Reviewer's report

Title: Columnar cell lesions of the canine mammary gland: pathological features and immunophenotypic analysis compared with the human breast

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Reviewer: Adelina Gama

Reviewer's report:

This paper describes the presence of columnar cell lesions on a series of canine mammary gland samples. This is the first description of such lesions in this species, which provides this manuscript of major significance. However, there are several points which need to be addressed to improve the comprehensibility of this paper.

Major Compulsory Revisions

Although the authors have applied the human breast classification, the chosen title: “Columnar cell lesions of the canine mammary gland: pathological features and immunophenotypic analysis compared with the human breast” implies a comparative study using both canine and human mammary samples. It would be more accurate the following title: “Columnar cell lesions of the canine mammary gland: pathological features and immunophenotypical analysis”.

In the 2nd paragraph of the Background section, the authors state: “CCLs to be divided into three broad categories: columnar cell change (CCC), columnar cell hyperplasia (CCH), and further subclassifications of these according to the absence or presence of cytological atypia, collectively known as flat epithelial atypia (FEA).”. This sentence on the classification of columnar cell lesions is not clear and should be clarified. There are two (not three) broad categories: columnar cell change (CCC) and columnar cell hyperplasia (CCH), each further subclassified according to the absence or presence of cytological atypia; the lesions of CCC and CCH with atypia are collectively known as flat epithelial atypia (FEA).

Material and Methods: despite 67 identified columnar cell lesions, the authors performed the immunohistochemical analysis in a rather small number of cases. Besides, there is a lack of information on which columnar cell lesions were used.

In the 2nd paragraph of Material and Methods section, the authors should clarify the classification applied in the present study. In the background section, CCC referred to Columnar Cell Change, but in this paragraph CCC is used for Columnar cell lesions without atypia? Please clarify.

In the 2nd paragraph of Results section, the authors should state “CCL without atypia were identified in 45/67” and not “CCC without atypia...” and then describe both CCC and CCH without atypia.
In the 2nd paragraph of the Results section, the authors state that columnar lesions without atypia were frequently associated with microcalcifications. How many cases were there with microcalcifications? And what about FEA cases? Were there any microcalcifications?

In the 4th paragraph of Results section, the authors state: “Interestingly, in situ carcinoma was more frequently observed in CCLs with atypia (FEA): 11/20 (Fig. 4)”. Although this is correct, this statement is misleading, given that 9 out of 20 in situ carcinomas were also associated with CCLs without atypia. Please comment.

The information regarding statistical associations is rather confusing. Instead of presenting figures (4 and 5), the authors should present their data in a table format, providing the number and percentage of each group of lesions, in addition to the P value.

The authors are advised to check the number of cases throughout the Results section, given that they do not always match with the numbers presented in the table. For example, the authors state: “CCCs were detected in association with 23 benign tumors…”, but in Table 1 the authors only mention 21 benign tumors.

The last sentence of the Discussion is confusing. Please rephrase it.

Table 1: the authors should remove the columns on DH. This additional information should be given in the text.

Figure 3A is out of focus and Figure 3B should be replaced by a more illustrative one. The authors must be aware that this is the first report of columnar lesions in canine mammary gland samples, and thus, it is important to present outstanding microphotographs.

Please eliminate Fig 4 and Fig. 5 (see comments above). In addition, the authors are advised to use a uniform nomenclature in the text and in table/figure legends. For example, the term “usual ductal hyperplasia” (UDH) is used in Fig. 5 legend but has not been mentioned in the text.

Minor Essential Revisions

In the abstract, the following sentence “characterized at dilated acini lined with a single layer of columnar epithelial cells” should be corrected, since the authors describe some columnar lesions with more than one epithelial cell layer (as described in the 2nd paragraph of the introduction and in the 2nd paragraph of the results section).

In the abstract, the sentence “The proliferation rate as measured by Ki67 appeared higher in the lesions analyzed.” is not very clear.

In Material and Methods, Ki-67 immunoreactivity scoring should be clarified.

In the Results section, the sentence “Associated lesions were represented only
by ductal and lobular hyperplasias.” is not correct, since the authors also
describe associated neoplastic lesions (Table 1).

In the 2nd paragraph of the Discussion, please introduce the missing reference
on “Hyperplastic breast lesions, such as duct hyperplasias without and with
atypia, have previously been described in the canine mammary gland.”

In the sentence: “Additional studies are needed to analyze the frequency of
columnar cells” (last paragraph), did the authors mean columnar cell lesions?

Discretionary Revisions

The authors should check the English language throughout the paper, in order to
improve the readability of the manuscript.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.