Vieira *et al.*
The Egyptian Journal of Otolaryngology (2023) 39:86
https://doi.org/10.1186/s43163-023-00439-7

The Egyptian Journal of Otolaryngology

LETTER TO THE EDITOR

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Tumor-associated tissue eosinophilia is associated with histological grade in canine squamous cell carcinoma

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To the Editor,

Not so long ago, we read an article from Sharma et al. (2021) in your prestigious journal that we found very interesting. The authors described an association between tumor-associated tissue eosinophilia (TATE) and tumor differentiation in head and neck squamous cell carcinoma (SCC) [1].

We found similar results by studying a series of 49 canine SCC biopsies, including cutaneous and oral tumors. Canine SCCs, considered the most common malignant neoplasm in dogs, were graded into well-differentiated, moderately differentiated, and poorly differentiated SCC. The eosinophils were colored with Congo Red staining and counted and scored into 3 grades, according to Sharma et al. [1]. In our study, eosinophils were present in all the cases, being abundant in 20 cases (40.8%) (Fig. 1), few in 16 (32.7%) (Fig. 2), and moderate in 13 (26.5%) tumors (Fig. 3). Significant differences were found in TATE in the different histological grades ($p < 0.0001$) (Table 1). Poorly differentiated tumors showed mostly a scarce infiltrate, i.e., few eosinophils. On the contrary, well-differentiated tumors showed, in general, an intense infiltrate of eosinophils. An association was also seen between TATE and the presence of vascular invasion ($p < 0.0001$). Canine SCC with emboli generally exhibited few eosinophils. TATE's associations with tumor differentiation and vascular invasion were also present when we considered only oral tumors. Comparing the location of the tumors, oral canine SCCs have more TATE than cutaneous SCCs. However, the differences were not statistically significant, contrary to what would be expected since, in the dog, oral SCC is more aggressive than cutaneous SCC.

There are no studies on canine tumors that allow comparison with ours. Even in human SCC, there is no consensus within the scientific community on this issue for human SCC. Both negative and positive outcomes have been related to TATE [2, 3]. Similar to the work of Sharma et al. [1], our results show that, in canine SCC, the presence of a higher number of eosinophils is associated with a higher histological differentiation of the tumors, which may result in a less aggressive biological behavior. Thus, the eosinophil count may be a criterion of aggressiveness and potentially a valuable and easy-to-determine prognostic factor in this type of cancer. Other studies show opposite results and indicate that TATE is related with oral SCC progression [3, 4]. However, this divergence may be due to methodological inconsistencies among the different studies. In this letter, we also like to emphasize the importance of comparative oncology studies. Comparative oncology allows us to understand cancer's origins better and translate this information into

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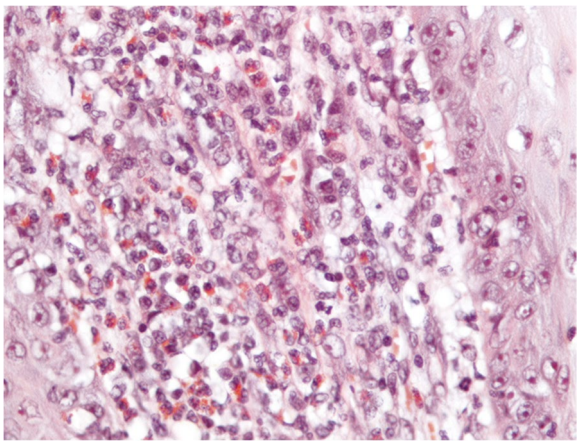

Fig. 1 Intense TATE in canine squamous cell carcinoma (Congo Red staining, 400×)

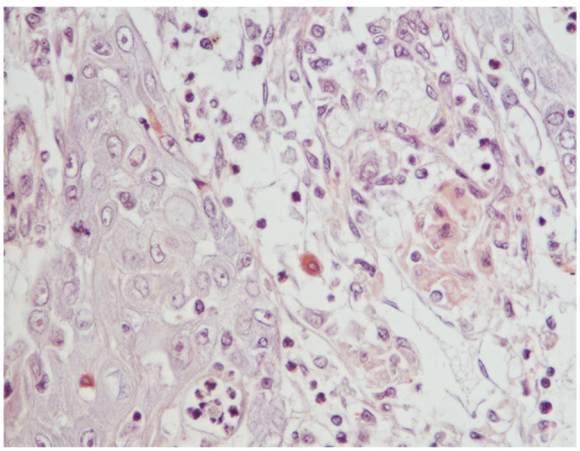

Fig. 2 Scarce TATE in canine squamous cell carcinoma (Congo Red staining, 400×)

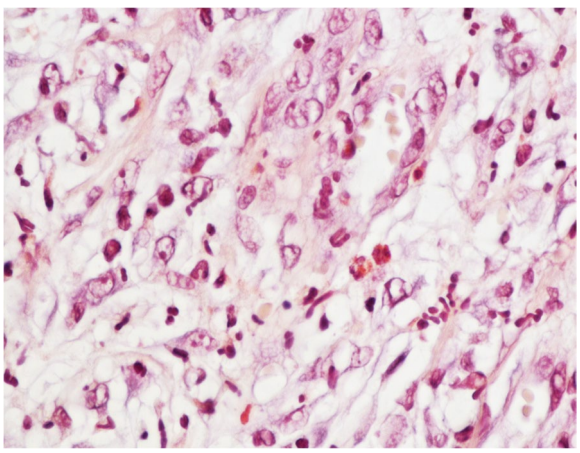

Fig. 3 Moderate TATE in canine squamous cell carcinoma (Congo Red staining, 600×)

Table 1 Association between TATE and histological differentiation

TATE	Histological differentiation						*p*-value
	Well-differentiated		Moderately differentiated		Poorly differentiated		
	n	%	*n*	%	*n*	%	
Scarce	0	0.0	3	6.1	13	26.5	< 00,001
Moderate	2	4.1	10	20.4	1	2.0	
Intense	11	22.4	9	18.4	0	0.0	

new forms of diagnosis and therapy that benefit both species. Given the similarities in pathophysiology and clinical course of the disease in canines and humans, dogs may be an important model for oncology comparative studies in a One Health concept.

Acknowledgements
Not applicable.

Authors' contributions
IP, design of the work; IP, the acquisition; ATV, MS, FS, and IP, analysis; FS, JP, and IP, interpretation of data; ATV, MS, FS, and JP have drafted the work or substantively revised it. All the authors have approved the submitted version (and any substantially modified version).

Funding
This work was supported by the projects UIDB/CVT/00772/2020 and LA/P/0059/2020 funded by the Portuguese Foundation for Science and Technology (FCT).

Availability of data and materials
The material was from UTAD Histopathology Lab. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable. Is a retrospective study with material from archives of the UTAD Laboratory of Histology and Pathological Anatomy. In the submission form of the material to the lab, there is a section with the informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 20 January 2023 Accepted: 23 March 2023
Published online: 19 May 2023

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