

1 **LETTER TO THE EDITOR**

2 **Letter to the editor re Parachini-Winter et al. "A case of canine high-grade T-cell lymphoma**  
3 **immunophenotypically consistent with T-zone lymphoma"**

4 Dear Editor,

5 Recently, we have read with interest the article "A case of canine high-grade T-cell lymphoma  
6 immunophenotypically consistent with T-zone lymphoma" by Parachini-Winter et al. <sup>1</sup> on Veterinary Clinical  
7 Pathology. This report describes an interesting case of canine Peripheral T Cell Lymphoma (PTCL) where  
8 neoplastic cells show a peculiar immunophenotype (CD45neg, CD5pos) with several similarities to T-zone  
9 lymphoma (TZL).

10 The case is accurately documented and the current literature on the topic is adequately evaluated.

11 However, some of the conclusions need further discussion in order to avoid incorrect messages to the  
12 readers.

13 The authors discredit describe the limit of flow cytometry (FC) in the T zone lymphoma diagnostic work-up  
14 stating that antibodies reactivities led to an incorrect diagnosis of TZL in this dog. Moreover, the authors  
15 suggest the necessity of lymphadenectomy and subsequent histopathological and immunohistochemical  
16 evaluation to diagnose TZL.

17 Based on our experience, we partially disagree with the aforementioned statement and below the principal  
18 issues are discussed.

19 The data obtained from cytology and flow cytometry in association with the most significant  
20 clinicopathological features such as complete blood cell count , are often sufficient for a final diagnosis of  
21 TZL with no need for histopathology. Indeed, in the current case description, many clinic-pathological  
22 features are in contrast with the classical presentation of canine TZL that have been reported previously.

23 First, the size of cells cytologically described as "*intermediated to occasionally large*" (this was also  
24 confirmed by the high Forward Scatter properties in FC) disagrees with the TZL morphological appearance.

25 TZL are characterized by small clear cells in most of the published case series . Second, the mitotic index  
26 reported as “1-5 mitotic figure per 50X field” is generally considered as high according to the updated Kiel  
27 classification<sup>2</sup>. Conversely, by definition TZL are classified as indolent low-grade lymphoma. Third, several  
28 case series reported blood infiltration as an almost constant hematological feature of TZL<sup>3</sup>, and this was not  
29 the case, even if flow cytometry was not performed on peripheral blood to check for a low percentage of  
30 neoplastic cells. Based on the above and our experience, the diagnosis of TZL should have been considered  
31 as highly improbable in this dog despite CD45 negativity.

32 Over the last 10 years our caseload recruited about 5000 FC phenotype canine lymphomas and CD45  
33 negativity was very rare in lymphoma subtypes other than TZL, but still, it may occur. In a recent  
34 retrospective case series we have described a dog with extranodal lymphoma where neoplastic cells were  
35 large-sized and CD45 negative, leading to a probable diagnosis of PTCL rather than TZL<sup>4</sup>. Other authors have  
36 also reported a T-cell lingual lymphoma with similar features<sup>5</sup> as also adequately addressed in the present  
37 paper.

38 The authors state that “*this case differs from previous research findings and the potential conclusion that*  
39 *flow cytometry alone is reliable to diagnose TZL in dogs*”. The conclusion that FC alone is able to diagnose  
40 TZL is an overinterpretation not supported by any of the quoted references.

41 In contrast in the paper from Martini et al 2016<sup>3</sup>, cases with “*a cytological diagnosis of small-clear cell*  
42 *lymphoma*” and a concomitant “*CD45-negative small T-cells*” phenotype based on FC were enrolled and in  
43 2015, Martini et al<sup>6</sup> clearly stated that “*the combined use of cytology and FC allows solving the differential*  
44 *diagnosis between small clear cell lymphoma and non-neoplastic reactive conditions when histopathology is*  
45 *not available*”. Finally, Harris et al<sup>5</sup> described cases “*based on a variable combination of cytology,*  
46 *histopathology, immunohistochemistry, immunophenotyping via flow cytometry and PCR for antigen*  
47 *receptor rearrangement assay*”.

48 From all the published data it is evident that an accurate analysis of more than one clinicopathological  
49 aspect is necessary to recognize TZL if lymphadenectomy and subsequent histopathology are not

50 considered. Furthermore, guidelines from ECLN have reported that FC should always be examined in light  
51 of cytological appearance in order to avoid a mis-diagnosis.

52 It is not our intention to minimize the importance of histopathology in the diagnosis and classification of  
53 canine lymphoma, as we always describe lymphadenectomy as a fundamental step in the lymphoma  
54 diagnostic workup. However, we are aware that many clinicians often treat dogs with lymphoma without a  
55 histopathological diagnosis, as shown by a recent survey<sup>7</sup> This is particularly true for low-grade lymphomas  
56 in which the indolent nature of the disease tends often to redirect towards non-invasive diagnostic  
57 techniques and a more prudent behavior.

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## 64 **References**

- 65 1. Parachini-Winter, Curran KM, Russell DS, Gorman E. A case of canine high-grade T-cell lymphoma  
66 immunophenotypically consistent with T-zone lymphoma. *Vet Clin Pathol.* 2018. doi:  
67 10.1111/vcp.12657
- 68 2. Fournel-Fleury C, Magnol JP, Bricaire P. et al. Cytohistological and immunological classification of  
69 canine malignant lymphomas: comparison with human non-Hodgkin's lymphomas. *J Comp Pathol.*  
70 1997;117(1):35-59

- 71 3. Martini V, Marconato L, Poggi A et al. Canine small clear cell/T-zone lymphoma: clinical  
72 presentation and outcome in a retrospective case series. *Vet Comp Oncol.* 2016;14 Suppl 1:117-  
73 126.
- 74 4. Martini V, Melega M, Riondato F et al, 2018 A retrospective study of flow cytometric  
75 characterization of suspected extranodal lymphomas in dogs. *J Vet Diagn Invest.* 2018. doi:  
76 10.1177/1040638718804301.
- 77 5. Harris LJ, Rout ED, Hughes KL et al. Clinicopathologic features of lingual canine T-zone lymphoma.  
78 *Vet Comp Oncol.* 2018;16(1):131-139
- 79 6. Martini V, Poggi A, Riondato F, et al. Flow-cytometric detection of phenotypic aberrancies in canine  
80 small clear cell lymphoma. *Vet Comp Oncol.* 2015;13(3):281-287
- 81 7. Regan RC, Kaplan MS and Bailey DB. Diagnostic evaluation and treatment recommendations for  
82 dogs with substage-a high-grade multicentric lymphoma: results of a survey of veterinarians. *Vet*  
83 *Comp Oncol.* 2013;11(4):287-295

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