



Retrospective evaluation of canine anal sac carcinoma (260 cases) in Brazil: late detection and failures in lymph node evaluation¹

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ABSTRACT.- Paiva F.N., Moreira S.H., Linhares L.C.M., Sueiro F.A.R., Nardi A.B. & Jark P.C. 2023. **Retrospective evaluation of canine anal sac carcinoma (260 cases) in Brazil: late detection and failures in lymph node evaluation.** *Pesquisa Veterinária Brasileira* 43:e07210, 2023. Faculdade de Ciências Agrárias e Veterinárias, Universidade Estadual Paulista “Júlio de Mesquita Filho”, Via de Acesso Prof. Paulo Donato Castellane Castellane s/n, Vila Industrial, Jaboticabal, SP 14884-900, Brazil. E-mail: n-paiva@hotmail.com

Anal sac neoplasms are common in companion animals, and the epidemiological profile has been extensively described in international studies; however, national data are still lacking. Data on the Brazilian reality of anal sac carcinoma cases' diagnosis and treatment are also scarce. The purpose of this study was to retrospectively evaluate cases of canine anal sac carcinoma and assess the profile of involvement, tumor size, and lymphatic invasion at the time of diagnosis. Information was obtained from Vetpat laboratory database, from 260 cases spanning a 12-year period (2010-2021). In histopathological evaluation at the time of diagnosis, data on sex, age, and race were described, as well as tumor size and lymphatic invasion. The presence of metastasis was also assessed in cases where lymph nodes were sampled. Simple descriptive statistical analysis was used to evaluate the data. Adult and elderly, female, and mixed-breed animals were more involved, indicating differences from international studies that can be attributed to sociocultural factors. In terms of tumor size, it was observed that 93% of the cases had the largest diameter above 2.5cm. Only 7% of the cases had the largest diameter below 2.5cm, demonstrating the often late diagnosis and the importance of rectal palpation examination during the general physical assessment of canine patients, particularly at an advanced age. Regarding lymphatic invasion and affected lymph nodes, 50% of the cases had lymphatic invasion described in the histopathological examination. However, only 5% of the lymph nodes were sent along with the primary tumor, indicating the disease's aggressive behavior but with possible metastases underdiagnosed.

INDEX TERMS: Anal sac apocrine adenocarcinoma, canine, diagnosis, epidemiology, neoplasm.

RESUMO.- [Avaliação retrospectiva do carcinoma de saco anal canino (260 casos) no Brasil: detecção tardia e falhas na avaliação dos linfonodos.] As neoplasias de saco anal possuem incidência importante nos animais de companhia, tendo o seu perfil epidemiológico de acometimento amplamente

descrito em estudos internacionais, entretanto dados nacionais ainda são escassos. De modo semelhante, dados acerca da realidade brasileira, associados ao diagnóstico e conduta desses casos, são inexistentes. O objetivo do presente trabalho foi avaliar, de forma retrospectiva, os casos de carcinoma de saco anal canino, avaliando o perfil de acometimento, o tamanho tumoral e a invasão linfática no momento do diagnóstico. Foi obtido informações de 260 casos, respectivo a um período de 12 anos (2010-2021), proveniente do banco de dados do laboratório Vetpat. Foram descritos os dados acerca do sexo, idade e raça, bem como o tamanho tumoral e presença de invasão linfática em avaliação histopatológica no momento do diagnóstico. Os casos que cursavam com envio dos linfonodos também foram avaliados quanto a presença de metástase. Os

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dados foram avaliados mediante análise estatística descritiva simples. Foi encontrado um maior acometimento em animais adultos a idosos, do sexo feminino e sem raça definida, evidenciando diferenças em relação a estudos internacionais, que podem ser atribuídas a fatores socioculturais. Em relação ao tamanho tumoral, observou-se que 93% dos casos apresentavam o maior diâmetro acima de 2,5cm e apenas 7% dos casos apresentavam o maior diâmetro abaixo de 2,5cm, evidenciando o diagnóstico frequentemente tardio, bem como a importância do exame de palpação retal durante a avaliação física geral de pacientes caninos, principalmente em idade avançada. Quanto a avaliação da invasão linfática e linfonodos acometidos, 50% dos casos cursavam com invasão linfática descrita em exame histopatológico, entretanto em apenas 5% dos casos os linfonodos foram enviados junto ao tumor primário, evidenciando o comportamento agressivo da doença, porém com metástases possivelmente subdiagnosticadas.

TERMOS DE INDEXAÇÃO: Adenocarcinoma apócrino do saco anal, caninos, epidemiologia, diagnóstico, neoplasia.

INTRODUCTION

Anal sac neoplasms develop in the apocrine glands inside the anal sacs and are common in companion animals. Anal sac carcinomas account for 17% of perianal tumors and 2% of all cutaneous neoplasms in dogs (Goldschmidt & Goldschmidt 2017, Liptak & Turek 2019), but they are rare in cats. Adenomas are uncommon in both species (Rodigheri et al. 2016, Goldschmidt & Goldschmidt 2017, Liptak & Turek 2019).

Its progression is initially subtle, with intradermal and subcutaneous masses discernible only on rectal palpation, with the most advanced cases forming external masses of large dimensions and varying appearance (Williams et al. 2003, Rodigheri et al. 2016, Goldschmidt & Goldschmidt 2017, Liptak & Turek, 2019). In terms of behavior, the neoplasm exhibits variable local aggressiveness but with a high metastatic potential, with approximately 26% to 96% of cases coursing with local metastasis and 0% to 42% of cases with distant metastasis, from the time of initial diagnosis (Bennett et al. 2002, Williams et al. 2003, Goldschmidt & Goldschmidt 2017).

The treatment of choice consists of surgical excision, which may later be combined with adjuvant techniques (Potanas et al. 2015, Barnes & Demetriou 2017, Chambers et al. 2020, Heaton et al. 2020, Liptak & Turek 2019). Clinical staging, tumor diameter, presence of regional, and distant metastases, presence of paraneoplastic hypercalcemia, and tumor histology are described as prognostic factors (Rodigheri et al. 2016, Wouda et al. 2016, Goldschmidt & Goldschmidt 2017, Pradel et al. 2018, Liptak & Turek 2019).

The epidemiological profile described in international studies primarily involves adult and elderly animals (Williams et al. 2003, Polton & Brearley 2007, Polton et al. 2007, Knudsen et al. 2013, Palladino et al. 2016, McQuown et al. 2017, Meier et al. 2017, Pradel et al. 2018, Elliott 2019) without a confirmed sexual predisposition (Williams et al. 2003, Polton et al. 2006, 2007, Polton & Brearley 2007, Knudsen et al. 2013, Pradel et al. 2018, Elliott 2019). Regarding the racial factor, the predisposition has been described primarily in the Dachshund, Cocker Spaniel, and German Shepherd breeds (Williams et al. 2003, Polton et al. 2006, Polton & Brearley 2007, Polton et al. 2007, McQuown et al. 2017, Pradel et al. 2018, Elliott 2019), and in dogs weighing

between 22 and 26kg, demonstrating the involvement mainly in medium-sized breeds (Turek et al. 2003, Williams et al. 2003, Palladino et al. 2016, McQuown et al. 2017, Schlag et al. 2020). There have been no studies that describe the epidemiological profile in Brazil, which may differ from international studies due to the country's sociocultural aspects.

This study aims to describe the epidemiological profile found in canine patients with anal sac carcinomas, as well as the tumor size and presence of lymphatic invasion at the microscopic level, as observed at the time of diagnosis.

MATERIALS AND METHODS

The database used was provided by Vetpat laboratory and covered a 12-year period (2010-2021). The search was carried out using the species "canine" and the "carcinoma of the anal sac" diagnosis in the laboratory's operating system. The search result on a retrospective survey of canine cases with histopathological diagnosis of anal sac carcinoma. Cases where the diagnosis was not confirmed and other neoplastic types and animal species were excluded.

Information about race, gender, and age was collected, as well as tumor size and the presence of lymphatic vascular invasion in histopathological evaluation. The presence of metastasis was also assessed in cases with lymph node referral.

The age was divided into age groups adapted from Creevy et al. (2019), with animals aged up to four years considered "young", animals aged between five and 10 years considered "adults", and animals aged over 10 years considered "elderly".

Only cases where the entire tumor was sent were considered for tumor size evaluation, allowing for total measurement. Tumors were divided based on a 2.5-cm cutoff point determined by the tumor staging model proposed by Polton & Brearley (2007). This evaluation did not include cases of tumor fragments being sent. There was no clinical information about the animals' comorbidities, general clinical status, or medical history. Simple descriptive statistical analysis was used to evaluate retrospective epidemiological data.

The Animal Use Ethics Committee (CEUA) of the "Faculdade de Ciências Agrárias e Veterinárias" (FCAV), of the "Universidade Estadual Paulista 'Júlio de Mesquita Filho'" (Unesp), Jaboticabal campus, approved the study under Protocol No. 1678/21.

RESULTS

Following the initial review of the database, 272 cases were accessed. Twelve originally accessed cases were excluded because the diagnosis had not been confirmed, leaving 260 cases for the retrospective analysis. The obtained data were exactly reproduced as they appeared in the system.

The epidemiological profile of the patients was first evaluated, which included the gender, age, and breed of the affected animals. In terms of gender, females accounted for 163/260 (63%), and males accounted for 97/260 (37%) of the cases. In terms of age, an average of 11.2 years was observed, with a minimum age of three and a maximum of 17 years. Table 1 summarizes the results based on age groups.

When the racial profile was examined, involvement was found in 24 different breeds and mixed-breed animals. Mixed-breed animals were the most common, accounting for 92/260 (35.4%) of the cases, followed by Poodles 42/260 (16.1%), Cocker Spaniels 27/260 (10.4%), and Dachshunds 16/260 (6.1%). Table 2 describes the other races, which accounted for less than 5% of cases.

Table 1. Epidemiological profile according to established age groups

Age group	Absolute value	Percentage
Young	4	1.60%
Adult	83	31.90%
Elderly	135	51.90%
Not informed	38	14.60%

Age division in groups adapted from Creevy et al. (2019), considering animals aged up to 4 years as "young", animals aged between 5 and 10 years as "adults", and animals aged over 10 years as "elderly".

Table 2. Racial profile found in dogs

Racial profile	Absolute value	Percentage
Mixed-breed	92	35.40%
Poodle	42	16.10%
Cocker Spaniel	27	10.40%
Dachshund	16	6.10%
Maltese	9	3.50%
Labrador	8	3.10%
German Shepherd	8	3.10%
Pinscher	6	2.30%
Yorkshire	6	2.30%
Beagle	5	1.90%
Boxer	5	1.90%
Chow-chow	4	1.50%
Shih-tzu	4	1.50%
Basset hound	3	1.20%
Golden Retriever	3	1.20%
Schnauzer	3	1.20%
Other*	10	3.80%
Not informed	9	3.50%

* Including races that accounted for less than 1% of cases.

The size of the lesions at the time of diagnosis was only assessed in 178 cases where the tumor mass was sent in its entirety. The largest diameter in 166/178 (93%) cases was greater than 2.5cm, and the largest diameter in 12/178 (7%) cases was less than 2.5cm.

The case with the largest diameter was 14.5cm in diameter and affected a medium-sized dog. There were 8/178 (4%) cases where the largest tumor diameter measured more than 10cm, affecting animals of various sizes. The largest tumor diameter measured 5.4cm on average.

Regarding lymphatic invasion in the primary tumor, 130 (50%) cases had invasion described in the histopathological examination. However, only 13 (5%) cases had lymph nodes sent along with the primary tumor, all diagnosed with metastasis.

DISCUSSION

In the current study, a higher frequency of females was observed, exceeding 60% of the cases, in agreement with Williams et al. (2003), Polton et al. (2007), and Meier et al. (2017). This finding, however, contradicts several other studies that found a higher involvement in males (Turek et al. 2003, Williams et al. 2003, Polton et al. 2006, Polton & Brearley 2007, Knudsen et al. 2013, Potanas et al. 2015, Pradel et al. 2018, Elliott 2019). In castrated males, a possible predisposition has also been

suggested (Turek et al. 2003, Urie et al. 2012, Knudsen et al. 2013, Palladino et al. 2016, Rodigheri et al. 2016, Wouda et al. 2016, Barnes & Demetriou 2017, Goldschmidt & Goldschmidt 2017, McQuown et al. 2017, Pradel et al. 2018, Elliott 2019, Heaton et al. 2020, Liptak & Turek 2019, Schlag et al. 2020). However, reproductive status was not assessed in this study. The findings regarding sexual predisposition are contradictory and can be attributed to regional differences, as there is no proven hormonal involvement in this neoplastic type; it is not possible to exclude hormonal influence in the early stages of the disease (Liptak & Turek 2019).

The age profile revealed that animals over the age of ten were more likely to be involved, followed by those between the ages of five and 10, with a higher frequency in animals considered adults and elderly, who were the most affected age groups (Rodigheri et al. 2016, Goldschmidt & Goldschmidt 2017, Liptak & Turek 2019). The mean age of onset, 11.2 years, remained within the range described in previous studies, which ranged from 9 to 11.5 years (Bennett et al. 2002, Turek et al. 2003, Williams et al. 2003, Polton & Brearley 2007, Polton et al. 2007, Urie et al. 2012, Knudsen et al. 2013, Potanas et al. 2015, Palladino et al. 2016, Wouda et al. 2016, Barnes & Demetriou 2017, McQuown et al. 2017, Meier et al. 2017, Pollard et al. 2017, Pradel et al. 2018, Skorupski et al. 2018, Elliott 2019, Chambers et al. 2020, Heaton et al. 2020, Schlag et al. 2020).

In terms of racial profile, animals of the mixed breed were described as the most affected group, a finding confirmed by Brazilian studies and linked to sociocultural patterns in the country rather than genetic predisposition. The Poodle breed, which was described with the highest frequency among defined breed animals in the current study, is not commonly described with a significant incidence, appearing among the most common breeds only in the Heaton et al. (2020) study and occurring with low incidence in Bennett et al. (2002) and Wouda et al. (2016). The high frequency observed in the Poodle breed may be due to the breed's popularity in Brazil rather than genetic predisposition.

The second and third most frequently observed breeds in the study were Cocker Spaniel and Dachshund, both of which have a predisposition already described in the literature (Turek et al. 2003, Polton et al. 2006, Polton & Brearley 2007, Polton et al. 2007, Rodigheri et al. 2016, Barnes & Demetriou 2017, Goldschmidt & Goldschmidt 2017, Pradel et al. 2018, Elliott 2019, Chambers et al. 2020, Liptak & Turek 2019).

Tumor size was determined by measuring the largest tumor diameter, which yielded a mean result of 5.4cm, with only 7% of cases having the largest diameter of less than 2.5cm, classified as T1 according to Polton & Brearley (2007) proposed anal sac carcinoma staging model. Turek et al. (2003), Pradel et al. (2018), Skorupski et al. (2018), Chambers et al. (2020), and Schlag et al. (2020) reported tumor averages of less than 2.5cm. In contrast, Heaton et al. (2020) reported a tumor average of 3.0cm, which is also considered low.

There were also 4% of cases where the largest tumor diameter was greater than 10cm, which was not observed in similar studies where no cases were recorded in these dimensions (Turek et al. 2003, Polton & Brearley 2007, Polton et al. 2007, Pradel et al. 2018, Skorupski et al. 2018, Chambers et al. 2020, Heaton et al. 2020, Schlag et al. 2020). Meier et al. (2017) reported a case with a tumor measurement

of 12cm, which was still less than the largest diameter of 14.5cm observed in this study. The findings show that this neoplastic type is frequently diagnosed late, as evidenced by the tumor dimensions, which tend to be large in most cases. This suggests that the initial diagnostic approach and clinical evaluation in veterinary practice may have failed.

The presence of lymphatic vascular invasion has been described as an important prognostic factor in cases of anal sac carcinoma, with values ranging from 10% to 61% (Pradel et al. 2018, Morello et al. 2021, Wong et al. 2021), values similar to those found in the current study. Furthermore, this parameter has been linked to a possible predictor of metastatic involvement (Schlag et al. 2020), as demonstrated by Morello et al. (2021), who found lymphatic vascular involvement in 61% of cases and clinically palpable lymph nodes on rectal examination, with metastasis confirmed in 48.57% of cases through in histopathological examination. Given the study's findings, it is believed that metastatic involvement in lymph nodes has been underdiagnosed.

Lymphadenectomy in conjunction with surgical excision of the primary tumor has been recommended in this neoplastic type, providing greater survival and a better prognosis for the patient (Polton & Brearley 2007, Wouda et al. 2016). However, given the lymph node referral rate observed of only 5% of cases and the disease's extremely aggressive and metastatic behavior, it is clear that the recommendation is still not widely followed.

CONCLUSIONS

The study depicted the profile of the animals most affected by anal sac carcinoma, which was concentrated in females, mixed breeds, and animals of advanced age, a finding that was not entirely consistent with literature data, indicating that the sociocultural issues in the country can influence the frequency of this neoplastic type.

The findings referring to the high tumor size frequently observed at the time of diagnosis, combined with the high rate of lymphatic invasion and the low rate of lymph node referral, highlight the clinician's shortcomings in dealing with this type of tumor. We reinforce two key points in this manner. Initially, the need for greater attention to evaluating rectal palpation, particularly in geriatric animals, allows for an early diagnosis of the neoplasm. Second, there is a greater need for lymphatic evaluation in affected patients to ensure proper staging and a more accurate approach in each case.

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Conflict of interest statement.- The authors declare no conflicts of interest.

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