



## Renal intravascular lymphoma in a dog

Renata Dalcol Mazaro<sup>1\*</sup>  Rafael Almeida Figuera<sup>1</sup> Flávia Serena da Luz<sup>1</sup> Alana Pivoto Herbichi<sup>2</sup>

<sup>1</sup>Programa de Pós-Graduação em Medicina Veterinária, Departamento de Patologia, Universidade Federal de Santa Maria (UFSM), 97105-900, Santa Maria, RS, Brasil. E-mail: renatamazarovet@gmail.com. \*Corresponding author.

<sup>2</sup>Departamento de Medicina Veterinária, Universidade Federal de Santa Maria (UFSM), Santa Maria, RS, Brasil.

**ABSTRACT:** A 10-year-old male large mixed breed dog was presented with skin ulcers and fracture on the right hind limb caused by vehicle collision. Given required limb amputation, and as being a shelter senior dog, euthanasia was requested by the owner and a complete post-mortem examination was conducted immediately after death. Gross changes were consistent with marked bilateral nephromegaly. Histopathological examination of the kidneys revealed round cells filling blood vessels. Immunohistochemically, the round cells were positive for CD3 antibody. Based on these findings, in absence of involvement of the bone marrow and peripheral blood, and inexistence of primary extravascular masses, the tumor was classified as T-cell intravascular lymphoma. To the author's knowledge, this is the first report describing intravascular lymphoma involving the kidneys alone in a dog.

**Key words:** renal lymphomas, T-cell lymphomas, intravascular lymphomas, dog.

## Linfoma intravascular renal em um cão

**RESUMO:** Um canino, macho, de 10 anos, sem raça definida (SRD), e grande porte, chegou para atendimento apresentando fratura em membro pélvico direito devido a atropelamento por veículo automotivo. Adicionalmente, foram observadas úlceras cutâneas ao nível da fratura. Devido à necessidade de amputação do membro e, por ser um cão idoso, o proprietário optou pela eutanásia, realizando-se necropsia imediatamente após a morte do paciente. Os achados macroscópicos foram consistentes com acentuada nefromegalia bilateral. A avaliação histopatológica dos rins revelou células redondas neoplásicas obliterando vasos sanguíneos. Imunohistoquimicamente, essas células foram positivas para CD3. Baseando-se nos achados histopatológicos, na ausência de envolvimento da medula óssea e do sangue periférico e, na inexistência de massas primárias extravasculares, o tumor foi classificado como linfoma intravascular de células T. Possivelmente, este é o primeiro relato de linfoma intravascular envolvendo unicamente os rins de um cão.

**Palavras-chave:** linfomas renais, linfomas de células T, linfomas intravasculares, cão.

Intravascular lymphoma [World Health Organization (WHO)], also known as angiotropic large cell lymphoma (Lukes-Collins Classification), angioendotheliotropic lymphoma (Kiel Classification), malignant angioendotheliomatosis (ZUCKERMAN et al., 2006), intravascular lymphomatosis (ZUCKERMAN et al., 2006), and systemic proliferative angioendotheliomatosis (PFLEGER & TAPPEINER, 1959), is a rare subtype of lymphoma characterised by proliferation of neoplastic lymphocytes within blood vessels, particularly capillaries, with no or minimal involvement of the parenchyma (VALLI et al., 2002; VALLI, 2007; VALLI et al., 2016, 2017). In dogs, immunohistochemistry has revealed staining patterns consistent with lymphoma of both T-cell and B-cell origin, as well as staining patterns of neither T-cell or

B-cell origin (KENT et al., 2001; MCDONOUGH et al., 2002; RIDGE & SWINNEY, 2004; MACHADO et al., 2011). Differently, human intravascular lymphomas are most often consistent with B-cell origin. The diagnosis rests on the histopathological and immunohistochemical findings in absence of involvement of bone marrow and peripheral blood, as well as lack of primary extravascular masses (VALLI et al., 2007, 2017). In most of the cases so far described both in man and dogs, this subtype of lymphoma occurs frequently in central nervous system (CNS), mainly in the brain, and primary clinical signs generally reflected thalamic-cortical lesions (LANE et al., 2002; MCDONOUGH et al., 2002; ZUCKERMAN et al., 2006; MACHADO et al., 2011). Additionally, other organs can be affected concomitantly, and for that reason, some authors

have characterized the intravascular lymphoma as a multisystemic disease (MCDONOUGH et al., 2002). Therefore, the aim of this report is to describe a case of intravascular lymphoma involving only the kidneys of a dog.

A 10-year-old male large mixed breed dog was admitted to Hospital Veterinário Universitário of Universidade Federal de Santa Maria (UFSM), Rio Grande do Sul, Brazil, presented skin ulcers and fracture on the right hindlimb caused by vehicle collision. Haematological examination and serum biochemistry were normal. Given required limb amputation (requiring intensive postoperative care), as being a senior dog, and belonging to a shelter with many dogs and cats, euthanasia was requested by the owner and a complete post-mortem examination was conducted immediately after death. Gross changes were consistent with marked bilateral nephromegaly. In addition, the kidneys were diffusely pale in colour, irregular contours

(Figure 1A), and soft on sectioning. On the cutting surface there was marked corticomedullary changes, as the medulla was five times larger than the cortex (Figure 1A). Other than the renal lesion, no other gross abnormalities were observed.

Samples from kidneys, lungs, lymph nodes, tonsils, intestines, adrenals, liver, heart, spleen, bone marrow, skin, pancreas, stomach, thyroid, urinary bladder, and brain were fixed in 10% neutral buffered formalin, processed routinely and embedded in paraffin wax. Sections these organs were stained with haematoxylin and eosin (HE). Immunohistochemistry (IHC) was performed on renal tissue specimens using the EnVision System (Dako). Briefly, endogenous peroxidases were blocked with peroxidase-blocking solution for 15 min at room temperature. Antigen retrieval was performed used Tris-EDTA buffer solution in a steamer for 10 min. Slides were incubated with primary antibodies (for 60 min) specific for: CD3 (Dako; prediluted), and

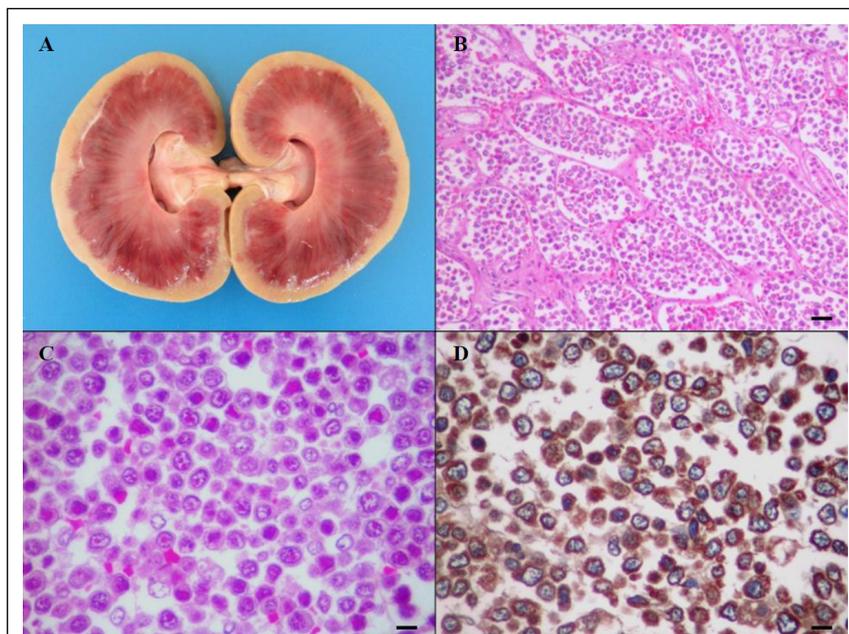


Figure 1 A - Cortical pallor, and corticomedullary dissociation. B - Intravascular lymphoma, a densely cellular proliferation fills small and medium-sized blood vessels located in the medullary region and corticomedullary junction, altering the architecture of the kidney. HE. Bar, 50  $\mu$ m. C - Intravascular lymphoma, neoplastic lymphocytes have scant to moderate eosinophilic cytoplasm, with round to irregular indented nucleus containing coarsely clumped chromatin associated with 1 or 2 prominent eosinophilic nucleoli. HE. Bar, 20  $\mu$ m. D - Intravascular lymphoma, marked CD3 cytoplasmic immunopositivity of neoplastic lymphocytes. IHC. Bar, 20  $\mu$ m.

CD79 $\alpha$  (Dako; prediluted). 3,3'-diaminobenzidine tetrahydrochloride (DAB) was used as chromogen and sections were counterstained with Harris haematoxylin. As negative controls, a duplicate of each section was incubated with Tris-EDTA buffer solution. Normal canine tonsil was used as a positive control.

Histopathological examination of the kidneys revealed a densely cellular proliferation filling small and medium-sized blood vessels located in the medullary region and corticomedullary junction, altering the architecture (Figure 1B). The renal cortex was unaffected. These cells were round with a high nucleus to cytoplasm ratio (Figure 1C). The cytoplasm was scant to moderate, and eosinophilic. A round to irregular indented nucleus containing an coarsely clumped chromatin associated with 1 or 2 prominent eosinophilic nucleoli was observed (Figure 1C). Binucleate cells were occasional. The mitotic rate of the neoplastic population was 2 per 10x40 high power field. Necrotic cells with pyknotic or karyorrhectic nuclei were scattered among neoplastic cells. An initial diagnosis of a renal intravascular lymphoma was reported. Histopathological examination of other tissues did not reveal any changes.

Immunohistochemical staining with CD3 antibody revealed diffuse intense cytoplasmic staining of the population of neoplastic cells (Fig. 1D), whereas staining with CD79 $\alpha$  antibody was not observed. Normal lymphocytes (CD3 or CD79 $\alpha$  positive) were not found among neoplastic lymphocytes. Based on these histological and immunohistochemical features, in absence of involvement of bone marrow (leukemia) and peripheral blood [absence of neoplastic lymphocytes in the bloodstream (leukemia or a terminal stage lymphoma)], and lack of primary extravascular masses (multicentric lymphoma, mediastinal lymphoma or alimentary lymphoma), the tumor was classified as T-cell intravascular lymphoma.

Intravascular lymphoma was first described in humans as proliferative systemic angioendotheliomatosis, implying a diffuse malignant proliferation of endothelial cells (PFLEGER & TAPPEINER, 1959). Subsequently, this neoplasm was first reported in dogs as cerebral angioendotheliomatosis (SUMMERS & DE LAHUNTA, 1985). Later, with advent of immunohistochemistry, it was demonstrated that neoplastic cells were lymphocytes, using the term angiotropic large-cell lymphoma to describe this neoplasm (SHEIBANI et al., 1986).

Based on several reports (KENT et al., 2001; LANE et al., 2002; MCDONOUGH et al., 2002; MACHADO et al., 2011; OLIVEIRA et al., 2015; DEGL'LNOCENTI et al., 2018), intravascular lymphoma in dogs is a tumor characterized by predominant involvement of the CNS with or without the involvement of other organs. In the present case, the kidneys were exclusively affected although renal involvement has been described as part of multisystemic disease (MCDONOUGH et al., 2002). Therefore, to our knowledge, this is the first report of intravascular lymphoma affecting only the kidneys in a dog.

Histologically, the differential diagnosis for intravascular lymphoma includes a angiotropic lymphoma, named lymphomatoid granulomatosis. This neoplasm is a angiocentric and angiodestructive lymphoproliferative disease characterized by atypical lymphocytes and plasmacytoid cells, that surround and destroy blood vessels (FITZGERALD et al., 1991; PARK et al., 2007). Additionally, the neoplastic cells are admixed with histiocytes, plasma cells, small lymphocytes and lesser numbers of eosinophils or neutrophils (VALLI et al., 2016), differently from the exclusive presence of T-cells observed in this case.

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## DECLARATION OF CONFLICT OF INTERESTS

The authors declare no conflict of interest. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results

## AUTHORS' CONTRIBUTION

The authors contributed equally to the manuscript.

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