CANINE T-CELL LYMPHOMA: CLASSIFICATION, TREATMENT AND PROGNOSIS

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June, 2024

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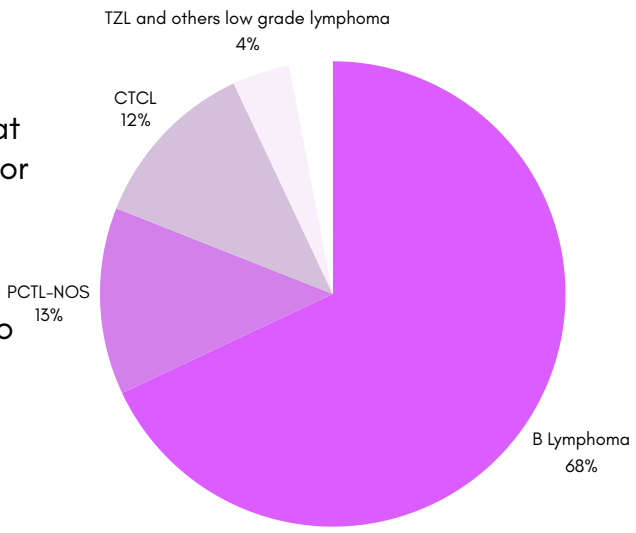
Lymphomas are neoplasms originating from lymphocytes that can develop in lymphoid tissues or in almost any body tissue.
Main objective: to provide a detailed description of T-cell lymphoma subtypes according to the World Health Organisation (WHO) classification.



CLASSIFICATION

Throughout history there have been several classifications of t-cell lymphoma. The WHO (1999) classification is the current system used to classify animal lymphomas. It takes into account tissue architecture, localisation and a limited set of immunohistochemical findings.

The characteristic molecules of T-cell subtypes (Comazzi and Riondato 2021)

Target	Reactivity
CD3	T cells
CD5	T cells and a subset of B cells
CD4	T-helper cells
CD8	T-cytotoxic cells
CD34	Madurez celular
CD45	All leukocytes
CD44	All hematopoietic cells
CD18	All leukocytes
MHC II	Monocytes, Histiocytes, Lymphocytes
TCR	Most T cells
CD25	Activated hymphocytes
CD11d	Splenic T cells and histiocytes
Ki67	Proliferating cells

The WHO stages for canine multicentric lymphoma (Owen, 1980):

Stage	
I	Single node or lymphoid tissue in single organ (excluding bone marrow)
II	Regional involvement of multiple lymph nodes (+- tonsils)
III	Generalized lymph node involvement
IV	Stage I-III with involvement of liver and/or spleen
V	Stage I-IV with involvement of blood or bone marrow
Substage	
a	Absence of systemic signs
b	Presence of systemic signs (fever, >10% weight loss, hypercalcemia)

SURVIVAL

<60 days	130-250 days	325-510 days	>800 days
ALL, HS-TCL, EATL1, English Bulldog T-Cell Leukemia and Intravascular Large T-Cell Lymphoma	TLBL, PCTL-NOS, HC-TCL and CTCL	EATL2	CLL and TZL

T-cell lymphoma types in dogs according to the WHO classification:

Precursor T-Cell Neoplasms	Immunophenotype
T-Acute Lymphoblastic Leukemia (ALL)	CD34+, CD3+, CD4±, CD5±, CD8±, MHCII-
Lymphoblastic T-Cell Lymphoma (TLBL)	CD3+, CD4+, CD5±, CD8±, MHCII-/low, TCR αβ
English Bulldog T-Cell Leukemia	CD45+CD4-CD8-CD5+ CD3+, MHC II-
Mature T-Cell Neoplasms	**Immunophenotype**
Chronic Lymphocytic Leukemia (CLL)	CD3+, CD4±, CD5±, CD8±, MHCII+, TCR αβ > γδ
Peripheral T-Cell Lymphoma, Not Otherwise Specified (PCTL-NOS)	CD3+, CD4±, CD5±, CD8±, MHCII low /+
T-Zone Lymphoma (TZL)	CD3+, CD4±, CD5±, CD8±, MHCII+, CD45-, CD21 low/mod
Cutaneous T-Cell Lymphoma (CTCL)	CD3+, CD4-, CD5±, CD8+, MHCII+, TCR αβ or γδ
Cutaneous Epitheliotropic T-Cell Lymphoma	CD3+, CD8+, TCRγδ+ , CD5-
Sézary Syndrome	CD3+, CD4-/CD8+
Cutaneous Non-Epitheliotropic T-Cell Lymphoma	CD3±, CD18+, CD45+, CD4±/CD8±, CD5±
Subcutaneous Panniculitis-Like Lymphoma	CD3, CD79a/CD20/Pax5
Anaplastic Large Cell Lymphoma	Not well studied
Intravascular Large T-Cell Lymphoma	CD3+/IgG-/CD79a-
Enteropathy-Associated T-Cell Lymphoma (EATL)	CD4+/CD8-, TCR+, CD3, CD30
Hepatosplenic T-Cell Lymphoma (HS-TCL)	CD3+, CD4-, CD8+, MHCII+, CD11b+, TCR γδ, granzyme B+
Hepatocytotropic T-Cell Lymphoma (HC-TCL)	CD3+, CD4-, CD8+, MHCII+, CD11b-, TCR γδ

TREATMENT

Comparison of different protocols

	L-CHOP	L-MOPP	VELCAP-TSE	LOPP
ORR (%)	96	78	73	97
DFI (days)	104	189	175	178
OTS (days)	235	270	237	323
Toxicity (%)	nr	67	90	42

Abbreviations: CHOP, cyclophosphamide, doxorubicin, vincristine and prednisolone; DFI, disease-free interval; MOPP, mechlorethamine, vincristine, prednisolone and procarbazine; ORR, overall response rate; OST, overall survival time; VELCAP-TSE, vincristine, l-asparaginase, cyclophosphamide, doxorubicin, lomusine, actinomycin, procarbazine and prednisolone; nr: not reported.

OUTCOMES

- Accurate classification is crucial to establish prognosis and appropriate treatment and for this purpose immunophenotyping must be performed.
- Treatment of canine T-cell lymphoma remains a challenge due to the lower response rate and shorter survival.
- Future research should focus on identifying new treatments and understanding the genetic and molecular basis of T-cell lymphoma.