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ORIGINAL RESEARCH

Clinical Staging and Histopathological Grading of Inguinal Squamous Cell Carcinoma in Dogs: A Case Series Study

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Introduction: Canine cutaneous squamous cell carcinoma (SCC) is a locally invasive tumor with a variable prognosis.

Materials and Methods: This study evaluated clinical stage and histopathological grade as prognostic factors. Eleven dogs with inguinal SCC underwent surgery. All dogs presented varying degrees of atopic skin owing to prolonged outdoor ultraviolet (UV) exposure. Tumors are located primarily in the ventro inguinal area, affecting the prepuce and scrotum in males. Clinical staging (TNM system) was performed through abdominal ultrasound and palpation of regional lymph nodes, and histopathologically, Broder grading was applied.

Discussion: The survival time (ST) and disease-free interval (DFI) were analyzed, and the median ST was 738 days for Grade 1 tumors compared with 135 days for Grade 4 tumors. Staging correlated with metastatic risk (1/11 patients).

Conclusion: This study highlights the importance of histological grade as a prognostic factor for canine cutaneous SCC and surgery as a treatment of choice and emphasizes the need for further studies on disease progression and treatment outcomes in veterinary medicine.

Keywords: dog, cutaneous squamous cell carcinoma, atopic skin, histological grade, treatment

Introduction

Squamous cell carcinoma (SCC) is an epithelial tumor that can arise at various sites in dogs. This tumor represents 3.9% to 10.4% of all canine skin tumors. It is the most common form of cancer in the oral cavity and is also present in other locations, such as the nasal cavity, mammary glands, lungs, bladder or vagina.[1] Dogs with thin, nonpigmented haircoats along the ventrum and flank are at increased risk of SCC, and chronic dermatitis in these areas increases the incidence of SCC.[2,3] The reported mean age at the onset of cutaneous SCC in dogs is 8.3–9.1 years. Dalmatians, boxers, bull terriers, beagles, Norwegian elkhounds, basset hounds, and pointers have a relatively high probability of suffering, but no sex predilection has been demonstrated.[3] The etiology of cutaneous SCC is associated with multiple factors, most notably, exposure to ultraviolet (UV) radiation,[4–6] which causes direct DNA damage and promotes mutations in key genes. Genetic alterations play key roles in the development of this disease.[7] Cutaneous SCC is considered locally invasive, with a variable rate of metastasis and prognosis linked to tumor location and disease progression. The treatment of choice is surgery, which permits histological evaluation and is important in determining prognosis. If the tumor is well differentiated and surgical excision is complete, the rates of recurrence and metastasis are low.[8] There are limited reports on other therapies, such as nonsteroidal anti-inflammatory drugs, retinoids, chemotherapy, and radiation, without good results. The latter, radiation therapy, has been utilized for SCC arising in other locations but has not been well described for cutaneous SCC in dogs, although it can be combined in cases of incomplete or nonsurgical patients. Early diagnosis

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and treatment are key to patient prognosis.[8,9] The purpose of this prospective analysis was to evaluate the signalment, clinical features, behavior, and outcomes of dogs diagnosed with cutaneous SCC with histopathologic actinic changes surgically treated at our institution.

Materials and Methods

Case Selection

This prospective study was conducted from 2020–2023 and was approved by the Ethics Committee on Animal Use of the Veterinary School of the Universidad de Las Palmas de Gran Canaria (ULPGC) (Protocol Number 58/2018), and the treatment of the animals was aligned with the veterinary best practices. The inclusion criterion was surgical patients with a histological diagnosis of cutaneous SCC of the ventro inguinal area (Figures 1–4). The exclusion criteria were other SCC locations, the presence of other tumors at the same time, metastasis at the time of diagnosis, or treatment with any other therapy. The patients were followed every week for 1 month until complete healing was achieved. The reviews were subsequently performed every 3 months by assessing the operated area, performing fine needle aspiration if necessary, performing abdominal ultrasound to rule out the involvement of lymph nodes or other organs during a year, and collecting blood for future studies. Ultrasound studies revealed the size and echogenicity of the iliac lymph nodes, and if changes were observed, fine needle aspiration (FNA) was performed. In addition, as previously mentioned, 8 mL blood samples were taken at each review with the oral consent of the owners to obtain samples of different types. Patient data, such as age, sex, breed, clinical stage, Broder grade, disease-free survival, and overall survival, were recorded.

Clinical Staging

Clinical staging was performed according to Bukhari et al[9] for human SCC, which evaluates primary tumor size (T), regional lymph node involvement (N), and distant metastasis (M).

Tumor staging was based on physical examination, inguinal node measurement, and abdominal ultrasound to evaluate the possibility of disease progression and plan surgery.

Treatment

The surgical process was defined as a resection with 1–2 cm soft tissue lateral and deep margins with a view to achieve histologically complete resection, in addition to performing lymph node resection if the margins were enlarged. Moreover, during surgery, healthy skin was removed from the patient, and a part of the tumor lesion was preserved for future studies.

Margin quality was obtained from the histopathological report and was characterized as complete or incomplete. Margins were categorized as complete if no tumor cells were present at the edges of the resection and as incomplete if any tumor cells contacted the edges of the resection in addition to vascular/lymphatic infiltration in the dermis or lymph node metastasis.

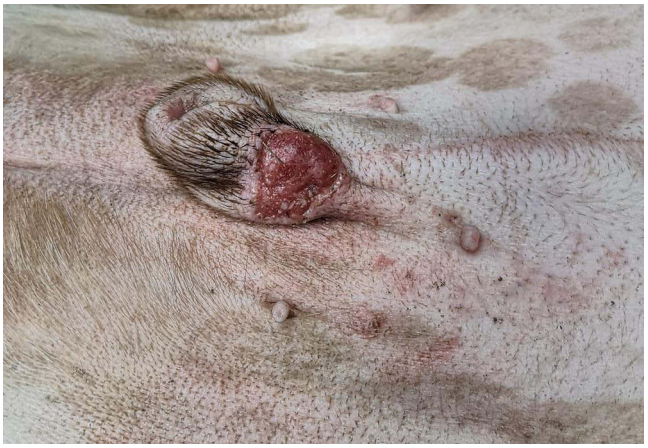

Figure 1 Preputial injury in a male dog (stage I).

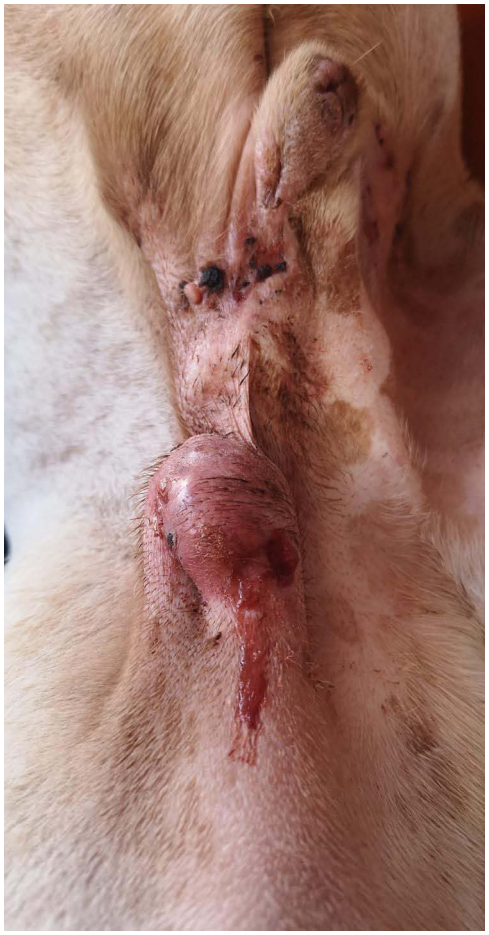

Figure 2 Caudal preputial injury in a male dog (stage II).

Histopathological diagnoses were reviewed and performed according to the Veterinary Pathology Section of the Veterinary School of ULPGC. The tumor tissue was fixed in formalin, and 4 µm thick sections were prepared routinely and stained with hematoxylin–eosin. A broder classification was performed once the results were obtained, according to Goldschmidt and Goldschmidt.[2] Tumors were classified as well differentiated (grade 1), moderately differentiated (grades 2 and 3), or poorly differentiated (grade 4). The infiltration stage was graded from 1 to 4 according to the depth and affected tissues. Grade 1, in situ carcinoma; grade 2, dermis or submucosal invasion; grade 3, muscle, nervous ganglia, gland, and adjacent adipose tissue invasion; and grade 4, deep invasion, including bone tissue invasion.

Follow-up

Patient follow-up was performed every 4 months, and disease progression was assessed. The response to treatment was evaluated according to the criteria for evaluating the response of solid tumors 30 days after the procedure (RECIST Guidelines).[10] The disease-free interval (DFI) was calculated as the time from definitive surgery to local recurrence, development, or progression of detectable metastases. The survival time (ST) was calculated as the time from definitive surgery to death attributed to the disease or if the dog was alive at the last follow-up. Patients lost to follow-up and those with unrelated deaths were excluded from the response evaluation.

Results

Eleven dogs met the study inclusion criteria and underwent complete surgery for the removal of cutaneous SCC, which was confirmed by histological evaluation. The median age at diagnosis was 9 years (IQR (6,9)). The dog breeds included in this study were American Staffordshire Terrier (3), American Pit Bull (4), and mixed breeds (3), of which 4 were

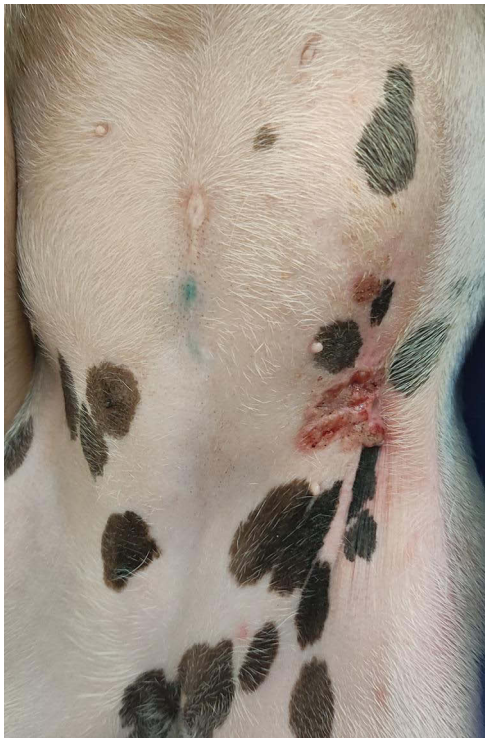

Figure 3 Inguinal injury in a female dog (stage I).

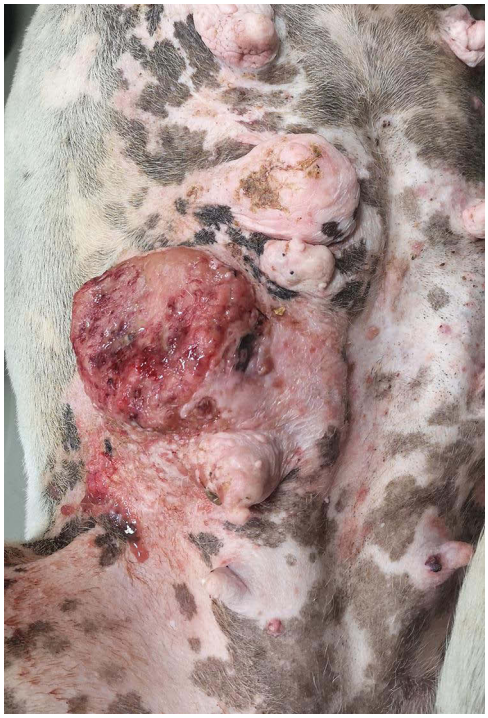

Figure 4 Inguinal injury in a female dog (stage II).

female and 7 were male. In addition, all dogs had different levels of atopic dermatitis due to continuous exposure to outdoor UV rays. The median follow-up period was 734 days (iq(395,1087)). Table 1.

All tumors are located in the ventro inguinal zone, affecting parts of the foreskin, including the scrotum, in males. Multiple lesions were observed in these cases, with the largest lesion used as a reference. Therefore, 5/11 dogs had lesions < 2 cm, 4/11 had lesions between 2 and 5 cm, and 2/11 had lesions greater than 5 cm. The inguinal lymph nodes were palpated, and 6 dogs showed an increase in size in one of them. Finally, an abdominal ultrasound was performed, in which an increase in the bilateral iliac nodes was observed in all animals that were diagnosed as reactive owing to their shape and similarity in size, in addition to FNA in cases where it was possible. On the basis of these data, we performed clinical staging. The results are presented in Table 2.

Table 1 Individual Information of 11 Dogs with Dermal Squamous Cell Carcinoma

Pt	Sex	Age	Breed	Primary Tumor size	Inguinal/Iliacs Lymph Nodes
1	Male	6	American Stafford	< 2 cm	Enlarged inguinal/no iliacs
2	Male	6	Mix pitbull	> 2 cm < 5 cm	Enlarged inguinal/iliacs reactive
3	Male	9	Pitbull	> 2 cm < 5 cm	Enlarged inguinal/iliacs reactive
4	Male	6	Pitbull	> 2 cm < 5 cm	Enlarged inguinal/iliacs reactive
5	Female	5	Mix Stafford	< 2 cm	Not palpable/iliacs reactive
6	Female	9	Pitbull	< 2 cm	Not palpable/iliacs reactive
7	Male	9	American Stafford	> 5 cm	Enlarged inguinal/iliacs reactive
8	Female	8	Pitbull	< 2 cm	None palpable
9	Male	11	Mix pitbull	< 2 cm	Not palpable/iliacs reactive
10	Female	11	Pitbull	> 5 cm	Enlarged inguinal/iliacs reactive
11	Male	9	American Stafford	> 2 cm < 5 cm	None palpable

Abbreviation: Pt, patient.

Table 2 Clinical Staging of Dogs

Pt	Staging	Tumor Size	Lymph Node	Distant Metastasis
1	I	T1	N0	M0
2	II	T2	N0	M0
3	II	T2	N0	M0
4	II	T2	N0	M0
5	I	T1	N0	M0
6	I	T1	N0	M0
7	III	T4	N1	M0
8	I	T1	N0	M0
9	I	T1	N0	M0
10	II	T3	N0	M0
11	II	T2	N0	M0

Abbreviation: Pt, patient.

Table 3 Follow-up of 11 Dogs

Pt	Clinical Staging	Broder Grade	DFI (days)	ST (days)
1	I	1	1095	1095
2	II	2	728	1089
3	II	2	730	730
4	II	2	575	575
5	I	1	755	755
6	I	2	734	734
7	III	4	64	135
8	I	1	365	365
9	I	2	189	365
10	II	3	240	365
11	II	2	227	227

Abbreviations: Pt, patient. DFI, disease-free interval. ST, survival time.

According to Bukhari et al for human SCC, five dogs were classified as stage I, five as stage II, and one as stage III. The latter was the only patient with inguinal node metastasis at the time of diagnosis, and none presented with distant metastasis (Table 2).

After staging, all dogs received NSAIDs for 2 weeks prior to surgery to improve skin quality and reduce primary lesions. At the time of the intervention, 6 dogs had one of the inguinal lymph nodes removed because of an increase in size.

Ten tumors were completely excised, and 1 tumor was incompletely excised on histologic evaluation.

When histopathological grading was considered, three tumors were well differentiated (Broder grade 1), seven were moderately differentiated (Broder grades 2 and 3), and one was poorly differentiated (Broder grade 4) (Table 3). Animals with Grade 1 tumors had a median ST of 738 days, and animals with Grade 2 and 3 tumors had a median ST of 620 days. Only one patient with a grade 4 tumor with inguinal node metastasis showed vascular and lymphatic invasion and 135 days of ST (Table 3).

The dogs underwent only one intervention in the period of one year, except for the animal with infiltrative margins that recurred after 64 days and underwent a second palliative surgery, although no disease-free time was obtained. The ST was maintained for 135 days until euthanization was performed because of disease progression.

During a period of one year, 11 dogs were monitored, and disease progression was evaluated via abdominal ultrasound every three months. The patient did not exhibit any changes during the first imaging test.

Ten of these dogs were alive at the end of the study, and one died of disease progression. Three of the 11 dogs experienced tumor recurrence. Two of them occurred during the study period, that is, in less than a year, and the other occurred after two years without its presence. We proceeded with the same dynamics as the main tumor; prior ultrasound and surgery were performed. In none of the three cases was removal of the internal lymph nodes necessary because no changes were observed with respect to previous ultrasound studies.

All dogs included in the study, with the exception of one, were alive without recurrence.

Discussion

Inguinal squamous cell carcinoma is a rare but locally aggressive tumor in canines. The mean age of the affected dogs in this study was 8 years, which is consistent with previous reports, and no sex predilection was observed.[1,2] Pit bulls and American Staffordshire Terriers were the most prevalent breeds in the study population. This type of tumor shows a predisposition in white-coated animals and typically develops in lightly pigmented or nonpigmented skin, likely induced by damage caused by chronic exposure to UV light.[6,8]

This is particularly relevant in the Canary Islands, where the subtropical climate and long hours of sunlight contribute to the incidence of ulcerated ventro inguinal skin lesions diagnosed as SCC. However, it also offers an opportunity to study this type of tumor in greater depth.

Histological lesions suggestive of exposure to chronic solar radiation were observed in all cutaneous SCC patients. These alterations have been reported in cases of SCC in humans and animals and are considered preneoplastic lesions associated with prolonged solar radiation.[6] Histological examination of these lesions revealed changes suggestive of chronic solar radiation exposure, which is consistent with similar reports in both human and animal cases of SCCs. SCCs in sun-exposed areas should be considered different entities from tumors in non sun exposed areas, warranting different treatments and prognoses.[2,3] Furthermore, it should be noted that patients present with dermatitis prior to the development of lesions, one of the causes related to the appearance of the tumor according to the literature.[5,6]

In relation to these changes described in patients with dermatitis, moderately differentiated lesions without lymph node involvement (stage II), such as the most common presentation, have been observed. This finding suggests that even with a moderate to severe evolution of the tumor, it is a disease that can have a good prognosis. Hence, it is important to diagnose this type of tumor in a timely manner and not to confuse it with other skin lesions.

It is a locally aggressive tumor; therefore, accurate staging is essential. Intervention and sample analysis are necessary to obtain good local control of the disease. This study evaluated the response of canine inguinal SCC to aggressive surgical treatment and investigated whether there was any difference between clinical stage and disease progression.[8,10] In all cases except one, local infiltration of the tumor tended to be moderate without metastasizing to the locoregional lymph node, even though the latter was found to be enlarged during examination. Therefore, although other treatments currently exist, they have not been shown to increase survival time (ST) as surgery gas has been achieved, even in lesions that may appear macroscopically out of control. Thus, our experience suggests that surgery remains the best standalone treatment option.[11,12]

Compared with SCC in humans, the appearance of lymph nodes or distant metastases is very rare in dogs and often presents with a high degree of metastasis.[11,13] In our study, only one patient presented with node metastasis at the time of surgery despite the presence of multiple injuries in other dogs.

Recurrence was more commonly observed in dogs with dedifferentiated lesions and deep dermal effects. A possible explanation is that these animals had more advanced disease at presentation in addition to histological grading. Although this does not constitute a sufficient number of cases to serve as a reference, the results presented here contribute to veterinary medicine, in which histological grading continues to be the main prognostic factor for cutaneous SCCs, with few studies on the follow-up of SCCs in animals.

SCCs may result in long survival times in dogs with early diagnosis and adequate surgical treatment. Understanding the different mechanisms used by tumor cells in this process may help in therapy and prognosis. Further studies are needed to better understand the behavior of canine squamous cell carcinoma, as current studies on this tumor are limited. Moreover, additional investigations are needed to evaluate this type of tumor at the molecular level, which will help identify potential therapeutic targets for future treatments.

Conclusion

Despite limited case numbers, this study represents a cohort of dogs with inguinal SCC treated uniformly and followed for ≥1 year. Timely diagnosis and aggressive surgical intervention yielded favorable outcomes, with histologic grading being the strongest prognostic indicator. These findings contrast with previous studies that included heterogeneous populations and tumor locations. Further investigations are needed to refine therapeutic strategies and improve understanding of canine SCC biology.

Institutional Review Board Statement

The study was approved by the Institutional Review Board (or Ethics Committee) of ULPGC (protocol code OEBA-ULPGC 33/2020R1).

Informed Consent Statement

Informed consent was obtained from all the subjects involved in the study.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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