Biological behaviour and clinical outcome in 42 cats with sarcoids (cutaneous fibropapillomas)

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Abstract
Feline sarcoids (or cutaneous fibropapillomas) are rare dermal neoplasms. There are currently no reported statistics concerning their clinical behaviour. Our objective with this retrospective, multi-institutional study was to describe the clinical presentation and biological behaviour of sarcoids in cats and to determine the oncologic outcome following surgical resection. Medical records from a laboratory database and six contributing institutions were searched to identify cats with histologically confirmed sarcoids. Forty-two cats were included in the study. The majority of sarcoids occurred on the face, particularly rostral locations such as the lips and nasal planum. Complete and incomplete histologic excision was achieved in 18 and 21 cats, respectively. The overall local recurrence rate was 40.5%. Complete histologic excision was associated with a significantly lower local recurrence rate (11.1%) and longer disease-free interval (not reached) compared with cats with incompletely excised sarcoids (66.7% and 250 days, respectively). The 1- and 2-year local recurrence rates were 0% and 7%, respectively, for cats with complete histologic excision, and 67% at both time intervals for cats with incomplete histologic excision. Five of the cats (83.3%) treated with curative-intent surgical revision following local tumour recurrence had no further local recurrence. All cats that died secondary to tumour-related causes had initial incomplete histologic excision and were euthanized because of local recurrence. Wide surgical resection of feline sarcoids is recommended to achieve complete histologic excision, local tumour control and a potential cure. For cats with incomplete histologic excision or local tumour recurrence, repeat surgical resection is recommended.

KEYWORDS
cats, fibropapilloma, oncology, oral and maxillofacial surgery, sarcoid, soft tissue neoplasia

1 | INTRODUCTION

Feline sarcoids (also known as cutaneous fibropapillomas) are rare dermal neoplasms that share many similarities with equine sarcoids. Bovine papillomavirus (BPV) types 1, 2 and 13 have been identified in equine sarcoids.¹ Similar to equine sarcoids, cross-species infection of a novel BPV type (BPV-14) has been confirmed to play a causal role in the development of feline sarcoids.²⁻⁶

Equine sarcoids are the most common cutaneous neoplasm in horses with six different clinical manifestations reported.⁷⁻⁸ In cats,
however, these different morphologies have not been described. Clinically, feline sarcoids present as firm, nodular, alopecic cutaneous masses that may measure up to 2 cm in diameter and are often focally ulcerated (Figure 1). They appear to have a predilection for the face (especially the nasal planum, philtrum, nares, upper lip and pinna), but have also been reported on the digits, neck, ventral abdomen and tail. Occasionally, lesions may be seen in the oral cavity. This anatomical distribution may be more of a reflection of the territorial marking behaviours seen in this species, such as scent rubbing and spraying.

Feline sarcoids are most commonly seen in domestic shorthair or domestic longhair cats in rural areas. Young, male cats with known exposure to cattle are believed to be predisposed. The lesions show behavioural and histologic characteristics that are virtually identical to equine sarcoids; they are slow growing and often locally infiltrative. Histologically, they are characterized by a fibroblastic proliferation with intimate association of an overlying, hyperplastic epithelial surface with pseudopapillomatous hyperplasia, that is, long rete pegs extending into the spindloid tumour (Figure 2). BPV-14 DNA has not been detected in non-sarcoid samples from cats. However, identification of BPV-14 nucleic acid is rarely necessary for definitive diagnosis because of the distinctive clinical presentation and histologic features of sarcoids in cats.

Feline sarcoids are often treated with surgery but incomplete excision is common, resulting in local tumour recurrence characterized by a markedly increased growth rate. Metastasis has not been reported. As with equine sarcoids, adjunctive radiation therapy using (90) Strontium plesiotherapy (Sr90) and immunotherapy have been reported to improve outcome in other papillomavirus-associated lesions in cats.

To the best of the authors’ knowledge, there are currently no reported statistics concerning the clinical behaviour of sarcoids in cats. Our objectives with this retrospective, multi-institutional study were to describe the clinical presentation and biological behaviour of sarcoids in cats and to determine the oncologic outcome following surgical resection.

2 METHODS

Medical records and a laboratory database were searched for the keywords of sarcoid and fibropapilloma in the histopathology report from six contributing institutions and a commercial laboratory from January 1, 2006 to December 31, 2017 to identify cats with histologically confirmed sarcoids. Cats that were not treated surgically or did not have >2 months follow-up information were excluded.

Medical records were reviewed and data were abstracted. Signalment and clinical presentation information included age, bodyweight, sex and neuter status, breed, presenting clinical signs, tumour location, presence of solitary or multiple tumours, tumour size (maximum dimension in cm) and known exposure to cattle (yes, possible, no). Information collected on preoperative diagnostic evaluation included complete blood count, serum biochemistry, preoperative tumour sampling (fine-needle aspirate, incisional biopsy, punch biopsy) and clinical staging (lymph node aspirates, head and neck imaging and thoracic imaging) test results. Surgical information included descriptions of lateral and deep surgical margins, method of closure (primary closure, random or axial pattern flap, second intention), intraoperative and postoperative complications, completeness of histologic excision (with complete histologic excision defined as a histologic tumour-free margin >0 mm), width of lateral and deep histologic margins and mitotic rate (per 10 high power fields [HPFs]). Details regarding adjunctive therapy (radiation therapy, chemotherapy, other) were also collected.

Oncologic outcomes examined included local tumour recurrence, regional or distant metastasis and survival. Time to local recurrence
(disease-free interval [DFI]) was defined as the interval between surgery and diagnosis of local recurrence. Treatment of local recurrence was recorded (none, revision surgery, chemotherapy, radiation therapy immunotherapy). If metastasis occurred, the site of metastasis was recorded. Time to metastasis (metastasis-free interval) was defined as the interval between surgery and diagnosis of metastatic disease. The status at the time of data abstraction was recorded with the date of last follow-up or death. Overall survival time (ST) was calculated from the date of surgery. The reason for death was recorded if cats died or were euthanized. Deaths were considered tumour-related if associated with treatment, local tumour recurrence or metastasis.

2.1 Statistical analysis

Continuous variables were tested for normality using skewness, kurtosis and Shapiro Wilk tests. If data were normally distributed, mean and SD were used for description. If data were non-normally distributed, median and range were used. Frequencies and percentages were used to describe categorical variables.

Kaplan Meier methodology was used to calculate the median DFI and median ST (MST) with 95% confidence interval (CI). Cats were censored in the DFI analysis if they did not develop local recurrence by the date of their last follow-up or death. Cats were censored in the survival analysis if they were lost to follow-up or alive at the last follow-up. Univariable cox proportional hazards regression was performed to assess for associations between DFI and ST. Variables assessed included mass size, mass location, mitotic rate, completeness of histologic excision, histologic tumour-free margin width and adjunctive treatments (chemotherapy, metronomic chemotherapy, radiation therapy, other treatments). Additionally, whether the sarcoid recurred locally was evaluated for association with ST.

Statistical analysis was performed using commercially available software (SAS version 9.4, SAS Institute Inc., Cary, North Carolina.). A P-value of <.05 was considered statistically significant for this analysis.

2.2 Cell line validation statement

Cell line validation was not conducted because cell lines were not used in this retrospective study.

3 RESULTS

3.1 Patient characteristics

Forty-two cats met the inclusion criteria. The median age was 9.0 years [range, 0.1-19.0 years] with a mean body weight of 4.8 kg (SD ± 1.5 kg). There were 25 neutered males (59.5%) and 17 spayed females (40.5%). Breeds included 32 domestic shorthair cats, 4 domestic longhair cats, 3 domestic medium hair cats and 1 each of Himalayan, Maine Coon mix and Ragdoll cats.

A mass was the presenting complaint in all cats, with sneezing observed in one case (2.4%). Twenty-nine sarcoids (69.0%) were located on the face (eight on the lip, six on the nasal planum, four on the eyelid, two on the pinna, one in the nasal cavity and eight on other locations on the head), five on the paw, three on the flank, two on the neck and three with an unknown location. Forty cats (95.2%) presented with a single mass. Two cats presented with separate masses located on the lip and nasal planum. The median maximum tumour dimension was 1.0 cm (range, 0.3-4.5 cm).

Six of the 42 cats (14.3%) had known exposure to cattle, four cats (9.5%) had possible exposure to cattle, 17 cats (40.5%) had no exposure to cattle and exposure to cattle was unknown in the remaining 15 cats (35.7%).

3.2 Initial staging

Fine-needle aspirates were performed in 11 cases; mesenchymal or spindle cells were noted in two cats and samples were non-diagnostic in the remaining nine cats. Incisional or punch biopsies were performed in eight cats; sarcoid or cutaneous fibropapilloma was diagnosed in four cats, one cat was diagnosed with suppurrative dermatitis and granulation tissue formation, and histopathology reports were not available for the other three cats.

Head and neck radiographs and CT scans were performed in two cases each: no bone involvement was reported in any cat. Thoracic radiographs were performed in six cats and a thoracic CT scan was performed in one cat; pulmonary metastasis was not evident in any cat. Lymph node status was not evaluated in any cat.

3.3 Surgery and histopathology

All cats were treated surgically. Descriptions of surgical margins were recorded in five cats; three sarcoids were resected with 1 cm lateral margins and full thickness of the lip or nasal planum for deep margins, and two sarcoids were excised with 0.5 cm lateral margins. The resultant defect was closed primarily in 33 cats, and the wound defect was closed with a labial advancement flap in three cats and an angularis oris axial pattern flap in one cat. The wound closure technique was not recorded in the remaining five cats. Postoperative complications occurred in five cats (11.9%) with wound dehiscence in each of these five cats. Dehiscence was associated with a surgical site infection and secondary trauma in one cat each.

Complete histologic excision was achieved in 18 cats and 21 cats had incomplete excision. Margin status was not reported in three cats. Median lateral and deep histologic margins were 2 mm (range, 0.6-10 mm) and 1.6 mm (range, 0.2-10 mm), respectively. The mitotic rate was available in 32 cats; the median mitotic rate was 2 per 10 HPFs (range, 0-29 per 10 HPFs).
3.4 | Adjuvant therapy

Five cats were treated with an adjuvant modality following incomplete histologic excision; no cats with complete histologic excision were treated in the postoperative setting. The adjuvant treatment protocols and outcomes for these five cats are summarized in Table 1.

3.5 | Local tumour recurrence and metastasis

Local tumour recurrence was diagnosed in 17 cats (40.5%). The median DFI was significantly decreased with incomplete histologic excision and adjuvant treatment with immunotherapy. There were no statistically significant associations between DFI and tumour size, tumour location, preoperative biopsy, histologic tumour-free margin width (lateral and deep) or mitotic rate. A summary of local recurrence rates and median DFI overall and for prognostic factors is presented in Table 2.

3.6 | Survival

At the time of data collection, 13 cats were still alive (median time of last follow-up 1332 days; range, 745-3618 days), five cats had died because of tumour-related reasons, 14 cats had died because of reasons unrelated to their sarcoid (median time of last follow-up

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### Table 1

<table>
<thead>
<tr>
<th>Cat</th>
<th>Radiation therapy</th>
<th>Chemotherapy</th>
<th>Immunotherapy</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>1</td>
<td>19 fractions of 3 Gy delivered Monday-to-Friday; total dose 57 Gy</td>
<td>—</td>
<td>—</td>
<td>• Local tumour recurrence at 356 d&lt;br&gt;• Local tumour recurrence treated with Sr90 plesiotherapy&lt;br&gt;• Alive and disease-free at 3573 d</td>
</tr>
<tr>
<td>2</td>
<td>Four fractions of 4 Gy delivered twice daily on two consecutive days; repeated 4 wk later; total dose 32 Gy</td>
<td>Toceranib (3.6 mg/kg PO Monday-Wednesday-Friday for 3 wk; dose reduced to 3.2 mg/kg PO Monday-Wednesday-Friday for 4 wk; then discontinued) and prednisolone (1.2 mg/kg PO q 24 h for 15 wk; dose reduced to 0.6 mg/kg PO q 24 h)</td>
<td>Interferon (dose and duration not recorded)</td>
<td>• Local tumour recurrence at 223 d&lt;br&gt;• Local tumour recurrence not treated&lt;br&gt;• Alive with local tumour recurrence at 1193 d</td>
</tr>
<tr>
<td>3</td>
<td>Strontium 90 plesiotherapy; six overlapping fields; total dose 120 Gy</td>
<td>—</td>
<td>—</td>
<td>• Local tumour recurrence at 279 d&lt;br&gt;• Local tumour recurrence treated with cytoreductive surgery and a second course of Sr90 plesiotherapy&lt;br&gt;• Second local failure and euthanized at 681 d because of local tumour recurrence</td>
</tr>
<tr>
<td>4</td>
<td>—</td>
<td>Alternating doxorubicin (1 mg/m²) and carboplatin (200 mg/m²) IV q 3 wk; two doses each for four total doses</td>
<td>—</td>
<td>• Local tumour recurrence at 250 d&lt;br&gt;• Local tumour recurrence treated with cytoreductive surgery&lt;br&gt;• Euthanized at 264 d because of local tumour progression</td>
</tr>
<tr>
<td>5</td>
<td>—</td>
<td>—</td>
<td>Imiquimod 5% cream (topical q 48 h)</td>
<td>• Local tumour recurrence and possible nodal metastasis at 83 d&lt;br&gt;• Local tumour recurrence not treated&lt;br&gt;• Euthanasia at 83 d because of local tumour recurrence and possible nodal metastasis</td>
</tr>
</tbody>
</table>
Abbreviations: CI, confidence interval; DFI, disease-free interval.

Second local recurrence after 232 days, treated with surgery and adjuvant immunotherapy. Third local recurrence after 173 days, not treated.

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

Second local recurrence after 249 days, treated with Sr90 plesiotherapy.

Abbreviations: CI, confidence interval; DFI, disease-free interval.

Local tumour recurrence rates and DFI overall and for statistically significant factors for median DFI

<table>
<thead>
<tr>
<th>Local tumour recurrence rate</th>
<th>DFI</th>
<th>Statistical results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>40.5% (17/42)</td>
<td>Not reached</td>
</tr>
<tr>
<td>Complete histologic excision</td>
<td>11.1% (2/18)</td>
<td>Not reached</td>
</tr>
<tr>
<td>Incomplete histologic excision</td>
<td>66.7% (14/21)</td>
<td>153 d</td>
</tr>
<tr>
<td>Immunotherapy treatment</td>
<td>100% (2/2)</td>
<td>153 d</td>
</tr>
<tr>
<td>No immunotherapy treatment</td>
<td>37.5% (15/40)</td>
<td>Not reached</td>
</tr>
</tbody>
</table>

Postoperatively was treated with surgery alone and had no further evidence of recurrent disease after 1276 days. One cat was lost to follow-up at 838 days with a third episode of local tumour recurrence following surgical treatment of two previous local recurrences at 182 and 578 days postoperatively.

The overall MST was 1809 days (range, 826-2172 days). There was no significant difference in MST between cats with complete and incomplete histologic excision, cats treated or not treated with adjuvant immunotherapy, and cats with or without local tumour recurrence. There was a statistically significant difference (P = .01) in overall MST between treatment groups for cats with local tumour recurrence.

The overall MST for cats that did not develop local tumour recurrence was 1862 days (range, 764-2172 days). For cats with local tumour recurrence, the overall MSTs were 328 days (range, 83-846 days) and 1809 days for cats that had no treatment and cats that were treated with surgical revision only, respectively. The lower limit of the range for cats treated with repeat surgical resection was 1151 days and the upper limit could not be calculated. The MST for cats treated with surgical revision in combination with adjuvant modalities could not be calculated as there were too few cats with tumour-related deaths. Only one cat was treated with radiation therapy alone following local recurrence; this cat was still alive at the time of data collection, 3573 days following initial surgery. The overall 1- and 2-year survival rates were 92% and 74%, respectively, for cats that did not develop local tumour recurrence, 38% at both time intervals for cats with untreated local recurrence, 100% at both time intervals for cats with local tumour recurrence treated with surgical revision only, and 100% and 67%, respectively, for cats with local tumour recurrence treated with a combination of surgical revision and adjuvant modalities (Figure 3).

4 | DISCUSSION

Sarcoids are most commonly diagnosed in young to middle-aged domestic shorthair or domestic longhair cats. The signalment and clinical presentation of the cats described herein were largely consistent with previous reports of cats with sarcoids; however, a predilection for sarcoids in male cats was not observed in the present study. The majority of sarcoids occur on the face, especially rostral locations such as the lips or nasal planum.
Results of this study suggest that feline sarcoids, while sharing many histologic similarities with equine sarcoids, are also comparable with non-vaccine-associated soft tissue sarcomas in cats based on their similar biologic behaviour, with a high local recurrence rate following incomplete histologic excision and low metastatic risk.\(^1\)\(^6\)\(^7\) The local recurrence rate following surgical resection was 40.5% in the present study. This is comparable to the previously reported 38.9% and 42.6% local recurrence rates in cats with sarcoids and non-vaccine-associated soft tissue sarcomas, respectively.\(^6\)\(^7\) In our study, complete histologic excision was associated with a significantly lower local recurrence rate (11.1%) and longer DFI (not reached) compared with cats with incompletely excised sarcoids (66.7% and 153 days, respectively). Moreover, local tumour recurrence was the most common reason for disease-related death in cats with sarcoids, both in the present study and previously reported studies.\(^6\)\(^10\) In the present study, five (29.4%) of the cats with local tumour recurrence were euthanized because of their recurrent disease and these were the only cats that died because of disease-related reasons. Of note, all five cats had incomplete histologic excision at their initial surgery. The most important prognostic factor for local recurrence following surgical resection soft tissue sarcomas in cats is complete histologic excision.\(^1\)\(^8\) The difficulty in achieving complete histologic excision of feline sarcoids is their predilection for the head, especially rostrally, which can make wide surgical resection challenging and result in a suboptimal cosmetic outcome. However, initial wide surgical resection should be recommended because this provides the best opportunity for complete histologic excision and long-term tumour control. Although radiation therapy is often recommended for improving local tumour control following incomplete histologic excision of soft tissue sarcomas in both cats and dogs,\(^1\)\(^9\) three cats were treated with various forms and protocols of radiation therapy in the present study and all developed local tumour recurrence. The use of adjuvant immunotherapy was also not efficacious in preventing local tumour recurrence following incomplete histologic excision in the two cats in our study, despite its demonstrated efficacy in treating equine sarcomas.\(^1\)\(^3\) This finding emphasizes that the primary goal in treating cats with sarcoids should be wide surgical resection with complete histologic excision.

Further surgical resection is recommended for cats with either incomplete histologic excision or local recurrence. A statistically significant difference was noted between STs of cats following local tumour recurrence when separated out into treatment groups. Cats with untreated local recurrence had a significantly shorter MST (328 days) than cats with treated local tumour recurrence (1809 days). Furthermore, five (83.3%) cats treated with curative-intent surgical revision had no further local recurrence. Local tumour recurrence was successfully treated in one cat with Sr90 plesiotherapy. Sr90 plesiotherapy has been described as the sole treatment in one cat with a sarcoid; however, this cat had progressive disease.\(^2\)\(^0\)

Many of the limitations of our study were inherent to retrospective studies. There was limited information available regarding the initial surgical procedures, so surgical intent could not be evaluated in many cases. Therefore, we were unable to determine how surgical intent may have impacted the clinical outcome of cases in this study beyond histologic completeness of excision. The efficacy of adjuvant treatment modalities may have been affected by selection bias and the small number of cats in these groups. Postoperative staging exams and tests were not standardized and often not specifically described in the medical records. In many cases, cats presented to the referring veterinarian for different reasons and there was no specific reference to the sarcoid in the medical records. As a result, the incidence of local recurrence and metastasis may have been under-represented. A potential limitation is the definition of tumour-related death used in the present study, which was those associated with treatment of the sarcoid or as a result of local tumour recurrence or metastasis. The cause of death for five cats was unknown in the present study. While we cannot discount the possibility that some of these may have been

**FIGURE 3** Kaplan-Meier survival curve for cats with and without local tumour recurrence. The median survival time (MST) for cats that did not develop local tumour recurrence was 1862 days (range, 764-2172 days). For cats with local tumour recurrence, the MST for cats that had no treatment and cats that were treated with surgical revision only were 328 days (range, 83-846 days) and 1809 days, respectively [Colour figure can be viewed at wileyonlinelibrary.com]
tumour-related deaths, the likelihood of this is low as all tumour-related deaths in study reported herein were because of local tumour recurrence, and the owners and referring veterinarians of the five cats with an unknown cause of death all stated that there was no evidence of local tumour recurrence.

Based on the findings of our study, we recommend that cats with sarcoids be treated with wide surgical resection for the best opportunity to achieve complete histologic excision, local tumour control and a potential cure. For cats with incomplete histologic excision or local tumour recurrence, repeat surgical resection is recommended.

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CONFLICT OF INTEREST
The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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