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da Fonseca Sapin, Carolina; Cerqueira Silva-Mariano, Luisa; Nunes Bassi, Jordana; Borelli Grecco, Fabiane

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PATHOLOGY

Anatomo-pathological and epidemiological analysis of urinary tract lesions in dogs

Análise anatomopatológica e epidemiologica de lesões do trato urinário de cães

Carolina da Fonseca Sapin[I] Luisa Cerqueira Silva-Mariano[I] Jordana Nunes Bassi[I] Fabiane Borelli Grecco[I*]

ABSTRACT

In dogs, diseases of the urinary tract are common and can be caused by disorders of varied etiology. The objective of this study was to classify qualitatively and quantitatively urinary tract lesions of 363 dogs, which were classified according to its anatomical distribution and etiology. The data was obtained from the revision of 36 years of protocols from the Regional Laboratory of Diagnosis (LRD/UFPel) and it represents 4.0% of diagnoses from a total of 8980 for that period and species. Renal injury accounted for 93.1% of cases, with 309 being primary kidney lesions; from which the main lesions were the tubulointerstitial nephritis (142 cases) often associated with Leptospirosis (47). Injuries of lower urinary tract accounted for 6.9% of the cases where acute cystitis stands out (19). In this study, renal failure, acute or chronic, represented an important cause of death in dogs.

Key words: *dogs, urinary tract, kidney, nefritis.*

RESUMO

Em cães, as doenças do trato urinário são frequentes e podem ser causadas por desordens de etiologia variada. O objetivo deste trabalho foi classificar qualitativa e quantitativamente lesões do trato urinário de 363 cães, as quais foram classificadas de acordo com a distribuição anatômica e etiologia. Os dados foram obtidos em uma revisão de protocolos de 36 anos do LRD/UFPel e corresponderam a 4,0% do total de 8980 diagnósticos realizados no período para a espécie. As lesões renais representaram 93,1%, sendo 309 primárias do rim; dentre as principais lesões, está a nefrite tubulo-intersticial (142 casos), geralmente associada à Leptospirose (47). O trato urinário inferior representou 6,9% dos casos, destacando-se cistite aguda (19). Neste estudo, a insuficiência renal, aguda ou crônica, representou importante causa mortis *em cães.*

Palavras-chave: *cães, trato urinário, rim, nefrite.*

INTRODUCTION

In dogs, diseases of the urinary tract are common (MAXIE & NEWMAN, 2007) and may be caused by disorders of varied etiology that induce structural and functional changes of the organs and which are diagnosed through its clinical aspects and histopathology (INKELMANN et al., 2012a). However, pathological studies of the urinary tract of small animals are rare and are mostly related to conditions of familial kidney disease or specific diseases (RHA et al., 2000). In the veterinary literature, urinary tract lesions have mainly been classified according to their distribution and etiopathogenesis (NEWMAN et al., 2013), associating them to clinical and epidemiological factors and to the resulting impact of these lesions occurrence (LULICH et al., 2008). Many injuries can be considered incidental necropsy findings (MAXIE & NEWMAN, 2007) but can be the cause of death or reason for euthanasia in this animal species, especially when associated with acute or chronic renal failure (KHAN et al., 2015).

The objective of this study was to classify qualitatively and quantitatively the urinary tract lesions of 363 dogs between 1978-2014 at the Regional Laboratory of Diagnosis (LRD) of the College of Veterinary in the Universidade Federal de Pelotas (UFPel).

MATERIALS AND METHODS

Protocols of biopsies and necropsies between 1978 and 2014 were analyzed and those protocols where

[I]Setor de Patologia Animal, Laboratório Regional de Diagnóstico, Faculdade de Veterinária, Universidade Federal de Pelotas (UFPel), 96010-140, Pelotas, RS, Brasil. E-mail: fabigrecco@ig.com.br. *Corresponding author.

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the diagnosis involved urinary tract lesions were selected, whether it was in relation to its anatomical distribution and/or etiology. The lesions were separated and quantified according to its description in the protocols, and were after classified in single and multiple, so the same animal, could have multiple lesions classified. It was evaluated the clinical history, epidemiological data (breed, sex and age) and type of urinary tract injury. Concerning the breed, the dogs were classified as pure breed (PB) or mixed breed (MB). Regarding age, the method used was described by FIGHERA et al. (2008) which ranks as puppies (under one year old animals), adults (one to nine years) and elderly (over 9 years). Those lesions were grouped regarding its distribution in the urinary tract as kidney lesions and/or lower urinary tract lesions (LUT) (MAXIE & NEWMAN, 2007; NEWMAN et al., 2013).

Kidney lesions were classified according to the distribution and nature in tubule-interstitial, glomerular, renal pelvis injuries, circulatory disorders, neoplasms, birth defects or kidney fibroplasia. Tubulointerstitial lesions were classified as tubulointerstitial nephritis, granulomatous nephritis, acute tubular necrosis (nephrosis), tubular dilation and presence of bile pigment in the tubular epithelium. Glomerular lesions were divided into: membranoproliferative glomerulonephritis, membranous glomerulonephritis, proliferative glomerulonephritis and glomerulosclerosis. Pelvis injuries were clustered into: pyelonephritis, hydronephrosis and kidney injuries caused by parasites. Circulatory disorders included: infarct, congestion/hyperemia, hemorrhage and edema. Neoplasms were classified as primary or metastatic. In kidney fibroplasia cases of renal fibrosis were allocated. In other lesions were included kidney stones and renal amyloidosis.

In the LUT, lesions were classified as inflammatory, obstructive, acquired anatomical variations, circulatory disorders, neoplasms and congenital diseases. Inflammatory lesions included acute cystitis, chronic cystitis and acute urethritis. Obstructive lesions were divided into urolithiasis and hydroureter. The rupture of the bladder, urethral rupture and urethral stricture were classified as acquired anatomical variations. In the group of circulatory disorders were considered cases of bleeding and congestion. Neoplasms were defined as primary or metastatic and congenital diseases were classified as dysplasia, renal cysts and agenesis.

RESULTS

A total of 8980 samples were obtained from dogs, including necropsies, biopsies, and cultures, at the LRD-UFPel between 1978 and 2014; from which 363 indicated the presence of a lesion in the urinary tract, representing 4.04% of the total diagnoses over this time period. Of these, 163 (44.9%) had only single lesions and 200 (55.1%) had multiple lesions. Renal injury was observed in 338 (93.1%) animals and 50 (6.9%) dogs had lesions localized in the lower urinary tract. Renal injury was considered to be primary in 309 of the samples (Figure 1) and secondary in the other 54. Table 1 shows the distribution, morphological diagnosis and frequency of the 685 renal lesions. Tubulointerstitial injuries accounted for a total of 313 of the lesions (45.7%), with acute tubular necrosis predominating (144). Tubular dilation associated with acute tubular necrosis was identified in 18 cases. Tubulointerstitial nephritis associated with leptospirosis was diagnosed in 47 cases.

Glomerular lesions accounted for 21% (144) of renal lesions. Glomerulonephritis (40) was classified according to the histological results: 20 were categorized as membrano-proliferative glomerulonephritis, 17 as membranous glomerulonephritis, and three as proliferative glomerulonephritis. Four female animals with glomerulonephritis (three with the membranoproliferative type and one with the proliferative type) had pyometra. Glomerulosclerosis (102) was the most frequently observed glomerular lesion, occurring predominately in cases with chronic renal failure/uremia. Most of the animals had concomitant glomerulonephritis and glomerulosclerosis. Glomerular amyloidosis was also identified in two animals.

Kidney fibroplasia was found in 129 cases (7 were puppies, 70 adults, and 39 elderly), and the lesion was associated with chronic renal failure. Other renal changes observed included 7 cases of granulomatous nephritis associated with different etiologies. The presence of bile pigment associated with liver failure was also observed in 2 cases. Circulatory disorders were diagnosed in 42 dogs, ranked in decreasing as congestion/hyperemia (19), hemorrhage (13), infarct (9), and edema (1). One case of bleeding was resulted from rupture of the renal artery.

Of a total of 41 injuries of the renal pelvis, parasitism by ***Dioctophyma renale*** was the most represented with 16 cases, followed by pyelonephritis (14), and hydronephrosis (11). The main cause of hydronephrosis was urolithiasis. In this study, 98.6% of obstructive lesions were caused by uroliths. These were observed in the renal pelvis, often associated with hydronephrosis, hydroureter, and rupture of the bladder and urethra. In cases of renal

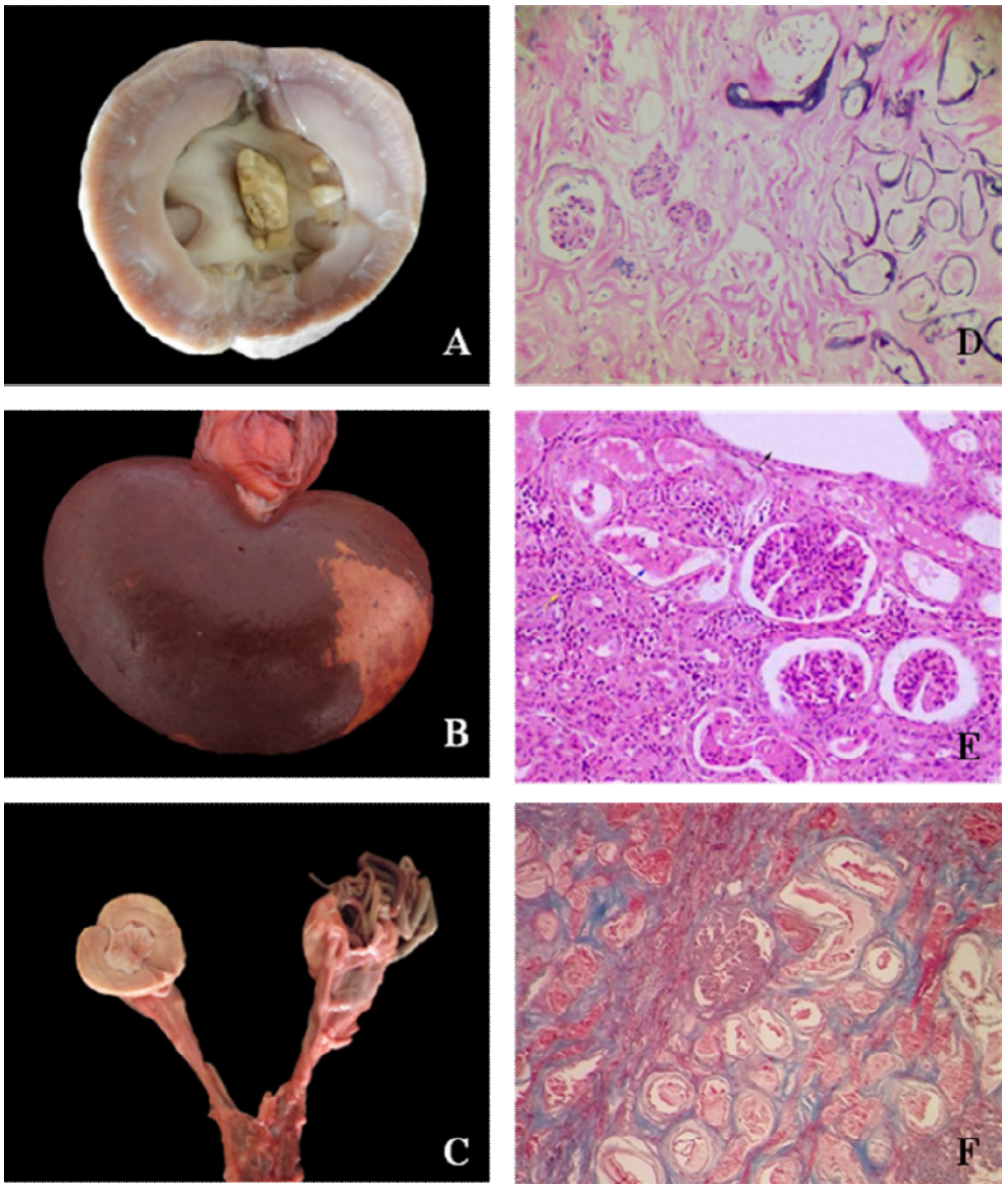

Figure 1 - Urolith obstructing the renal pelvis (A); Renal infarct (B); Exemplary of ***D. renale*** in right kidney and hydronephrosis in contralateral kidney (C); Calcification of tubules and glomeruli (10x) H&E (D); Tubulointerstitial nephritis, tubular dilation, acute tubular necrosis (arrows) and glomerulosclerosis (20x) H&E (E); Primitive conjunctive tissue evidenced by Masson's Trichrome (40x) (F). Figures from the personal archive of authors.

neoplasia, primary renal carcinoma was the most frequent diagnose (7). A single case of mammary adenocarcinoma with renal metastasis was reported in this study. We also identified a case of renal cysts and a case of agenesis associated with urolithiasis.

Results from LUT lesions (60) are shown in table 2. Inflammatory LUT injuries accounted for 25 (41.7%) cases, 19 had acute cystitis, and five had chronic cystitis and one had acute urethritis. We observed 19 obstructive LUT lesions, of which 18 were urolithiasis and one hydroureter resulting from urolithiasis. Acquired anatomical variations associated with rupture of the bladder (8) or urethra (1), were related to trauma and only one case was reported to be caused by urolithiasis. Neoplasms diagnosed were urinary bladder polyp (1), bladder

Table 1 - Classification of 685 renal lesions.

Renal Lesions	Nº/%	Sex	Breed	Age
Tubulointerstitial injuries	313*/45.7			
Acute tubular necrosis	144/46	50 F; 69 M; 25 UN	84 PB; 41 MB; 19 UN	19 P; 73 AD; 37 ED; 15 UN
Tubular dilation	18/5.8	10 F; 7 M; 1 UN	15 PB; 1 MB; 2 UN	1 P; 14 AD; 1 ED; 2 UN
Tubulointerstitial nephritis	142/45.4	53 F; 65 M; 24 UN	69 PB; 59 MB; 14 UN	23 P; 68 AD; 29 ED; 22 UN
Granulomatous nephritis	7/2.2	3 F; 2 M; 2 UN	2 PB; 3 MB; 2 UN	4 AD; 1 ED; 2 UN
Presenceof bile pigment	2/0.6	2 F	1 PB; 1 MB	1 AD; 1 UN
Glomerular lesions	144*/21			
Membrano-proliferative glomerulonephritis	20/13.9	12 F; 3 M; 5 UN	14 PB; 1 MB; 5 UN	1P; 10 AD; 6 ED; 3 UN
Membranous glomerulonephritis	17/11.8	6 F; 9 M; 2 UN	10 PB; 6 MB; 1 UN	13 AD; 3 ED; 1 UN
Proliferative glomerulonephritis	3/2.1	2 F; 1 M	3 PB	1 ED; 2 UN
Glomerulosclerosis	102/70.8	38 F; 56 M; 8 UN	59 PB; 32 MB; 11 UN	6 P; 56 AD; 31 ED; 9 UN
Glomerular amyloidosis	2/1.4	1 M; 1 UN	1 PB; 1 MB	1 AD; 1 UN
Renal fibrosis	129*/18.8			
Fibroplasia	129/100	48 F; 70 M; 11 UN	72 PB; 40 MB; 17 UN	7 P; 70 AD; 39 ED; 12 UN
Circulatory disorders	42*/6.1			
Infarct	9/21.4	2 F; 5 M; 2 UN	8 PB; 1 MB	1 P; 5 AD; 3 ED
Congestion/Hyperemia	19/45.2	10 F; 5 M; 4 UN	7 PB; 7 MB; 4 UN	5 P; 13 AD; 1 ED
Hemorrhage	13/31	2 F; 5 M; 6 UN	6 PB; 6 MB; 1 UN	3 P; 8 AD; 2 UN
Edema	1/2.4	1 F	1 PB	1 AD
Lesions of the renal pelvis	41*/6			
Pyelonephritis	14/34.1	4 F; 10 M	8 PB; 5 MB; 1 UN	1 P; 5 AD; 8 ED
Hydronephrosis	11/26.8	3 F; 7 M; 1 UN	6 PB; 1 MB; 4 UN	1 P; 4 AD; 3 ED; 3 UN
Parasitism by ***Dioctophyma renale***	16/39.1	5 F; 9 M; 2 UN	4 PB; 11 MB; 1 UN	10 AD; 3 ED; 3 UN
Neoplasm	8*/1.2			
Primary	7/87.5	4 F; 2 M; 1 UN	6 PB; 1 UN	2 AD; 4 ED; 1 UN
Metastases	1/12.5	1 F	1 PB	1 ED
Developmental abnormalities	8*/1.2			
Renal dysplasia	6/75	1 F; 4 M;1 UN	3 PB; 2 MB; 1 UN	2 P; 4 AD
Renal cysts	1/12.5	1 M	1 MB	1 AD
Agenesis	1/12.5	1 M	1 MB	1 AD
Total	685			

F= females; M= males; * = amount corresponding to total of each group; PB= pure breed; MB = mixed breed; P = puppies; AD = adults; ED= elderly; UN= uninformed.

adenoma (1), bladder papilloma (1), bladder papillary infiltrative transitional cell carcinoma (2), and squamous bladder cells carcinoma (1). Only one case of circulatory disorder was recorded which was associated with congestion.

DISCUSSION

The kidney is particularly susceptible to toxicity due to the high blood flow to it in relation to its mass and the unique property of the renal tubular epithelium in the concentration of urine and its components, including drugs and chemicals (NEWMAN, 2013). Structural and functional differences in renal blood flow (RBF) and glomerular filtration rate (GFR) significantly contribute to the increased susceptibility of elderly animals to the nephrotoxic response when compared to younger animals (KHAN, 2015). In this study, approximately 70% of the subjects were aged animals and were affected by a variety of diseases, such as glomerulosclerosis and fibroplasia that had led to chronic renal failure. However, age of animals was not a determining factor in the development of acute renal failure but instead represented a 'triggering' event.

According to KHAN et al. (2015), acute renal failure is characterized by rapid failure of glomerular filtration rate, which can develop in a few hours or over a number of weeks, with a consequent

Table 2 - Classification of 60 lesions of lower urinary tract.

Lesions of lower urinary tract	Nº/%	Sex	Breed	Age
Inflammatory lesions	25*/41.7			
Acute cystitis	19/76	4 F; 14 M; 1 UN	9 PB; 6 MB; 4 UN	7 AD; 9 ED; 3 UN
Chronic cystitis	5/20	2 F; 2 M; 1 UN	4 PB; 1 MB	4 AD; 1 ED
Acute urethritis	1/4	1 M	1PB	1P
Obstructive lesions	19*/31.6			
Urolithiasis	18/94.8	2 F; 11 M; 5 UN	5 PB; 9 MB; 4 UN	10 AD; 5 ED; 3 UN
Hydroureter	1/5.2	1 M	1 UN	1 AD
Acquired anatomical variations	9*/15			
Rupture of the bladder	8/88.9	1 F; 5 M; 2 UN	3 PB; 3 MB; 2 UN	1 P; 5 AD; 1 ED; 1 UN
Rupture of urethra	1/11.1	1 M	1 UN	1 P
Neoplasms	6*/10			
Primary	6/100	4 F; 2 M	6 PB	3 AD; 3 ED
Circulatory disorders	1*/1.7			
Congestion	1/100	1 M	1 PB	1 AD
Total	60			

F= females; M= males; * = amount corresponding to total of each group; PB= pure breed; MB = mixed breed; P = puppies; AD = adults; ED= elderly; UN= uninformed.

retention of nitrogenous products (prerenal azotemia) causing damage to the parenchyma and eventually the entire organ. With the progression of this process, occurs the formation of cylinders causing obstruction of urinary flow (post-renal azotemia). KHAN et al. (2015) classified acute renal damage that was similar to that described in this study as acute tubular necrosis, interstitial nephritis, and glomerulonephritis. Data concerning the classification of acute tubular necrosis presented in this study were not consistent with the protocols described in KHAN's study. In this research, Leptospirosis was the main cause of interstitial nephritis. TOCHETTO et al. (2012) reported that in 53 cases of leptospirosis, interstitial nephritis was the characterizing lesion of the disease. Colonization of the kidney by bacteria begins in the interstitial capillary tubes and reachs the thin tubule, causing degeneration and concomitant tubular necrosis and an inflammatory response.

Glomerular lesions in this study accounted for 21% (144) of renal lesions, and were the second most frequent group. Glomerular diseases are often associated with membranous proliferative changes that included a significant increase in mesangial cells and basement membrane mesangial substance, thickening of basement membranes and division of the basement membrane when combined with granular deposits of immunoglobulin (NEWMAN, 2013). In this study, four female animals had glomerulonephritis (3 membranoproliferative type and 1 proliferative type) associated with pyometra. Renal changes in cases of pyometra are secondary to glomerulonephritis caused by deposition of immunocomplex containing bacterial endotoxins that alter the response of the renal tubule to antidiuretic hormone (NEWMAN, 2013).

Glomerulosclerosis (102) was the most frequently observed form of glomerular injury, occurring mainly in cases of chronic renal failure/ uremia. Most of animals in the study had concomitant glomerulonephritis and glomerulosclerosis. These are key symptoms of chronic kidney disease that is characterized by the formation of a vicious cycle that includes progressive loss of nephrons with replacement by fibrous connective tissue. The mechanism suggested for this, although not yet fully understood, involves systemic hypertension and intra-renal glomerular hyperfiltration, hypertrophy and/or tubular atrophy of cells (KHAN et al., 2015). Cases of glomerulosclerosis identified in this study progressed to renal fibroplasia. Fibroplasia also occurs in the repair infarcts and in other renal necrotic lesions (NEWMAN, 2013). Extensive glomerular amyloidosis leads to a reduction in the efficiency of the glomeruli, proteinuria, and kidney failure in dogs; there is a high incidence of thrombosis of the pulmonary arteries in affected animals (NEWMAN, 2013). Although NEWMAN (2013) noted an increase in the frequency of pulmonary thrombosis this was not observed in the two cases of glomerular amyloidosis reported in this study.

Dioctophyma renale infection was reported in 16 animals. Most animals parasitized by this nematode were mixed breed and wandering animals, this can be explained by the indiscriminate eating habits of these animals (KOMMERS et al., 1999), in addition to direct contact with contaminated water. In this study, renal changes observed in parasitized animals were characterized by bone metaplasia in the renal capsule and the presence of bioperculated eggs in the lung parenchyma. These had a rough and thick bark-like appearance and had elicited no tissue response suggesting an erratic migration of the parasite.

Obstructive changes caused by uroliths can occur anywhere in the urinary tract, including the pelvic urinary bladder (INKELMANN et al., 2012b). In our study, male dogs were the most likely to be affected because they have a longer and thinner urethra (NEWMAN et al., 2013). One of the most common causes of the development of calculi is an imbalanced diet (MONFERDINI & OLIVEIRA, 2009). In the present research, most dogs affected by uroliths were identified in the period between 1978-1989, when it was more common to feed dogs with home cooked food that did not have a proper balance of calcium and phosphate.

Primary urinary tract neoplasms occur infrequently in dogs. Primary renal tumors are rare and comprise about 1% of all tumors in dogs (NEWMAN et al., 2013). Animals in this study affected by primary metastatic renal tumors were more than five years of age, a finding consistent with the findings of KOBAYASHI et al. (2008). For renal neoplasms, primary renal carcinoma was the most frequent diagnose. Only one mammary adenocarcinoma case with renal metastasis was observed in this study. In other reports metastatic tumors were the most common (INKELMANN et al., 2011).

Abnormalities in urinary tract development are rare in dogs (HÜNNING et al., 2009; NEWMAN et al., 2013). In this paper, these cases represented 1.2% of renal lesions. We found two cases of renal dysplasia that were characterized as progressive juvenile nephropathy; one Shar Pei and one Shih Tzu, one year and a half, and eight months old respectively. Renal dysplasia is a congenital disease characterized by disruption of the renal parenchyma due to abnormalities in nephrogenesis, with development of structures inappropriate to the animal's stage of development (PICUTT &LEWIS, 1987). The case of renal agenesis described here resulted in the death of the animal, as it was associated with urolithiasis of the contralateral kidney.

Among the LUT injuries described in this paper, inflammatory causes were the most common. Cystitis in dogs is among the most common diseases of the lower urinary tract (LULICH et al., 2008). For the animals in this study, cystitis was more frequently observed in females, with no obvious association reported for age or breed.

Obstructive lesions of LUT, the second most common cause of urinary tract changes described in this study, were associated with uroliths and caused hydroureter and/or rupture. Tumors of LUT were all primary and occurred in the bladder in contrast to the results of INKELMANN et al. (2012b), who report a higher number of metastatic tumors. With significant increases in the dog population, increases in life expectancy, and poor feeding practices by many owners, we suggested that the incidence of lesions of the urinary tract is likely to increase and accurate characterization of the changes and will be important in the diagnoses of this condition.

CONCLUSION

Most diagnoses in this study were of primary lesions of the kidney, demonstrating the importance of a thorough clinical pathology analysis of the animal, since kidney failure, either acute or chronic, is a significant cause of death in dogs. The most frequent injury of the LUT was the acute or chronic cystitis, indicating that it deserves special attention from veterinary practitioners, as may occur the evolution of this injury and lead to worsening of the disease. The knowledge of renal alterations could be a key factor in preventive actions in order to avoid an undesirable prognosis for the animal. Besides, the correct classification of this data will contribute to the best comprehension of these alterations and its implications.

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