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CASE REPORT

Companion or pet animals

# Imaging features of unilateral renal T-cell lymphoma occurring simultaneously in the urinary bladder wall and contralateral ureter with secondary polycythaemia in a dog

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A six-years-old neutered male Labrador Retriever was presented with haematuria and inappetence of one-week duration. Physical examination revealed mild abdominal pain and the blood cell count showed moderate polycythaemia, with a slight increase of the erythropoietin levels. Urinalysis demonstrated proteinuria, haematuria and isosthenuria and urinary sediment revealed mild amount of lymphoid cells. After performing a complete imaging study (radiographs, ultrasound and CT scan), a unilateral renal lymphoma with secondary extranodal lymphoma of the urinary tract (bladder wall and left ureter) was suspected. Fine-needle aspirates of both kidneys, ureter and bladder masses were obtained, and a tentative diagnosis of lymphoma was made. Positive PCR antigen receptor rearrangement indicated a T-cell origin. The owners opted for euthanasia and declined necropsy. CT was essential for the evaluation of this case, not only depicted renal lesions, but also identified accurately extension to adjacent anatomic structures helping to determine the systemic spread of the disease.

**KEYWORDS**
computed tomography (CT), dogs, renal lymphoma, ureter lymphoma

## BACKGROUND

Lymphoma is a common haematopoietic neoplasm in dogs and cats that often occurs in multicentric, gastrointestinal, mediastinal and cutaneous forms, with the primary extranodal presentation being less frequent.[1] The prevalence of primary renal lymphoma is unknown in dogs, and a small number of cases have been sporadically published in the veterinary literature.[2] On the other hand, lymphoma of the urinary tract involving the kidney, ureter and bladder is a very rare presentation in dogs and humans, described in very few cases.[3,4]

Different canine renal tumours such as carcinomas, sarcomas and lymphomas have been found to be associated with non-primary erythrocytosis[5]; moreover, in a recent study with a population of twenty-nine dogs with presumed primary renal lymphoma, secondary polycythaemia was observed in 51% of cases.[2] This type of polycythaemia is due to an increase in the production of erythropoietin (EPO) or an EPO-like substance, in the absence of systemic hypoxia, which could be originated by both benign and malignant disorders.[5] According to the reviewed literature, only a reduced number of cases of renal lymphoma combined with secondary erythrocytosis have been reported in dogs.[5–7]

Although a biopsy is mandatory to reach the definitive diagnosis of renal T-cell lymphoma, abdominal ultrasound has been widely used to initially assess the renal appearance.[6] However, in certain cases the use of CT can improve the accuracy of the diagnosis since it depicts in better detail the involvement of other organs.[8]

The objective of this report is to describe a case of a unilateral renal T-cell lymphoma and secondary polycythaemia simultaneously involving the lower contralateral ureter and the bladder in a dog, which was detected by imaging and confirmed by clinical pathology, flow cytometry and clonality.

## CASE PRESENTATION

A six-year-old neutered male Labrador Retriever was presented to VTHUM following a one-week history of haematuria, urinary incontinence, polydipsia and inappetence. The owners reported that the dog had a 4-week history of apathy,

lethargy and weight loss. Physical examination only revealed mild to moderate abdominal pain on cranial abdomen palpation. The remainder of the physical examination was unremarkable.

## INVESTIGATIONS

Initial diagnostic tests included a complete blood cell count (CBC), serum biochemical profile, urinalysis, abdominal radiographs and ultrasonographic examination.

Significant changes in the CBC included moderate polycythaemia. The red blood cell (RBC) count was $8.9 \times 10^6/\mu l$ (reference interval (RI), 5.69-8.56 $\times$ $10^6/\mu l$), hematocrit (HCT) was 62% (RI: 38%−58%) and hemoglobin (Hb) was 212 g/L (RI: 137–206 g/L). A normal concurrent total plasma protein (59 g/L; RI: 54–72 g/L) was also measured. The remainder of the CBC was within normal limits. On biochemistry, abnormalities consisted of moderate azotemia (urea: 99.1 mg/dl; RI: 20–50 mg/dl, creatinine: 2.53 mg/dl; RI: 0.5-1.5 mg/dl), mild hypoalbuminemia (2.2 g/dL; RI: 2.5-3.6 g/dL) and increase in the acute phase protein profile (CRP: 70.3 $\mu$g/ml; RI: < 12, ferritin: 875.7 $\mu$g/L; RI:60-190 $\mu$g/L). Urinalysis collected by ultrasound-guided cystocentesis demonstrated proteinuria (3+), a pH of 6.0, haematuria (3+) and isosthenuria (urine specific gravity was 1.013; RI: 1.015-1.045). The urine protein/creatinine ratio was elevated (6.024). Analysis of the sediment revealed some lymphoid cells. A urine bacterial culture was also performed showing no bacterial growth. All these data suggested the presence of renal failure and active inflammation.

On the abdominal radiographs, loss of serosal detail in the cranial abdomen was observed, and the right kidney was enlarged (4.5 times L2)[9] extending from T12-T13 to L3-L4, causing ventral displacement of the intestinal loops on the left lateral view (Figure 1). Thoracic radiographs were unremarkable.

Abdominal ultrasound was performed using a 3–8 MHz micro-convex and 4–13 MHz linear array transducers (MyLab Twice, Esaote, Barcelona, Spain). Ultrasound examination revealed an enlarged unstructured right kidney (13.2 × 7.5 cm) with loss of cortico-medullary distinction and heterogeneous echotexture, and a moderate dilated renal pelvis (1.5 × 1.2 cm) (Figure 2). The left kidney had a normal size (left kidney to aorta ratio: 8.5; RI: 5.5–9.1)[10] but presented a severe hydronephrosis (2.6 cm) (Figure 2). The left ureter was moderately dilated (0.8 cm) and could be followed presenting a mass 7 cm from the origin of the ureter. The ureteral mass was fusiform-shaped (2 × 4.5 cm), and hypoechoic compared to the renal cortex (Figure 2). In the caudodorsal aspect of the bladder at the trigone, there was a broad-based slightly heterogeneous mass of irregular borders (1 cm width x 3.3 cm length), being hyperechoic compared to the ureteral mass previously described (Figure 2). It was difficult to assess if the urethra was affected. The right medial iliac lymph node was enlarged (2.5 × 3.7 cm), hypoechoic and oval-shaped with reactive perinodal fat.

In order to characterize all the lesions observed in the ultrasonographic study, a CT scan of the abdomen was proposed. Plain and postcontrast (immediate and 5 minutes after contrast media administration) CT scans were carried out after administration of intravenous iodinated contrast medium (Iopromide 300mgI/ml [Ultravist 300, Bayer, Barcelona. Spain] at 800 mgI/kg and at 4 ml/s into cephalic vein catheter using a power injector (A-60, Nemoto, Tokyo, Japan). The patient was examined in sternal recumbency under general anaesthesia using a dual slice CT scanner

**LEARNING POINTS/TAKE-HOME MESSAGES**

- Urinary tract lymphoma, although not common in dogs, should be considered the main differential diagnosis when ultrasonographic and computed tomographic changes are detected at renal, ureter and urinary bladder level.
- While a larger number of cases are necessary to standardise the ultrasonographic and computed tomographic findings of the lymphoma at the ureter, the ultrasonographic features could be those of a hypoechogenic homogeneous mass, and the tomographic appearance that of a soft tissue mass with homogeneous contrast enhancement.
- Computed tomography is an essential method to perform to aid in the diagnosis of urinary tract lymphoma.

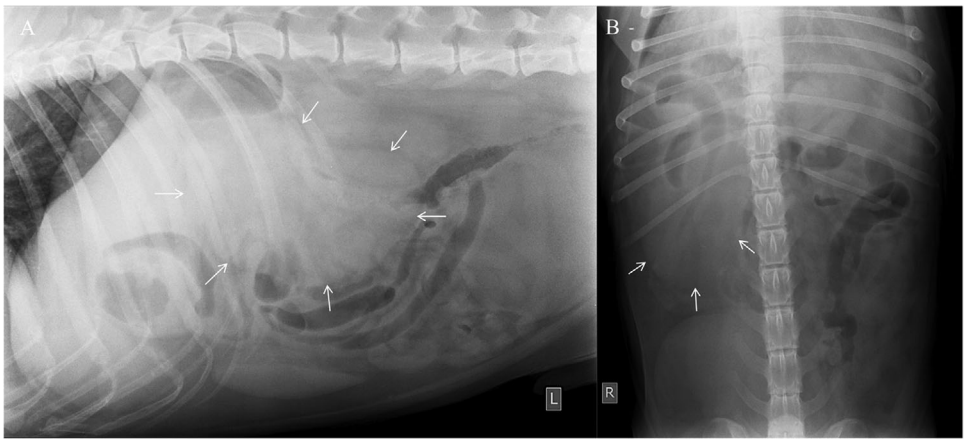


**FIGURE 1** Left lateral (A) and ventrodorsal (B) abdominal radiographs. Silhouette of the right kidney (arrows) is enlarged extending from T13 to L4, showing a ventral displacement of the intestinal loops. Loss of serosal detail in the cranial abdomen is also observed

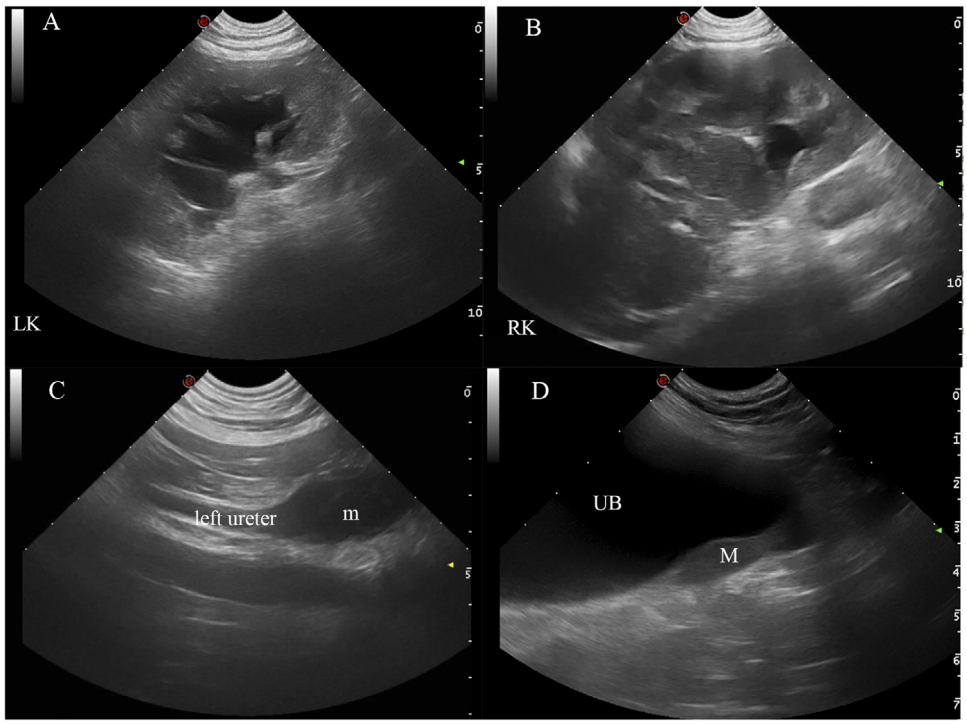


**FIGURE 2** Ultrasonographic images of the left kidney showing severe hydronephrosis (A), enlarged unstructured right kidney with loss of corticomedullary distinction and heterogeneous echotexture (B), left ureter moderately dilated presenting a hypoechoic mass (C) and urinary bladder with a hypoechoic broad-based mass at the level of the trigone (D)
Abbreviations: LK, left kidney; m, ureteral mass; M, bladder mass; RK, right kidney; UB, Urinary bladder.

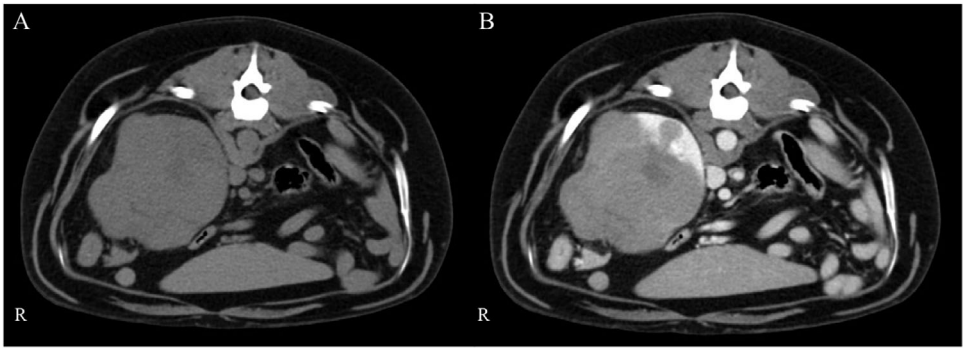


**FIGURE 3** Computed tomographic images. Transverse views before (A) and after contrast administration (B) where an enlarged mass on the cranial pole of the right kidney was seen. The mass was isoattenuating compare to the kidney in the pre-contrast phase with homogeneous enhancement in the post-contrast phases, being hypoattenuating to the normal renal parenchyma

(General Electric HiSpeed, General Electric Healthcare, Madrid, Spain). The CT technical parameters were 120 kV tube voltage, 80 mAs tube current, 1s tube rotation time, helical scan mode, collimator pitch of 1, 2 mm slice thickness and reconstructions interval with 50 % overlap. The display field of view was 35 cm, and matrix dimension was 512 × 512. Reformatted images in sagittal, dorsal planes, maximum intensity projection and volume rendering were obtained. Images were reviewed in a PACS workstation in soft tissue (WW = 400, WL = 40) and bone windows (WW = 1500, WL = 300). Adjustments to image window width and level were made as needed.

A large, irregular soft tissue mass within the cranial pole of the right kidney was present (dimensions: 9.5 cm length x 7 cm width x 8 cm height), causing loss of the normal renal architecture. The mass was isoattenuating compare to the kidney (43 HU) with a small hypoattenuated area (22UH) in the pre-contrast phase. After contrast administration the mass showed homogeneous enhancement in the immediate and 5 minutes post-contrast phases (64 HU and 75 HU respectively) being hypoattenuating to the normal renal parenchyma (Figures 3 and 4). The small hypoattenuated lesion did not show contrast uptake and was interpreted as a necrotic area. The left kidney presented normal size with slightly irregular contour. Both renal pelvis were distended (approximately 2.1 cm right kidney and 3.2 cm left kidney) suggesting bilateral urinary tract obstruction. In the 5 minutes post-contrast series, the right renal pelvis was totally filled with contrast enhancing urine and the left renal pelvis showed layering of nonenhancing and contrast-enhancing urine. The left ureter was moderately distended (0.85 cm) coursing along the abdomen, showing an ovoid-shaped soft tissue mass (40 HU) (dimensions: 5.8 cm

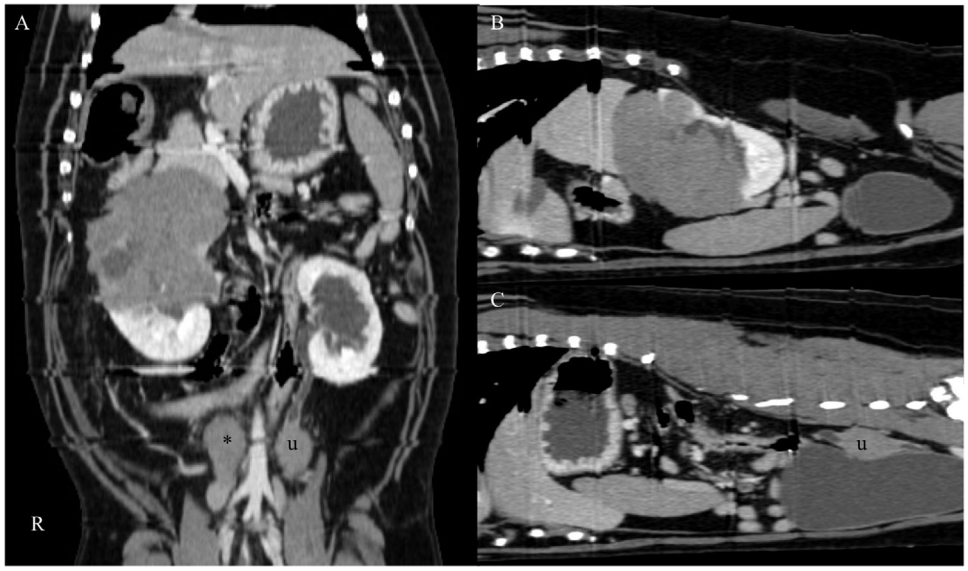


**FIGURE 4** Computed tomographic images after contrast administration. In the dorsal reconstruction view, an enlarged mass on the cranial pole of the right kidney, severe hydronephrosis of the left kidney, enlargement of the right medial iliac lymph node (*) and the ureteral mass (u) of the left ureter was seen (A). Sagittal reconstruction view of the right side of the abdomen showing the enlarged mass of the right kidney (B). Sagittal reconstruction view towards the left side of the abdomen where the ureteral mass (u) was nicely depicted dorsal to the urinary bladder (C)

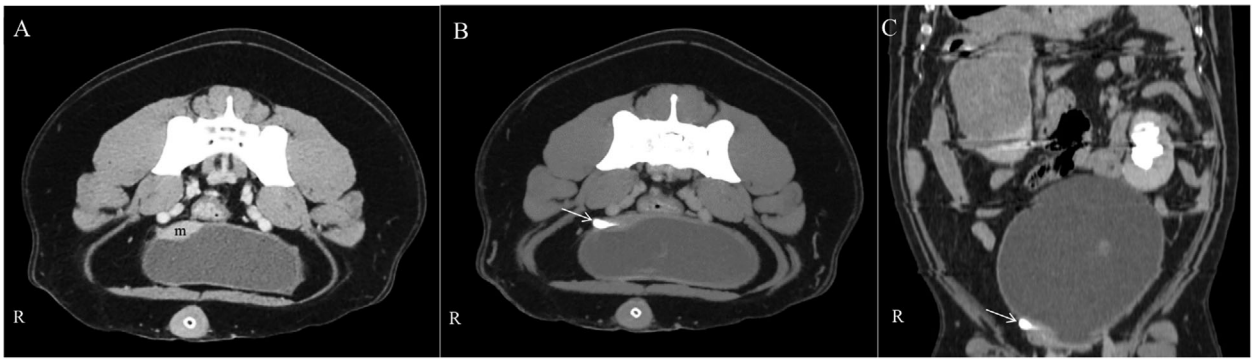


**FIGURE 5** Computed tomographic images. Transverse views (A and B) and dorsal reconstruction view (C) of the urinary bladder. A mass (m) arising from the right dorsal bladder wall at the level of the bladder trigone was observed (A). Note the right ureter with contrast ending in the bladder mass (arrow) (B and C)

length x 3 cm width x 2.2 cm height) located 6.5 cm caudal to the kidney (Figure 4). This mass showed homogeneous contrast enhancement in the post-contrast study (68 HU). The portion of the ureter caudal to the mass, presented normal diameter.

In the urinary bladder, a broad-base soft tissue attenuating mass (39 HU) was observed involving the trigone and extending caudally to the bladder neck. The mass showed a homogeneous contrast enhancement (100 HU and 75 HU on the immediate and delayed post-contrast phases respectively) (Figure 5). On the delayed phase, the right ureter was mildly distended (0.42 cm) on its most distal portion with a contrast-enhanced urine path through the mass before draining into the bladder.

After 5 minutes post-contrast administration, there was a minimal amount of contrast media into the urinary bladder suggesting a delayed renal excretion.

The hepatic, splenic, aortic and right medial iliac lymph nodes were enlarged, round-shaped, soft tissue attenuated (33 HU) and showed a homogeneous contrast enhancement (70 HU).

Based on the ultrasonographic and CT findings a secondary extranodal lymphoma of the urinary tract was suspected.

Ultrasound-guided aspiration from kidneys, ureter and urinary bladder masses was obtained. The cytological examination of the samples revealed that main cell population was composed of round cells with a high nucleus-cytoplasmic ratio (Figure 6). A flow cytometry assay was performed testing from an FNA and cells in suspension with the following markers: CD45, CD14, CD18, CD21, CD3, CD5, CD4, CD8, CHCII, CD34 and CD79a. The cells were CD45 and CD3 positive but negative for all the other antibodies (Figure 6). A diagnosis of atypical T cell (CD3 positive) lymphoma was done. Positive PCR antigen receptor rearrangement also indicated a T-cell origin.

Erythropoietin levels were also measured and showed a slight increase (0.7 mUI/ml, RI: 0.41–0.65).

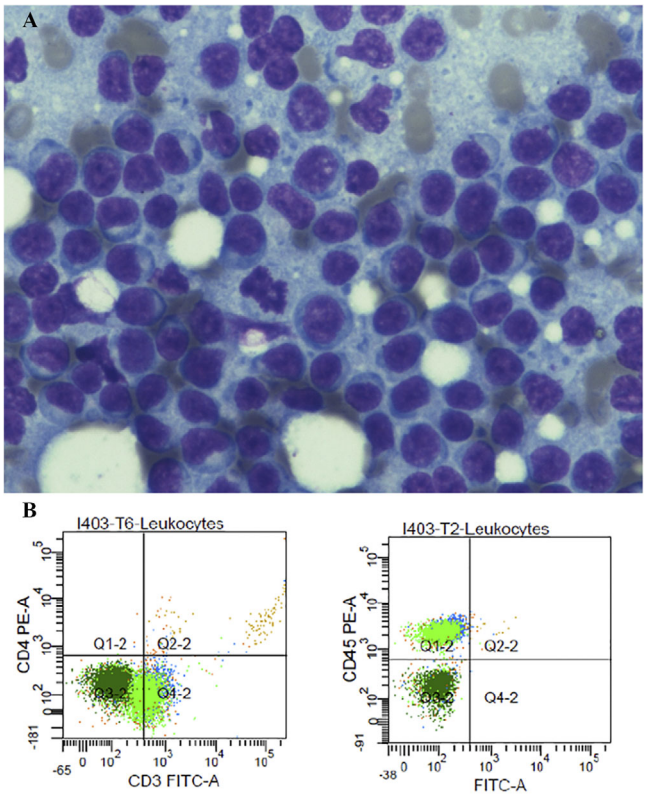


**FIGURE 6** Cytology of the left kidney showing intermedium large lymphocyte as the predominant cell type. H&E stain; x60 (A). Flow cytometry analysis of the kidney cytology showing a CD3 and CD45 positive cells and negative CD21, CD4, CD8 cells. A diagnosis of atypical T-cell (CD3 positive) lymphoma was done (B)

## DIFFERENTIAL DIAGNOSIS

On the basis of the imaging findings, clinical pathology, clonality and immunocytochemistry, the most likely diagnosis was a right renal lymphoma, simultaneously involving the contralateral ureter and the wall of the urinary bladder. Alternative differential diagnosis for the renal mass included tumours of epithelial origin: carcinoma, adenocarcinoma and transitional cell carcinoma, and non-epithelial neoplasms: hemangiosarcoma, fibrosarcoma and anaplastic sarcoma among others.[11,12] Differentials for the ureter mass were transitional cell carcinoma, leiomyoma and leiomyosarcoma, mast cell tumour, spindle cell sarcoma and other sarcomas.[13] And for the bladder mass, differential diagnosis included tumours of epithelial origin like the transitional cell carcinoma, followed by squamous cell carcinoma, adenocarcinoma and undifferentiated carcinoma; as non-epithelial origin tumours would be considered: leiomyomas and leiomyosarcomas, haemangiomas and haemangiosarcomas, fibromas and fibrosarcomas.[3]

## OUTCOME AND FOLLOW-UP

A guarded prognosis was given based upon the diagnosis, the owners declined any treatment, and the patient was humanely euthanised. A post-mortem examination was not allowed by the owners.

## DISCUSSION

Lymphoma is the most common hematopoietic neoplasm in dogs being the multicentric form the most frequent distribution pattern. Although renal involvement in canine multicentric lymphoma is common, primary renal lymphoma has rarely been reported,[5] being exceedingly infrequent to find primary extranodal lymphoma at the level of the urinary bladder or ureter.[14] In humans, the incidence of lymphoma at the level of the ureters has been found to be very low, since in a recent study of 1264 cases of primary urinary tract lymphoma, the ureters were affected in just 1.6% of patients.[4] According to the literature reviewed, there is only a single reported case of lymphoma involving ureters, kidneys and urinary bladder in a dog.[3] This referred case, like the one we present here, consisted of a T-cell lymphoma. However, our patient also had erythrocytosis, being, to the best of the author´s knowledge the first case that meets all these characteristics.

Erythrocytosis, also called polycythaemia, consists in an increase in the erythrocyte count. It is detected by an elevated RBC count, HCT, and/or haemoglobin concentration and could be relative or absolute.[15] The origin of a relative erythrocytosis may be due either to a haemoconcentration or to a transient physiologic erythrocytosis (due to splenic contraction).[5] On the other hand, absolute polycythaemia is caused by an increase in the total RBC mass, and it must be established whether it is primary (due to a myeloproliferative disorder) or secondary which results from excessive production of EPO.[15] By last, absolute secondary polycythaemia, can also be characterized as appropriate when it is associated with hypoxic stimulus, while it is inappropriate if the EPO production is autonomous and independent of systemic hypoxia.[5] In agreement with the case described by Froment and Gara-Boivin in 2015, it was very likely that the erythrocytosis observed in our patient was an inappropriate secondary type, since, although arterial blood gas analysis was not performed, the patient presented a normal cardiovascular examination, not supporting systemic hypoxia. Secondary polycythaemia due to inappropriately elevated EPO is an infrequent paraneoplastic syndrome associated with infiltrative renal neoplasia.[2,6] The increase in EPO production has been explained by two possible mechanisms, either the neoplastic cells are the ones that generate the ectopic production of EPO or an EPO-like substance, or the neoplastic infiltration produces compression of the renal tissue and vascular supply causing local renal hypoxia that would originate a physiologically-induced EPO production from hypoxic renal cells.[6] In the present case, there was a slight increase of EPO, most likely due to the presence of the renal neoplasia.[2,6]

For decades, abdominal ultrasound has been one of the main diagnostic tools to evaluate the kidneys when abnormalities in the renal architecture are suspected. Several studies have reported that the sonographic findings in dogs with renal lymphoma include renomegaly, hypoechoic lesions, pyelectasia and bilateral involvement; however, in our patient the sonographic appearance was that of a heterogeneous mass-type lesion that distorted the normal renal morphology, rather than hypoechoic nodules. The use of other techniques is a nonspecific requirement to reach the diagnosis;[2,11,16] however, in dogs weighing greater than 25 kg, patient factors such as body size, amount of intraperitoneal fat and interference from

gas artifact in the gastrointestinal tract can affect the quality and detail of the images acquired.[17] Multi-phase contrast-enhanced CT is used in dogs to assess pathologies affecting the kidney[18] while in humans, in addition to CT, MRI is also used for the evaluation of renal tumours in order to reduce the incidence of complications that may appear after a renal biopsy.[19] In a recent retrospective study, the tomographic findings of different canine kidney tumours were evaluated.[12] Although no significant differences were found between CT and histopathological findings and further studies are needed, renal lymphoma showed homogeneous enhancement, bilateral involvement and multiples masses, while renal cell carcinoma and hemangiosarcomas tended to show heterogeneous enhancement and unilateral renal involvement.[12] In our case, the CT study revealed a large, irregular soft tissue expansile mass within the cranial pole of the right kidney with homogeneous enhancement, hypodense compared with the adjacent normal renal tissue, in agreement with previous studies in humans and dogs.[8,12] In humans this finding is attributed to the fact that the lymphomatous tissue enhances less than the normal renal parenchyma, which helps to differentiate it from squamous cell carcinoma, which usually enhances in the arterial phase.[8] Both primary and secondary lymphoma involving the urinary bladder have been very rarely described in humans and dogs, especially those of T-cell origin.[14,20] Ultrasonographically, they cannot be differentiated from other urinary bladder tumours as they can appear either as heterogeneous mural masses or as a focal thickening affecting any part of the urinary bladder wall.[3,20] In the present case, a broad-based slightly heterogeneous mass of irregular borders was identified at the trigone level of the urinary bladder, which was observed as a soft tissue attenuating mass with homogeneous contrast enhancement at the CT study. To the best of our knowledge there are no other reports on the CT examination of canine bladder lymphoma with which to compare our findings; however in humans, bladder lymphoma, cannot be differentiated from the more common transitional cell carcinoma on the basis of CT attenuation values or enhancement patterns.[21] In humans, very few publications have been found reporting the involvement of the ureters with lymphoma.[4] In the reviewed literature, only one case of a dog with lymphoma affecting the ureters, as well as the right kidney and bladder, has been found, but its ultrasonographic or computed tomographic appearance was not described.[3] In our case, the mass affecting the ureter was homogeneously hypoechoic compared with the renal cortex by ultrasound and a soft tissue density mass with slight and homogeneous contrast uptake at the CT exam, being this the first description of a ureter lymphoma by these imaging modalities.

Lymphoma of the urinary tract is a rare presentation in dogs.[3,20] Differential diagnosis of lymphoma from other more common malignancies of the urinary tract can be difficult based solely on imaging techniques.[4] Hence, to reach the diagnosis cytologic exam is needed as well as a sensitive and specific test for canine lymphoma. In the present case, a flow cytometry assay and polymerase chain reaction clonality assay were used to assess the lymphoid population which indicated a T-cell origin.[5] Recently, urine flow cytometry has been reported to be a feasible method to aid in the diagnosis of urinary tract lymphoma.[22]

In our patient, the images obtained by CT offered greater detail of the lesions than the observed with ultrasound, their dimensions and degree of vascularization among others, specifically regarding the bladder and ureter tumour, in addition to better characterizing the morphology and internal architecture of the mass of the right kidney, facts that could not be accurately assessed by ultrasound. Hence, the information of the lesions obtained by means of contrast-enhanced CT helped in the understanding of the characteristics of the pathologies found, especially if we take into account that it has been the first description of this type of tumour at the level of a ureter.

To the best of our knowledge this is the first case report describing the computed tomographic features of a T-cell lymphoma affecting simultaneously one kidney, contralateral ureter and urinary bladder in a dog with polycythaemia. We emphasize the use of imaging techniques, especially CT, in cases of suspected urinary tract lymphoma, as it improves the precision of the diagnosis since it depicts the involvement of each affected organ in greater detail, combined with the use of cytology, immunohistochemistry, flow cytometry and clonality to characterise a B or T cell origin.

## CONFLICT OF INTEREST

The author declares that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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