidney was evident, and the distance between the cortical and medullary parts of the kidney was indeterminate and there was a third-grade dilatation of the pelvis. Lymphosarcoma was confirmed by biopsy with FNA of the left kidney.

Significant increases in TK1 and LDH activity were observed in the lymphosarcoma group compared with healthy ones. Severe activity of LDH (approximately 40 times of healthy cat's range) and high activity of TK1 (about 13 times of healthy cat's range) were observed in all lymphosarcoma cats (Table 1).

Table 1: Serum TK1 and LDH activity in lymphosarcoma and healthy groups. Mean ± SD

	Lymphosarcoma	Healthy
TK1 (U/l)	12.08±1.05†	1.16 ± 0.03
LDH (U/l)	98.25 ± 9.59†	3241.64 ± 68.82

*Data are expressed as Mean ± SD. † as superscript denotes significant difference in comparison with healthy group. ($P < 0.01$).

Discussion

In this study, all cats that were evaluated had clinical symptoms such as lethargy and sleepiness, vomiting, or diarrhea. Four cats have azotemia or increased nitrogen concentrations in the blood, which has led to further investigation by biopsy and sampling by FNA of kidneys and other tissues. Hypoechoic nodules have been commonly seen with histocytic sarcoma tumors, but hypoechoic lesions have been documented in this regard [11,12]. Hemangiocarcinoma and carcinoma are described as nodules or hypoechoic renal masses; however, they are commonly expanded unilaterally [13,14]. In this study, bilateral renal lesions were present in four cats. In humans, renal lymphoma lesions are usually bilateral and this is the opposite of carcinomas which are often unilateral [15,16]. The pelvic dilatation, renal enlargement, hypoechoic parenchymal lesions, and loss of cortical and central renal fragmentation were observed in our study. These ultrasonographic features are similar to those reported in previous reports of renal lymphoma in humans and cats [17,18]. There is a significant correlation between hypoechic thickness and renal lymphoma in cats [19]. In most cases, Ultrasound evaluation of the kidneys revealed abnormal conditions. However, in three cats, ultrasonographic findings were partial and non-specific. Mild renomegaly in particular could be misdiagnosed or overlooked in some cats with renal lymphosarcoma as there is a great interbreed variability of renal size in cats. 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. One cat with mild renal changes on the 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. The correlation between imaging findings and pathological observations has been observed in human cases. Repeat ultrasound scans and fine-needle aspirations may therefore be useful in cats with mild or nonspecific renal ultrasound findings, especially if presented with signs of renal impairment. Pyelectasis was reported in all 4 cats. Mild pelvic dilation may be due to several causes, including intravenous fluid administration and conditions affecting the glomerular filtration rate. Pyelectasis is a nonspecific finding and should be interpreted with caution. Three of the cats with pyelectasis in the current study had received fluid therapy before abdominal ultrasound. However, of these 3 cats, 2 had grade III pyelectasis and one grade II. These grades are considered unlikely to be due to fluid therapy alone. Hydronephrosis is commonly documented in humans with renal lymphoma [20]. Our findings suggest that pelvis dilation could also be an indicator of feline renal lymphosarcoma. There is little information available regarding the correlation between the severity of pyelectasis and specific diseases. Furthermore, the 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 pyelectasis are lacking. The terms mild, moderate, and severe are subjective. We attempted to improve the standardization of renal pelvis measurements in our study by introducing a grading system based on pelvic width measured in the sagittal plane. In one cat, 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 lymphosarcoma, but have been occasionally documented in humans [21]. While CT

examinations are not possible for all patients, particularly those who 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 [22]. Three cats 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 lymphosarcoma [23,24]. Renomegaly without distortion of the contour is most common in humans with Burkitt'slymphosarcoma, either primary or multicentric form, and is due to diffuse infiltration of neoplastic cells [25]. In our study renomegaly was found in 3 cats, but in 2 cases it was not associated with renal deformity, suggesting a similar behavior to Burkitt's lymphosarcoma. As healthy renal parenchyma does not contain lymphatic tissue, it has been hypothesized that the source of renal lymphosarcoma is the capsular lymphatics, the perirenal fat, or chronic inflammatory processes in the kidney with recruitment of lymphocytes and subsequent neoplastic transformation. As 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. Alternatively, multiple mass lesions could be a result of hematogenous dissemination as the smaller interlobular arteries extend into the cortical space [26]. 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 lymphosarcoma in lymph nodes and most nonlymphoid organs. Findings from the current study also support this sampling technique for cats with renal lymphosarcoma. Increased sensitivity can be achieved by repeat sampling or immunophenotyping [27]. In one of the cats in this study, repeated aspiration was effective in confirming lymphosarcoma. Percutaneous biopsy sampling and histopathology provided a more definitive diagnosis in cytologically inconclusive cases. No complications to renal biopsy occurred in these cats.

Conclusion

As a result of this study, five cats with renal lymphosarcoma disease had symptoms such as kidney enlargement, hypoechoic lesions, and bilateral renal complications. These findings suggest that the pathology of tumor spreading in cats and humans may be similar. A more comprehensive study may provide more insights than similarities. In some cats, kidneys affected by lymphosarcoma may not exhibit obvious ultrasound lesions. For these cases, other advanced imaging, ultrasonography, and kidney tissue sampling are recommended. A biopsy for cytology through FNA was a high-performance test to detect this disease in these cats.

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Conflict of interest

The authors declare that they have no competing interests.

Ethical approval

For this type of study formal consent is not required.

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