








Clinical Reports

Chronic kidney disease in a dog of the Teckel breed: case report

Doença renal crônica em cão da raça Teckel: relato de caso

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ABSTRACT

Chronic kidney disease (CKD) is a disease characterized by the gradual and functional loss of renal mass, affecting its physiology leading to clinical manifestations. The CKD reaches dogs of several breeds causing important clinical alterations. Some laboratory tests are determinant for the correct diagnosis and thus for the implementation of the most appropriate treatment. The urinalysis, urinary protein-creatinine ratio (UPC) evaluation, urea, and creatinine dosage together with the symmetric dimethylarginine dosage (SDMA), urinary tract ultrasonography and blood pressure monitoring, are the main methods used for diagnosis. In this way, this work aimed to report a case of CKD in a Teckel dog attended at the Veterinary Hospital of the Federal University of Jataí (UFJ), discussing the main clinical manifestations, laboratory, and image alterations, as well as the correct staging according to IRIS (Interest Renal International Society), from which the best treatment option to be adopted is determined.

RESUMO

A doença renal crônica (DRC) é uma enfermidade caracterizada pela perda gradual e funcional da massa renal, afetando sua fisiologia levando à manifestações clínicas. A DRC atinge cães de diversas raças causando alterações clínicas importantes. Alguns exames laboratoriais têm se mostrado determinantes para o diagnóstico correto e assim, para implementação do tratamento mais adequado. A urinálise, avaliação da relação proteína-creatinina urinária (UPC), dosagem de ureia e creatinina juntamente com a dosagem de dimetilarginina simétrica (SDMA), ultrassonografia do trato urinário e monitoração da pressão arterial, constituem os principais métodos utilizados para diagnóstico. Sendo assim, este trabalho teve como objetivo relatar um caso de DRC em um cão da raça Teckel atendido no Hospital Veterinário da Universidade Federal de Jataí (UFJ), discutindo as principais manifestações clínicas, alterações laboratoriais e de imagem, assim como o correto estadiamento de acordo com a IRIS (*Interest Renal International Society*), a partir do qual se determina a melhor opção de tratamento a ser adotada.

INTRODUCTION

Chronic kidney disease (CKD) is a progressive disease characterized by irreversible lesions in the renal parenchyma, resulting from the evolution of the primary disease, causing a decrease in the functional renal mass leading the kidneys to a loss in the performance of their functions, mainly related to the control of extracellular fluids (Hall et al., 2016; Galvão; Carvalho, 2017). For

Rodriguez (2012), CKD represents the progressive and irreversible loss of functional kidney tissue and often the determining cause of the initial renal injury is not possible, since the components of the nephron act independently.

The clinical manifestations presented by the patient with CKD are commonly observed in advanced phases of the disease, such as apathy, weight loss, lethargy,

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dehydration, emesis, polyuria, and polydipsia (Barbosa et al., 2019). In pets, DKC is characterized by a reduction in the glomerular filtration rate (GFR), remaining above 50% for a period longer than three months (Galvão; Carvalho, 2017). According to Thrall et al. (2015), GFR is a good indicator of renal function because it is directly related to the number of functional nephrons. Additionally, Hall et al. (2016) stated that GFR below 30% indicates imminent renal failure.

Normal serum concentrations of urea and creatinine are evaluated to indirectly measure the GFR. Urea is a compound formed in the liver from ammonia and bicarbonate, while creatinine is a metabolite of creatine and creatine phosphate in muscles. Both are excreted by the kidneys, but creatinine is not affected by extrarenal processes and is therefore a more reliable indicator of GFR. However, for there to be a considerable increase in plasma creatinine and urea, the kidney must have about 75% of its function compromised (Thrall et al., 2015; Barbosa et al., 2019).

The clinical diagnosis of CKD is obtained by detecting increased serum creatinine and urea concentrations (azotemia), in addition to changes present in urinalyses, such as decreased ability to concentrate urine, proteinuria, and cylindruria, associated with systemic arterial hypertension (SAH) and renal morphological changes observed in ultrasound examination (Hokamp et al., 2016). Thus, the loss of distinction between the cortical and medullary regions can be verified, as well as the increased thickness and echogenicity of the cortical region due to the replacement of functional renal tissue by fibrous scar tissue (Schmidt et al., 2016). In CKD, SAH, when identified, must be constantly monitored.

Nogueira; Poggiani (2013) reported that the main renal disorders capable of developing CKD in dogs are glomerulonephritis, amyloidosis, pyelonephritis, nephrolithiasis, polycystic kidney disease, and neoplasia. According to Thrall et al. (2015), urea and creatinine are not suitable biomarkers for early diagnosis of CKD, as their changes are seen later. Other biomarkers are more suitable for early detection of kidney problems, such as the measurement of serum levels of symmetric dimethylarginine (SDMA). This is an amino acid from the methylation of arginine, which is excreted by the kidneys, reflecting more reliably the renal function (Dahlem et al., 2017).

An important element in verifying the progression of kidney disease is the evaluation of urinary protein-creatinine (UPC), which allows the detection of proteinuria in the dog (Galvão; Carvalho, 2017). That relation estimates quantitatively the severity of the proteinuria, being the method of choice for its evaluation in the clinical routine (Rodriguez, 2012). According to Freitas et al. (2014), proteinuria accelerates the progression of renal disease, and its measurement

assists in monitoring renal function, and should not be evaluated in dogs with pyuria, hematuria, or bacteriuria, due to the chance of increasing post-renal albuminuria in the sample.

According to the International Renal Interest Society (IRIS), CKD can be classified into four stages, which consider clinical and laboratory parameters. The staging is initially based on serum creatinine and SDMA concentration, with sub staging considering proteinuria and blood pressure. To IRIS, in proteinuria-based sub staging, in all cases, UPC should be measured, with the ideal staging being based on two urine samples collected at an interval of at least two weeks. Sub staging based on blood pressure should be made from multiple measurements, preferably on different days during the animal's visit to the clinic.

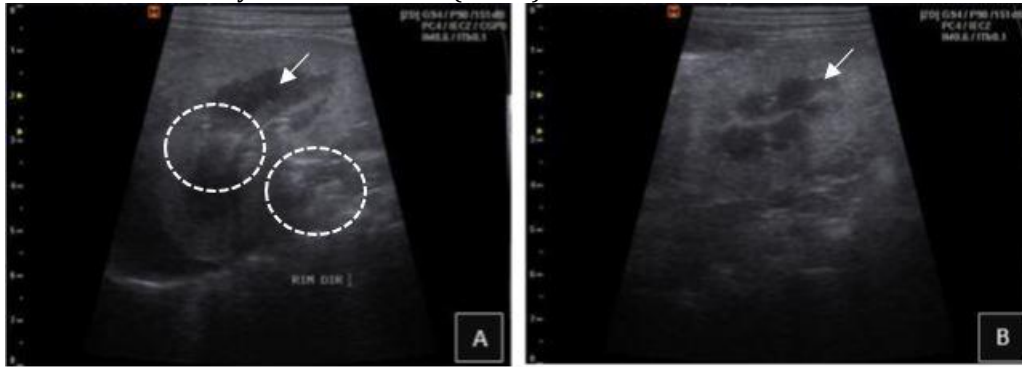
For staging-based treatment, some interventions are necessary, such as avoiding the use of nephrotoxic drugs, monitoring and controlling proteinuria and blood pressure, reducing dehydration with fluid therapy and, in more advanced stages, intervening in gastrointestinal problems such as emesis, nausea, and loss of appetite (IRIS, 2019). The nephroprotective treatment has aimed at controlling factors such as proteinuria, SAH, glomerular hypertension, and fibrosis to prevent the progression of CKD and increase patient survival. On the other hand, the symptomatic treatment aims to prevent the progression of the disease and development of the uremic syndrome. Thus, the objective of this work was to report a case of CKD in a Teckel dog attended at the Veterinary Hospital of the Federal University of Jataí (UFJ), presenting the main clinical manifestations, laboratory and imaging changes that led to the staging as recommended by IRIS (Interest Renal International Society).

CASE REPORT

A nine-years-old female Teckel breed, castrated, was treated at the Veterinary Hospital of the Federal University of Jataí (UFJ). The animal was agitated and breathless. The tutor reported polyuria and polydipsia. During the physical examination, tachypnea made respiratory auscultation impossible and no other visible alteration was verified during the physical evaluation.

Ultrasound (US) examination of the urinary system, complete blood count (CBC) and biochemical tests of liver and kidney function were requested. The US indicated changes suggestive of glomerulonephritis, with loss of corticomedullary definition, mainly in the right kidney (Figure 1) and the other tests showed no significant alterations. The patient was admitted for one day for observation and a therapeutic diagnosis with amoxicillin with clavulanic acid (250mg/5ml) orally, every 12 hours at a dose of 25 mg/kg for 15 days due to the initial diagnosis suggestive of nephritis.

Figure 1. A: Right kidney with evident loss of corticomedullary definition (arrow) and hyperechoic areas (circles). B: Left kidney with evident corticomedullary loss of definition (arrow).



In return, 14 days after the onset of antibiotic therapy, a new US was performed, systemic blood pressure (SBP) measured and requested urine collection by cystocentesis for the following day, due to the low volume contained in the urinary bladder. The US did not show improvement in the renal pattern, and the presumptive diagnosis of nephritis was disregarded, discontinuing antibiotic therapy. The SBP was measured by a non-invasive method, using Doppler, cuff size 2 (4.2 to 7.1 cm), and pear, and the cuff was placed in the middle portion of the left pelvic limb, obtaining a value of 240 mmHg. In the next day, cystocentesis was performed for urinalysis and UPC, in addition to CBC and renal and hepatic biochemical evaluations. Urinalysis, CBC, and biochemical evaluations did not present significant alterations; however, UPC was increased with a result of 0.93.

In two new SBP assessments, performed on alternate days also using the aforementioned non-invasive method, an average value of 240 mmHg was obtained. A new blood sample was collected and SDMA evaluation was requested, the result of which 18 µg/dl allowed the patient to be staged at CKD stage II, and, according to the results obtained in the SBP and UPC, it could also be classified as highly hypertensive and proteinuric. Given the clinical scenario, benazepril (0.5 mg/kg) orally SID (once a day) and omega 3 (500 mg) orally SID were prescribed for two weeks until further evaluation. Specific feed for patients with kidney diseases was also instituted together with the stimulation of water intake.

In return made 35 days after the start of antibiotic therapy, the patient underwent three SBP assessments performed sequentially, and the mean value obtained of 120 mmHg showed a decrease in systolic blood pressure when compared to the previously presented values. Continuing the treatment, benazepril 0.5 mg/kg was prescribed orally, SID for 60 days and Omega 3 (500mg) orally, SID for 40 days, in addition to maintenance of dietary management with specific feed for nephropathy.

Upon returning 62 days after starting antibiotic therapy, the patient was re-evaluated through three new measurements of SBP, urinalysis, and UPC. The mean value (105 mmHg) indicated a new decrease in SBP. In the urinalysis, there was no change, and the UPC value of

0.32 indicated remission of proteinuria, reallocating it to the range of values considered borderline. The tutor reported an improvement in the patient's general condition, with increased appetite and decreased polyuria and polydipsia. Therefore, medical and dietary therapy previously prescribed was maintained.

DISCUSSION

Due to the clinical manifestations presented by the geriatric canine patient, renal disease was considered among the diagnostic suspicions. Polyuria and polydipsia, as well as image changes, were suggestive of possible nephropathy. Chronic renal disease usually affects elderly animals, however, it can occur at any age, its clinical manifestations are initially quite non-specific, so the diagnosis becomes difficult, as well as determining the primary cause (Gerbers; Volkweis, 2017).

As verified in the ultrasonography, there was a loss of corticomedullary definition, as mentioned by Giménez; Laguía (2012) in cases of CKD. Rodriguez (2012) reported that in CKD the GFR is lower in the presence of kidney injury and can be detected in imaging and laboratory tests. This corroborates the findings of this report (glomerulonephritis and proteinuria). Additionally, Barbosa et al. (2019) found that primary glomerular diseases are among the main causes of CKD in dogs, coinciding with the patient's ultrasound finding.

Despite the non-detection of azotemia in the evaluations performed during the follow-up, the adoption of the IRIS recommendations (2019) allowed the classification of the patient in stage II of CKD, since she presented a high SDMA value of 18 mg/dl, being the reference range between 0 and 14 mg/dl. The measurement of serum levels of SDMA becomes a useful and reliable alternative for the identification of early kidney injury before serum creatinine levels are increased and the non-functional mass of the kidneys increases. Nability et al. (2015) stated that factors such as body mass, age, breed, gender, or exercise do not influence serum levels of SDMA. Therefore, none of these would justify the change in the serum value of SDMA for this patient, except for the kidney injury itself, so that it can be used to detect early kidney injuries.

In addition to the changes in the imaging examination, other changes also corroborated to the classification of the patient in stage II, such as persistent renal proteinuria and high blood pressure. For proteinuria evaluation, Freitas et al. (2014) proposed the protein quantification through the 24-hour urine collection as the most reliable method, consistent with the used one. The monitoring and control of proteinuria are essential for better prognosis of the patient, since the accumulation of protein is harmful to both renal tubules and glomeruli, causing the loss of nephrons and thus reducing renal function (Gerbers; Volkweis, 2017).

Systemic hypertension is a cardiovascular complication often seen in CKD and can be detected in about 85% of dogs with glomerular diseases, with hypertension directly linked to the activation of the renin-angiotensin-aldosterone system (Galvão et al., 2010). According to Gonsalez et al. (2018), the activation of this system acts as an acute compensatory response, but its prolonged activation contributes to alterations such as glomerular hypertension. Additionally, Rodriguez (2012) pointed out the activation of the system as being responsible for harmful effects on the kidneys, favoring proteinuria by albuminuria.

Another explanation for hypertension is that due to the reduction in GFR in CKD, the kidneys' ability to excrete sodium (Na⁺) and water decreases. This causes the expansion of the extracellular fluid, increasing cardiac output, and consequently, blood pressure (Nogueira; Poggiani, 2013). According to IRIS (2019), the final classification of the chronic renal patient regarding the systolic blood pressure should be made based on multiple measurements during different moments of the patient in the clinic, coinciding with that performed on the patient.

After the diagnosis of CKD, staging is important to guide the implementation of appropriate treatment and patient monitoring (IRIS, 2019). For blood pressure control, benazepril at a dose of 0.5 mg/kg SID was used. Benazepril has hepatic elimination, being beneficial in patients with renal disfunctions. Besides, the vasodilation caused by the drug reduces the intraglomerular pressure, increasing the GFR, thus reducing the appearance of proteinuria (Spinoza et al., 2017). Based on the use of benazepril, it was noticed that the patient showed reduced proteinuria value after reassessing UPC, evidencing its efficacy for the renal patient.

Moreover, the use of omega-3 intended to promote nephroprotection. For Panickar; Jewell (2018), the supplementation of the diet with omega-3 polyunsaturated fatty acids may act to reduce glomerular inflammation, consistent to the use of this drug as therapy for the renal patient of this report. Cortadellas et al. (2014) also reported that the use of omega-3 in the diet of dogs with proteinuria has beneficial effects on its reduction and in preventing deterioration of GFR.

The indication of renal diet for the patient intended to help increase its survival. In their study, Cortadellas et al. (2014) stated that dogs with specific diet indications for patients with kidney disease have survived more than those conventional feed, thus justifying such choice. Although the dosage of specific minerals was not performed, the indication of a renal diet aimed to indirectly adapt certain minerals in the patient's diet and thus promote life quality. Barbosa et al. (2019) observed that feeding without the moderate restriction of certain minerals may contribute to the worsening of the disease. In this way, the adequacy of sodium levels may contribute to blood pressure control and phosphorus control may reduce uremia manifestations and soft tissue calcification. Finally, the adequacy of protein levels can assist in the non-formation of nitrogenous non-protein compounds.

After the implementation of medication and dietary therapy associated with weekly monitoring, the patient presented stabilization of systemic blood pressure, as well as of the proteinuric condition. Because of the staging, the reserved prognosis required follow-up and monthly monitoring of the clinical condition. However, the patient did not return adequately for monthly follow-up and monitoring as requested.

CONCLUSIONS

In conclusion, chronic kidney disease in its initial stage has a non-specific clinical manifestation, with changes also found in other diseases. Clinical and laboratory evaluations are important for staging, which is performed based on the serum concentration of creatinine and SDMA. Although creatinine is not a good early marker of kidney damage, its joint assessment with SDMA characterizes an important parameter for choosing the most appropriate treatment for renal patients, since altered values of SDMA reveal kidney damage even before the serum increase in creatinine due to kidney disease. Thus, monitoring and follow-up of the chronic renal patient are essential for a better adaptation of the treatment used, which aims to increase the patient's survival, ensuring nephroprotection through the control of systemic blood pressure and proteinuria.

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