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HISTOPATHOLOGICAL COMPARISON OF RENAL INTERSTITIAL LESIONS IN DOGS WITH CHRONIC KIDNEY DISEASE OF DIFFERENT STAGES

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ABSTRACT

Objective: To compare the interstitial histopathological changes in the kidneys of dogs with chronic kidney disease (CKD) at different stages, evaluating the progression of fibrosis, inflammatory infiltration, and tubular atrophy, as well as their correlation with the clinical severity of the disease. CKD is one of the main causes of morbidity in dogs, characterized by a progressive and irreversible degeneration of the renal parenchyma.

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The development of interstitial fibrosis and the loss of the functional structure of the nephrons compromise renal capacity, leading to metabolic and hemodynamic dysfunctions. Histopathological analysis is essential to understand the evolution of the disease and direct more effective therapeutic approaches. In the early stages of CKD, mild to moderate interstitial inflammation and interstitial edema are observed, while in the advanced stages, extensive fibrosis and tubular atrophy predominate. The progression of renal fibrosis is associated with a worse prognosis, highlighting the importance of early diagnosis and appropriate clinical management.

Keywords: Histopathological evaluation. Interstitial fibrosis. Canine renal failure. Chronic nephropathy. Renal pathology.

INTRODUCTION

Chronic kidney disease (CKD) represents one of the major causes of canine morbidity and mortality, being defined by the progressive and irreversible deterioration of kidney function over time (Polzin, 2013). This condition can be triggered by various elements, such as glomerular, tubular, interstitial, and vascular diseases, as well as genetic predisposition and contact with nephrotoxics (Chew, DiBartola, & Schenck, 2011). Regardless of the initial cause, CKD usually progresses to a common end-stage of kidney failure, where the kidneys' ability to maintain the body's homeostasis is seriously impaired (Nabity *et al*., 2011).

Histopathological changes observed in the kidneys of dogs with CKD include interstitial fibrosis, tubular atrophy, lymphoplasmacytic inflammatory infiltration, and glomerular sclerosis (López-Novoa *et al*., 2011). The progression of these changes can be affected by elements such as blood pressure, proteinuria, glomerular hyperfiltration and chronic inflammatory response, according to McGrotty (2008). Research shows that interstitial fibrosis is one of the main histopathological signs of the advancement of CKD and has a strong link with the patient's prognosis (Brown *et al*., 2013).

The classification of CKD is performed by the International Renal Interest Society (IRIS) system, which divides the disease into four stages based on serum creatinine, SDMA, proteinuria, and blood pressure levels (IRIS, 2017). Each stage exhibits varied histopathological patterns, mirroring the evolution of renal interstitial changes over time. In the early stages, there is a discrete inflammatory infiltration and interstitial edema, while in the more advanced stages, broad interstitial fibrosis, vessel atrophy, and interstitial mineralization predominate (Vaden, 2011).

In this scenario, the objective of this study is to analyze the interstitial histopathological changes in the kidneys of dogs at different stages of chronic kidney disease (CKD), investigating the progression of fibrosis, inflammatory infiltration, and tubular atrophy, in addition to correlating them with the clinical severity of the disease. Understanding these changes is essential for creating more efficient treatment strategies and improving the prognosis of affected patients.

METHODOLOGY

The present study consists of a literature review based on the analysis of scientific articles, books and published guidelines on the histopathology of chronic

kidney disease in dogs. Databases such as PubMed, Google Scholar, and Scielo were consulted, using the descriptors "chronic kidney disease in dogs", "renal histopathology", "interstitial fibrosis", "canine nephropathy", and "progression of CKD".

Studies published between 2011 and 2017 that discuss the evolution of CKD and its morphological, inflammatory, and fibrotic aspects were included. In addition, reference guidelines, such as those defined by IRIS, were used to contextualize the categorization and diagnostic criteria of CKD.

The data collected were examined comparatively to recognize histopathological patterns and pathogenic mechanisms common among the analyzed researches. The main objective of the review was to detail the histopathological characteristics of CKD in several phases, associating microscopic findings with the clinical severity of the disease.

RESULTS AND DISCUSSIONS

Histopathological evaluation indicates that the advancement of CKD is strongly linked to the growth of interstitial fibrosis. This happens due to continuous inflammatory processes and the progressive replacement of the functional renal parenchyma by connective tissue (López-Novoa *et al*., 2011). Research indicates that lymphoplasmacytic inflammatory infiltration noted in the early stages of the disease is directly related to the body's attempt to repair tissue damage, despite eventually triggering a sequence of fibrogenic events (Brown *et al*., 2013).

During the early stages of CKD (IRIS 1 and 2), moderate interstitial inflammation, interstitial swelling, and mild tubular atrophy with little collagen deposition are noted. These results reinforce the idea that the initial inflammatory response aims to restore kidney function, but becomes inefficient as the disease progresses (McGrotty, 2008). In addition, the activation of the renin-angiotensin-aldosterone system (RAAS) helps in the formation of fibroblasts by inducing vasoconstriction and increasing the deposition of extracellular matrix (Nabity *et al*., 2011)

In the advanced stages (IRIS 3 and 4), there is a predominance of interstitial fibrosis, with a large amount of type I and III collagen, which replaces functional renal tissue. Tubular atrophy becomes more evident, marked by the dilation of the tubes and the presence of hyaline casts, while interstitial mineralization becomes common, indicating a considerable metabolic impact on the progression of the disease (Chew,

DiBartola & Schenck, 2011). These results are in line with research that indicates that the severity of interstitial fibrosis is strongly associated with decreased glomerular filtration rate and the growth of azotemia (Polzin, 2013).

The reduction of interstitial inflammation in more advanced stages can be justified by the gradual exchange of functional tissue for fibrous connective tissue, restricting the ability of immune response. This procedure leads to decreased mobilization of inflammatory cells and growth of extracellular matrix deposition, maintaining the renal fibrosis cycle (López-Novoa *et al*., 2011). Thus, the progression of CKD shows a shift from a predominantly inflammatory pattern to a fibrotic pattern, further decreasing renal functionality.

Comparative evaluation also reveals a higher prevalence of interstitial mineralization in dogs in advanced stages of CKD, possibly due to alterations in calcium and phosphorus metabolism, commonly noted in patients with chronic renal failure (Vaden, 2011). Research indicates that a lack of calcium and excess phosphorus stimulate the production of parathyroid hormone (PTH), resulting in bone demineralization and calcium deposition in kidney tissue (McGrotty, 2008).

Based on these results, the relevance of early diagnosis and the application of therapeutic strategies aimed at reducing interstitial inflammation and delaying the progression of renal fibrosis is emphasized. Appropriate management of CKD, which encompasses the control of proteinuria, blood pressure, and metabolic changes, can help maintain renal function and improve the prognosis of impacted patients (Polzin, 2013).

FINAL CONSIDERATIONS

The present study demonstrates that interstitial lesions in the kidneys of dogs with CKD become progressively more fibrotic and less inflammatory as the disease progresses. The progression of CKD shows a shift from a predominantly inflammatory pattern to a fibrotic pattern, resulting in a progressive decrease in kidney function. These results highlight the relevance of early diagnosis and appropriate treatment of CKD to delay the progression of interstitial fibrosis and maintain renal function for as long as possible.

In addition, renal histopathology remains an essential instrument for the diagnosis of CKD, enabling a detailed description of the structural changes related to

each phase of the disease. The application of therapeutic tactics aimed at reducing fibrosis and controlling aggravating factors can have a significant impact on improving the prognosis of affected dogs.

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