ORIGINAL ARTICLE

https://doi.org/10.21708/avb.2023.17.2.11357

Documentary research of clinical and epidemiological aspects of lymphoma in dogs treated at the federal rural university of Rio de Janeiro

Pesquisa documental dos aspectos clínicos e epidemiológicos do linfoma em cães atendidos na Universidade Federal Rural do Rio de Janeiro

Felipe Noleto de Paiva[1*], Danielle Carlos Silva[2], Pedro Carvalho Cassino[2], Thiago Souza Costa[3], Julio Israel Fernandes[3]

ABSTRACT: Lymphomas, malignant neoplasms that originate in the lymphocytes, have a high incidence in domestic animals. This paper aimed to describe the clinical and epidemiological findings of 200 cases of canine lymphoma evaluated over nine years (2011–2019) at the Oncology Service of the Veterinary Hospital at The Federal Rural University of Rio de Janeiro. A majority of mixed-breed canines (84/200-42%) were observed, followed by the Labrador Retriever, Pitbull, and Rottweiler with similar incidence (15/200-7.5%). The average age was 7.7 years and the most affected canines were aged approximately 3 and 11 years old (146/200-73%). As for the anatomical classification, the cases classified as multicentric (131/200-65,5%) were the most common, followed by cases of the cutaneous form (44/200-22%), alimentary form (7/200 - 3.5%), mediastinal form (5/200-2.5%), and extranodal form (16/200-6,5%). Among extranodal cases were described cases of ocular involvement (5/200-2.5%), oral cavity involvement (4/200-2%), cardiac involvement (3/200-1.5%), and pulmonary involvement (1/200-0.5%). The clinical manifestation observed was related to the affected region in the different anatomical forms. More studies of this nature are needed to profile the disease presentation and contribute to clinical identification and diagnosis.

KEYWORDS: Canine; lymphosarcoma; retrospective study; clinical manifestation.

RESUMO: Os linfomas são neoplasias malignas que se originam nos linfócitos, apresentando alta incidência em animais domésticos. Este trabalho teve como objetivo descrever os achados clínicos e epidemiológicos de 200 casos de linfoma canino avaliados ao longo de nove anos (2011-2019) no Serviço de Oncologia do Hospital Veterinário da Universidade Federal Rural do Rio de Janeiro. A maioria dos cães foi classificada como sem raça definida (84/200-42%), seguida pelo Labrador Retriever, Pitbull e Rottweiler com incidência semelhante (15/200-7,5%). A idade média foi de 7,7 anos e os caninos mais acometidos tinham aproximadamente 3 e 11 anos (146/200-73%). Quanto à classificação anatômica, os casos classificados como multicêntricos (131/200-65,5%) foram os mais comuns, seguidos pelos casos da forma cutânea (44/200-22%), forma alimentar (7/200 - 3,5 %), forma mediastinal (5/200-2,5%) e forma extranodal (16/200-6,5%). Entre os casos extranodais foram descritos casos de envolvimento ocular (5/200-2,5%), envolvimento da cavidade oral (4/200-2%), envolvimento cardíaco (3/200-1,5%) e envolvimento pulmonar (1/200-0,5 %). A manifestação clínica observada foi relacionada à região acometida nas diferentes formas anatômicas. Mais estudos dessa natureza são necessários para traçar o perfil de apresentação da doença e contribuir para a identificação e diagnóstico clínico.

PALAVRAS-CHAVE: Canino; linfossarcoma; estudo retrospectivo; manifestação clínica.

INTRODUCTION

The term 'lymphoma' comprises not just one disease but a spectrum of neoplastic processes that have in common their lymphoid cell origin and can develop in different organs and tissues due to the constant migration of lymphocytes through the body (ZANDVLIET, 2016; VAIL; THAMM; LIPTAK, 2020). Canine lymphoma has a high incidence in the clinical routine and represents approximately 20% of all tumors in the species (DALECK; DE NARDI, 2016; VAIL; THAMM; LIPTAK, 2020).

[1] Universidade Estadual Paulista (UNESP), campus de Jaboticabal
[2] Médico veterinário autônomo
[3] Universidade Federal Rural do Rio de Janeiro (UFRRJ)
*Corresponding author: n-paiva@hotmail.com
Received: 07/05/2022. Accepted: 05/03/2023

The first epidemiological studies of the disease date back to the 1960s in the United States and report an incidence of approximately 6% of canine malignant tumors, estimating 24 cases per 100,000 dogs (DORN; TAYLOR; HIBBARD, 1967). Studies are currently underway in different countries, with records estimated between 13 and 114 cases per 100,000 dogs (ZANDVLIET, 2016), and values of up to 7.5 cases per 1,000 dogs, in certain regions (ROOYEN; HOOIJBERG; REYERS, 2018), which shows a growing incidence curve.

In the canine species, lymphomas represent about 80%–90% of hematopoietic tumors (MEUTEN, 2017) and 7%–24% of all neoplasms (VAIL; THAMM; LIPTAK, 2020). The affected population includes all ages, with a higher incidence in animals of advanced age and scarce reports of the disease in animals aged below one year (DALECK; DE NARDI, 2016). There is no proven sexual predisposition, although some authors describe less involvement in non-castrated females (ZANDVLIET, 2016). Breeds reported to have the highest incidence include the Boxer, Rottweiler, Chow Chow, Beagle, Basset Hound, German Shepherd, Saint Bernard, Scottish Terrier, Airedale Terrier, Bulldog, and Bull Mastiff. Breeds reported to have a lower incidence include the Dachshund and the German Spitz (VAIL; THAMM; LIPTAK, 2020).

Lymphoma is classified anatomically according to the form of involvement in multicentric, gastrointestinal, mediastinal, cutaneous, and extranodal (DALECK; DE NARDI, 2016; MEUTEN, 2017; VAIL; THAMM; LIPTAK, 2020). Extranodal lymphomas comprise other sites of involvement and occur mainly in the ocular, renal, pulmonary, cardiac, urinary, nasal, oral, and neurological forms (KELLER et al., 1993; ZANDVLIET, 2016; MEUTEN, 2017).

This study aims to evaluate the profile of involvement of canine lymphoma in the sample space studied and to describe the clinical manifestations associated with the different anatomical forms.

MATERIAL AND METHODS

A retrospective study was conducted on cases of canine lymphoma treated by the oncology service of the Veterinary Hospital of the Federal Rural University of Rio de Janeiro (UFRRJ), which is located in the municipality of Seropédica in the state of Rio de Janeiro. The survey was conducted through the evaluation of medical records in physical format from the hospital's archive. The nine-year period between January 2011 and December 2019 was considered.

Epidemiological data on the breed, age, and sex of affected animals were collected. As for the clinical evaluation, data were initially collected on the affected organ/tissue, classifying the cases according to the anatomical location as previously described (DALECK; DE NARDI, 2016; MEUTEN, 2017; VAIL; THAMM; LIPTAK, 2020). Subsequently, data on the clinical manifestations were collected. Subclassifications were not considered in any anatomical form. Information was collected and compiled according to the description in the medical records. Statistical analyses were performed using simple descriptive analysis. The data collection procedure was performed per all necessary ethical guidelines and principles and the General Law for the Protection of Personal Data.

RESULTS AND DISCUSSIONS

A total of 213 medical records of dogs with 'initial suspicion of lymphoma were obtained; however, 13 records were discarded for not having diagnostic confirmation. The remaining 200 cases were confirmed by cytopathology and/or histopathology tests, according to the literature that describes both techniques as satisfactory in obtaining a definitive diagnosis (DALECK; DE NARDI, 2016; VAIL; THAMM; LIPTAK, 2020).

Regarding the racial pattern, the most affected animals were mongrel dogs with 84/200 (42%) cases; followed by Labrador Retriever animals with 15/200 (7.5%) cases; Pitbull with 15/200 (7.5%) cases; Rottweiler with 15/200 (7.5%) cases; Poodle with 12/200 (6%) cases; Golden Retriever with 7/200 (3.5%) cases; Cocker Spaniel with 6/200 (3.0%) cases; Dachshund with 6/200 (3.0%) cases; Pincher with 5/200 (2.5%) cases; Boxer with 4/200 (2.0%); Shih Tzu with 4/200 (2.0%) cases; Yorkshire with 4/200 (2.0%) cases; French Bulldog with 3/200 (1.5%) cases; Chow Chow with 3/200 (1.5%) cases; Sharpei with 3/200 (1.5%) cases. The other affected breeds accounted for no more than 1.0% of the cases and included the following breeds: Dalmatian, Fila Brasileiro, Belgian Shepherd, Cane Corso, Argentine Dogo, Great Dane, Fox Paulistinha, Maltese, Mastiff, German Shepherd, Swiss Shepherd, and Pug.

The higher prevalence of mongrel animals is often observed in epidemiological studies conducted in developing countries where such animals still represent a significant portion of the canine population (CARDOSO et al., 2003; MORENO; BRACARENSE, 2007; GAVAZZA et al., 2009; WANG; LEE; LIAO, 2016; SÁNCHEZ et al., 2019), which is related to cultural and socioeconomic issues. Thus, such a finding does not necessarily represent a predisposition.

Among animals with a defined breed, the Labrador Retriever, Pitbull, and Rottweiler breeds had similar frequencies and represented the most affected breeds. Labrador Retriever dogs are frequently described among the breeds with the highest incidence in different countries (VALLI et al., 2013; WANG; LEE; LIAO, 2016; COMAZZI et al., 2018; ROOYEN; HOOIJBERG; REYERS, 2018; PURZYCKA et al., 2020); similarly, the Rottweiler breed also has a marked incidence (MORENO; BRACARENSE, 2007; GAVAZZA et al., 2009; NERSCHBACH et al., 2014; CORA et al., 2016; YAU et al., 2017).

The Pitbull and Poodle breeds showed a high incidence in the study; however, they are not among the breeds with the highest incidence of canine lymphoma (DALECK; DE

NARDI, 2016). Both findings are explained by the popularity of these breeds in Brazil, which may have increased their representativeness in the study.

The Golden Retriever, Boxer, German Shepherd, and Cocker Spaniel breeds showed a high incidence in several similar national and international studies (KELLER et al., 1993; SEQUEIRA et al., 1999; HOSOYA et al., 2007; MORENO; BRACARENSE, 2007; GAVAZZA et al., 2009; PASTOR et al., 2009; PONCE et al., 2010; VALLI et al., 2013; NERSCHBACH et al., 2014; WANG; LEE; LIAO, 2016; CORA et al., 2016; YAU et al., 2017; COMAZZI et al., 2018; ROOYEN; HOOIJBERG; REYERS, 2018; PURZYCKA et al., 2020); however, in the present study, a medium-to-low incidence related to them was observed. Although races are considered predisposed regardless of geographic factors (COMAZZI et al., 2018), racial variations between countries, and territories represent an important variable, which justifies this finding. Among the other races observed, no significant differences in incidence were found in relation to data in the literature.

The ages of the dogs ranged from 7 months to 19 years, with an average of 7.7 years. The observed age ranges of animals affected with lymphoma are illustrated in the graph in Figure 1.

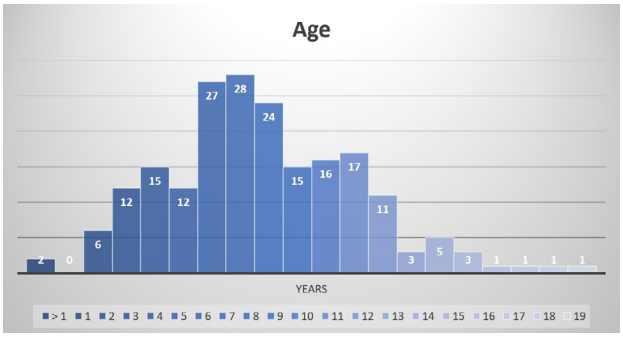
The age variation observed in the study, between 7 months, and 19 years, was greater than the variation observed in other similar studies, which remained with an average interval of 1 year to 18 years of age of onset (KELLER et al., 1993; CARDOSO et al., 2003; FIGHERA et al., 2006; GAVAZZA et al., 2009; PASTOR et al., 2009; NERSCHBACH et al., 2014; YAU et al., 2017; MORGAN et al., 2018; SÁNCHEZ et al. ., 2019).

The average age observed was similar to that described in the literature (7.0–9.1 years) (KELLER et al., 1993; GAVAZZA et al., 2009; PASTOR et al., 2009; CORA et al., 2016; YAU et al., 2017; COELHO et al., 2019; SÁNCHEZ et al., 2019). The most affected age group was the 3–11 years age group, which is in line with the findings of Moreno; Bracarense (2007) and Coelho et al. (2019), who reported a greater involvement from 2–10 years of age. Advanced age is a factor frequently associated with oncological diagnosis in veterinary medicine, and this was in cases of canine lymphoma.

As for sex, 111/200 (55.5%) female animals and 89/200 (44.5%) male animals were included in this study. The minimal difference between the two sexes is a finding consistent with what is described in the literature, which states that there is no sexual predisposition (CARDOSO et al., 2003; HOSOYA et al., 2007; MORENO; BRACARENSE, 2007; GAVAZZA et al., 2009; PASTOR et al., 2009; VALLI et al., 2013; NERSCHBACH et al., 2014; CORA et al., 2016; YAU et al., 2017; ZANDVLIET, 2016; ROOYEN; HOOIJBERG; REYERS, 2018; COELHO et al., 2019). Castration status was not assessed in this study.

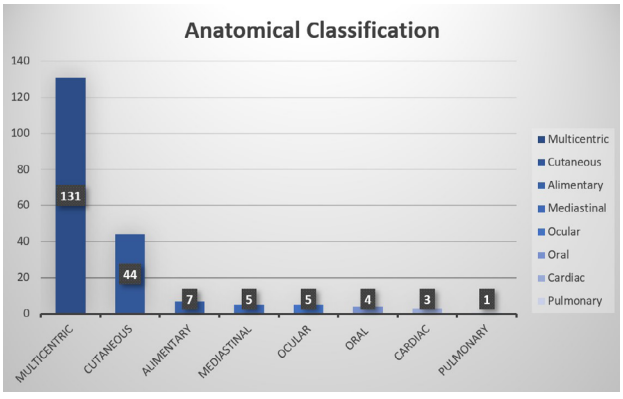
With regard to involvement, the cases were initially divided according to the previously described anatomical classification (DALECK; DE NARDI, 2016; MEUTEN, 2017; VAIL; THAMM; LIPTAK, 2020) and arranged in the graph of Figure 2.

Evaluating the different forms of presentation, the multicentric form was the most common and represented more than 60% of the cases, corroborating other findings reported in the literature (SEQUEIRA et al., 1999; CARDOSO et al., 2003; MORENO; BRACARENSE, 2007; GAVAZZA et al., 2009; CAPUA et al., 2011; CORA et al., 2016; DALECK; DE NARDI, 2016; YAU et al., 2017; COELHO et al., 2019;). The cutaneous form had the second highest incidence and accounted for 22% of cases. This frequency is higher than the ones reported in the studies conducted by Moreno, Bracarense (2007), Ponce et al. (2010), and You et al. (2017). The incidence was similar in the mediastinal and alimentary forms (both below 5%). These results are close to the values reported in the literature, according to which both vary around 5% of cases (SEQUEIRA et al., 1999; MORENO; BRACARENSE, 2007; GAVAZZA et al., 2009; CÁPUA et al., 2011; CORA et al., 2016; VAIL; THAMM; LIPTAK, 2020), although some authors report higher (CARDOSO et al., 2003; YAU et al., 2017; COELHO et al., 2019) or lower (PONCE et al.,



Source: personal archive.

Figure 1. Illustration of the ages of the canines diagnosed with lymphoma



Source: personal archive.

Figure 2. Illustration of the anatomical classification of canines diagnosed with lymphoma

2010) incidences. Extranodal cases accounted for 6.5% of the total, a lower value than that reported by Cardoso et al. (2003), Moreno Bracarense (2007), and Coelho et al. (2019), who reported values that ranged between 7.8% and 9.2%.

Among the 131 cases of multicentric lymphoma, 63/131 (48%) cases of generalized involvement in peripheral lymph nodes were observed. The remaining 68/131 (52%) cases had one or multiple lymph nodes affected, with 59/131 (45%) cases involving submandibular lymph nodes, 43/131 (32.8%) cases involving popliteal lymph nodes, 39/131 (39.7%) cases involving prescapular lymph nodes, 22/131 (16.7%) cases involving inguinal lymph nodes, 5/131 (3.8%) cases involving axillary lymph nodes, 15/131 (11.4%) cases involving internal abdominal lymph nodes, and 5/131 (3.8%) cases involving internal thoracic lymph nodes.

The cases of multicentric lymphoma mostly manifested with generalized lymph node enlargement, similar to that described in the literature (DOBSON; GERMAN, 1993; FIGHERA et al., 2006; GAVAZZA et al., 2009; DALECK; DE NARDI, 2016). In cases of regional lymphadenopathy, the most affected lymph nodes were the submandibular ones, followed by the popliteal, prescapular, inguinal, and axillary lymph nodes, with partially concordant data from Daleck and De Nardi (2016) who stated that lymphadenopathy tends to start in the submandibular and prescapular lymph nodes. The significantly lower involvement observed in inguinal and axillary lymph nodes can be explained by their deeper location, which can make it difficult to palpate and detect clinical signs. The involvement of deep abdominal and thoracic lymph nodes is described in the literature with low incidence values (DOBSON; GERMAN, 1993; FIGHERA et al., 2006).

Among the 44 cases of cutaneous lymphoma, 21/44 (47.7%) manifested as generalized lesions without the distinction of specific location, 17/44 (38.6%) manifested as multifocal lesions with the distinction of affected locations, and 6/44 (13.7%) manifested as focal lesions. Cases of focal and multifocal lesions were described according to their locations and showed 14/44 (31.8%) cases with the involvement of the trunk region, 7/44 (15.9%) cases with limb involvement, and 2/44 (4.5%) cases involving the head and neck region. Regarding the presentation and characterization of the skin lesions, 29/44 (65.9%) cases involved nodular lesions, 3/44 (6.8%) cases involved plaque lesions, and 3/44 (6.8%) cases involved nodular and plaque lesions, with the lesions not being reported in 9/44 (20.5%) cases.

The cutaneous manifestation occurred more commonly in a diffuse and multifocal form and less commonly in a localized form, which is in agreement with what is described in the literature (RISBON et al., 2006; FONTAINE et al., 2009; FONTAINE; HEIMANN; DAY, 2010). The most frequent location was the trunk, followed by the limbs, and the head and face, corroborating the findings of Fontaine, Heimann and Day (2009) who described a greater involvement of the trunk region, followed by the head and face region, and only posteriorly in the limbs. Macroscopically, the lesions manifested mainly in the nodular form and in plaques, corroborating what was described by similar studies (MOORE; OLIVRY, 1994; RISBON et al., 2006; FONTAINE et al., 2009; FONTAINE; HEIMANN; DAY, 2010; DALECK; DE NARDI, 2016; VAIL; THAMM; LIPTAK, 2020).

Out of the seven cases of alimentary lymphoma, 3/7 (42.8%) manifested as intestinal masses, 2/7 (28.6%) manifested as lymphadenopathy in mesenteric lymph nodes, 1/7 (14.3%) manifested with omental nodulation, and 1/7 (14.3%) manifested with gastric wall thickening. The most affected site was the intestines, a finding that is in agreement with those of similar studies (COUTO et al., 1989; COYLE; STEINBERG, 2004; FRANCES; LANE; LENARD, 2013; LANE et al., 2018). Gastric lesion, often described as having a high incidence (COUTO et al., 1989; COYLE; STEINBERG, 2004; FRANCES; LANE; LENARD, 2013), was less observed. The other locations observed in the study, in mesenteric lymph nodes, omentum, and gastric wall, were previously described with different incidence values (COUTO et al., 1989; COYLE; STEINBERG, 2004; FRANCES; LANE; LENARD, 2013; LANE et al., 2018; VAIL; THAMM; LIPTAK, 2020).

All cases of mediastinal lymphoma had mediastinal lymph node involvement. The total number of cases with increased mediastinal lymph node volume is in accordance with the findings of previous studies (DAY, 1997; LANA et al., 2006; DALECK; DE NARDI, 2016; REEVE et al., 2020; VAIL; THAMM; LIPTAK, 2020).

Among the five cases of ocular lymphoma, 3/5 (60%) cases manifested with intraocular masses, 1/5 (20%) with a retrobulbar mass, and 1/5 (20%) with a conjunctival mass. Intraocular involvement was the most feature according to previous studies (VASCELLARI; MULTARI; MUTINELLI, 2005; PATE et al., 2011; MCCOWAN et al., 2014; OTA-KUROKI et al., 2014; WIGGANS et al., 2014).

Among the four cases of lymphoma in the oral cavity, 2/4 (50%) cases manifested with a mass on the tongue, 1/4 (25%) with a mass in the maxilla, and 1/4 (25%) with a gingival mass. Lymphoma with an extranodal location in the oral cavity is seldom reported; thus, there is a paucity of comparative data. The tongue, maxilla, and gums have previously been identified as sites of occurrence (ITO et al., 2007; BERLATO et al., 2011).

Among the three cases of cardiac lymphoma, 2/3 (66.7%) cases manifested as cardiac masses and 1/3 (33.3%) as a pericardial mass. The manifestation of extranodal cardiac lymphoma has a description of more frequent cardiac involvement in the pericardial location per the findings of previous studies (ANAI et al., 2013; DALECK; DE NARDI, 2016; PEIXOTO et al., 2016).

The only case of pulmonary lymphoma presented as multiple pulmonary nodules. A similar manifestation was previously described by Blackwood, Sullivan and Lawson (1997) and Geyer et al. (2010).

The epidemiological data described here help to characterize the profile of greater involvement of lymphoma in dogs as well as the clinical manifestations most commonly associated with different anatomical forms of the disease. The differences observed in the profiles of affected animals (mainly in the racial profile) are explained by cultural variations related to the different geographic regions. The observed anatomical forms with varied macroscopic manifestations demonstrate the difficulty inherent in the clinical diagnosis of the disease.

CONCLUSION

In the present study, a higher incidence of canine lymphoma was observed in mixed-breed animals between 3 and 11 years of age, with greater involvement in females. The multicentric manifestation was described with the highest incidence, with the cutaneous manifestation in second place, followed by the alimentary, mediastinal, and extranodal forms. More studies of this nature are needed to corroborate the findings of the current one.

ACKNOWLEDGMENTS

We thank the Research Support Foundation of the State of Rio de Janeiro (FAPERJ) for funding this study. This study was partially funded by the Coordination for the Improvement of Higher Education Personnel-Brazil (CAPES).

REFERENCES

ANAI, L. B. et al. Linfoma Cardíaco Primário Em Cão. **Semina: Ciências Agrárias**, v. 34, n. 5, p. 2375-2380, 2013.

BERLATO, D. Radiotherapy in The Management of Localized Mucocutaneous Oral Lymphoma in Dogs: 14 Cases. **Veterinary and Comparative Oncology**, v. 10, n. 1, p. 16-23, 2011.

BLACKWOOD, L.; SULLIVAN, M.; LAWSON, H. Radiographic abnormalities in canine multicentric lymphoma: A review of 84 cases. **Journal of Small Animal Practice**, v. 38, n. 2, p. 62-69, 1997.

CÁPUA, M. L. B. et al. Linfoma canino: clínica, hematologia e tratamento com o protocolo de Madison-Wisconsin. **Ciência Rural**, v. 41, n. 7, p. 1245-1251, 2011.

CARDOSO, M. J. L. et al. Linfoma Canino: Revisão de Cinquenta e Quatro Casos. **Bioscience Journal**, v. 19, n. 3, p. 131-142, 2003.

COELHO, A. C. B. et al. Canine Lymphomas Diagnosed in Southern Brazil From 2000 To 2017: Epidemiology and Immunophenotype. **Pesquisa Veterinária Brasileira**, v. 39, n. 7, p. 492-498, 2019.

COMAZZI, S. et al. Breed-Associated Risks for Developing Canine Lymphoma Differ Among Countries: an European Canine Lymphoma Network Study. **Veterinary Research**, v. 14, n. 232, p. 1-7, 2018.

CORA, R. et al. Epidemiological Data Concerning Canine Lymphoma over a Ten-Year Period (2005-2014), in Cluj-Napoca, Romania. **Bulletin of University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca**, v. 73, n. 1, p. 83-88, 2016.

COUTO, C.G. et al. Gastrointestinal Lymphoma in 20 Dogs - A Retrospective Study. **Journal of Veterinary Internal Medicine**, v. 3, n. 2, p. 73-78, 1989.

COYLE, K.A.; STEINBERG, H. Characterization of Lymphocytes in Canine Gastrointestinal Lymphoma. **Veterinary Pathology**, v. 41, n. 2, p. 141-146, 2004.

DALECK, C. R.; DE NARDI, A. B. **Oncologia em cães e gatos**. 2. ed. Rio de Janeiro: Roca, 2016, 1075p.

DAY, M. J. Review of Thymic Pathology In 30 Cats And 36 Dogs. **Journal of Small Animal Practice**, v. 38, n. 9, p. 393-403, 1997.

DOBSON, J.M.; GERMAN, N.T. Canine Multicentric Lymphoma I: Clinicopathological Presentation of The Disease. **Journal of Small Animal Practice**, v. 34, n. 12, p. 594-598, 1993.

DORN, C.R.; TAYLOR, D.O.; HIBBARD, H. H. Epizootiologic Characteristics of Canine and Feline Leukemia and Lymphoma. **American Journal of Veterinary Research**, v. 28, n. 125, p. 993-1001, 1967.

FIGHERA, R.A. et al. Aspectos Clinicopatológicos De 43 Casos De Linfoma Em Cães. **Medvep - Revista Científica de Medicina Veterinária**, v. 4, n. 12, p. 139-146, 2006.

FONTAINE, J. et al. Canine Cutaneous Epitheliotropic T-Cell Lymphoma: A Review. **Veterinary and Comparative Oncology**, v. 7, n. 1, p. 1-14, 2009.

FONTAINE, J.; HEIMANN, M.; DAY, M. J. Canine Cutaneous Epitheliotropic T-Cell Lymphoma: A Review Of 30 Cases. **Veterinary Dermatology**, v. 21, n. 3, p. 267-275, 2010.

FRANCES, M.; LANE, A. E.; LENARD, Z. M. Sonographic Features of Gastrointestinal Lymphoma In 15 Dogs. **Journal of Small Animal Practice**, v.54, n. 9, p. 468-474, 2013.

GAVAZZA, A. et al. Clinical, Laboratory, Diagnostic and Prognostic Aspects of Canine Lymphoma: A Retrospective Study. **Comparative Clinical Pathology**, v. 18, n. 3, p. 291-299, 2009.

GEYER, N. E. et al. Radiographic Appearance of Confirmed Pulmonary Lymphoma in Cats and Dogs. **Veterinary Radiology & Ultrasound**, v. 51, n. 4, p. 386-390, 2010.

HOSOYA, K. et al. Comparison of COAP and UW-19 Protocols for Dogs with Multicentric Lymphoma. **Journal of Veterinary Internal Medicine**, n. 21, v. 6, p. 1355-1363, 2007.

ITO, T. et al. A Case of Atypical Canine Lymphoma with Oral Mass and Multiple Osteolysis. **Journal of Veterinary Medical Science**, v. 69, n. 9, p. 977-980, 2007.

KELLER, E. T. et al. Evaluation of Prognostic Factors and Sequential Combination Chemotherapy with Doxorubicin for Canine Lymphoma. **Journal of Veterinary Internal Medicine**, v. 7, n. 5, p. 289-295, 1993.

LANA, S. et al. Diagnosis of Mediastinal Masses in Dogs by Flow Cytometry. **Journal of Veterinary Internal Medicine**, v. 20, n. 5, p. 1161-1165, 2006.

LANE, J. et al. Low-Grade Gastrointestinal Lymphoma in Dogs: 20 Cases (2010 To 2016). **Journal of Small Animal Practice**, v. 59, n. 3, p.147-153, 2018.

MCCOWAN, C. et al. Conjunctival Lymphoma: Immunophenotype And Outcome in Five Dogs and Three Cats. **Veterinary Ophthalmology**, v. 17, n. 5, p. 531-537, 2014.

MEUTEN, D. J. **Tumors in Domestic Animals**. 5. ed. Ames: John Wiley & Sons Inc, 2017, 989p.

MOORE, P. F.; OLIVRY, T. Cutaneous lymphomas in companion animals. **Clinics in Dermatology**, v. 12, n. 4, p. 499-505, 1994.

MORENO, K.; BRACARENSE, A. P. F. R. L. Estudo Retrospectivo de Linfoma Canino no Período de 1990 - 2004 na Região Norte do Paraná. **Brazilian Journal of Veterinary Research and Animal Science**, v.44, p. 46-52, 2007.

MORGAN, E. et al. Canine T Cell Lymphoma Treated with Lomustine, Vincristine, Procarbazine, And Prednisolone Chemotherapy In 35 Dogs. **Veterinary and Comparative Oncology**, v.16, n.4, p. 622-629, 2018.

NERSCHBACH, V. et al. Splenic and Hepatic Ultrasound and Cytology in Canine Lymphoma: Effects of Findings on Stage Migration and Assessment of Prognosis. **Veterinary and Comparative Oncology**, v. 14, p. 82-93, 2014.

OTA-KUROKI, J. et al. Intraocular and Periocular Lymphoma in Dogs and Cats: A Retrospective Review Of 21 Cases (2001–2012). **Veterinary Ophthalmology**, v. 17, n. 6, p, 389-396, 2014.

PATE, D. O. et al. Diagnosis of intraocular lymphosarcoma in a dog by use of a polymerase chain reaction assay for antigen receptor rearrangement. **Journal of the American Veterinary Medical Association**, v. 238, n.5, p. 625-630, 2011.

PASTOR, M. et al. Genetic and Environmental Risk Indicators in Canine Non-Hodgkin's Lymphomas: Breed Associations and Geographic Distribution of 608 Cases Diagnosed throughout France over 1 Year. **Journal of Veterinary Internal Medicine**, v. 23, n. 2, p. 301-310, 2009.

PEIXOTO, T. C. et al. Linfoma Primário Cardíaco Associado À Leishmaniose Visceral Em Cão - Relato De Caso. **Brazilian Journal of Veterinary Medicine**, v. 38, n. 1, p. 47-54, 2016.

PONCE, F. et al. A Morphological Study of 608 Cases of Canine Malignant Lymphoma in France With a Focus on Comparative Similarities Between Canine and Human Lymphoma Morphology. **Veterinary Pathology**, v. 47, n. 3, p.414-433, 2010.

PURZYCKA, K. et al. Clinicopathological Characteristics and Prognostic Factors for Canine Multicentric Non-Indolent T-Cell Lymphoma: 107 Cases. **Veterinary and Comparative Oncology**, v. 18, n. 4, p. 656-663, 2020.

REEVE, E. J. et al. Mediastinal Lymphoma in Dogs Is Homogeneous Compared to Thymic Epithelial Neoplasia and Ismore Likely to Envelop the Cranial Vena Cava in CT Images. **Veterinary Radiology & Ultrasound**, v. 61, n. 1, p. 25-32, 2020.

RISBON, R. E. et al. Response of Canine Cutaneous Epitheliotropic Lymphoma to Lomustine (CCNU): A Retrospective Study of 46 Cases (1999–2004). **Journal of Veterinary Internal Medicine**, v. 20, n. 6, p. 1389-1397, 2006.

ROOYEN, L. J. V.; HOOIJBERG, E.; REYERS, F. Breed Prevalence of Canine Lymphoma in South Africa. **Journal Of The South African Veterinary Association**, v. 89, n.1, p.1-11, 2018.

SÁNCHEZ, D. et al. Canine Lymphoma: Pathological and Clinical Characteristics of Patients Treated at a Referral Hospital. **Veterinaria México OA**, v. 6, n. 2, p. 1-12, 2019.

SEQUEIRA, J. L. et al. Características Anatomoclínicas Dos Linfomas Caninos Na Região De Botucatu, São Paulo. **Arquivo Brasileiro de Medicina Veterinária e Zootecnia**, v. 51, n. 3, p. 1-9, 1999.

VAIL, D. M.; THAMM, D. H.; LIPTAK, J. M. **Withrow & MacEwen's Small Animal Clinical Oncology**. 6. ed. St. Louis: Elsevier, 2020, 842p.

VALLI, V. E. et al. Canine Lymphomas: Association of Classification Type, Disease Stage, Tumor Subtype, Mitotic Rate, and Treatment with Survival. **Veterinary Pathology**, v. 50, n. 5, p. 738-748, 2013.

VASCELLARI, M.; MULTARI, D.; MUTINELLI, F. Unicentric Extranodal Lymphoma of The Upper Eyelid Conjunctiva in A Dog. **Veterinary Ophthalmology**, v. 8, n. 1, p. 67-70, 2005.

WANG, S. L.; LEE, J. J.; LIAO, A. T. Comparison of Efficacy and Toxicity of Doxorubicin and Mitoxantrone in Combination Chemotherapy for Canine Lymphoma. **Canadian Veterinary Journal**, v. 57, n.3, p. 271-276, 2016.

WIGGANS, K. T. et al. Presumed Solitary Intraocular or Conjunctival Lymphoma in Dogs and Cats: 9 Cases (1985–2013). **Journal of the American Veterinary Medical Association**, v. 244, n. 4, p. 460-470, 2014.

YAU, P. P. Y. et al. Retrospective Study on The Occurrence of Canine Lymphoma and Associated Breed Risks in A Population of Dogs in NSW (2001–2009). **Australian Veterinary Journal**, v. 95, n.5, p. 149-155, 2017.

ZANDVLIET, M. Canine Lymphoma: A Review. **Veterinary Quarterly**, v. 36, n. 2, p. 76-104, 2016.