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Evaluation of scar revision after inadequate primary excision of cutaneous mast cell tumors in 85 dogs (2000–2013)

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Abstract

Objective: To determine the frequency of residual tumor, and factors associated with local recurrence and disease progression in dogs with incompletely excised mast cell tumors (MCT) following scar revision surgery.

Study Design: Retrospective study.

Animals: Eighty-five dogs.

Methods: Medical records from January 2000 to April 2013 were reviewed. Dogs with scar revision surgery after incomplete primary MCT excision were included. Recorded were signalment; initial tumor size, location and grade; time interval between primary excision and scar revision surgery; presence of MCT in the resected scar; local recurrence, lymph node metastasis, systemic metastasis, and cause of death.

Results: Eighty six tumors in 85 dogs were studied. Residual MCT was found in 23 (27%) resected scars. Seven (8%) scars with residual MCT had incomplete or narrow margins. Follow-up was available for 68 dogs (69 tumors; median 403 days; range 4–2939). Local recurrence was reported in three (4%) dogs at 212, 555, and 993 days. Disease progressed in 10 dogs (14.5%) with regional or systemic metastasis at a median of 207 days (64–1583). Margin status and presence of MCT in the resected scar were not associated with local recurrence or disease progression. Lymph node metastasis ($p = .004$), locoregional recurrence ($p = .013$), and disease progression ($p = .001$) were significantly more likely in Grade III tumors.

Conclusion: Twenty-seven percent of resected scars contained residual MCT, but recurrence was uncommon after surgical revision.

Clinical significance: Clinicians should primarily consider tumor grade when estimating the likelihood of local recurrence and disease progression and determining the need for ancillary treatment of MCT after scar resection.

1 | INTRODUCTION

Primary surgical excision is considered the standard of care for cutaneous mast cell tumors in dogs. Surgical margins of 1–3 cm lateral and one fascial plane deep to the observable or palpable tumor are advocated for achieving histologic margins devoid of neoplastic cells.[1-3] Alternatively, lateral margins equivalent to the maximal diameter of the tumor have also been shown to achieve good local tumor control.[4] Local recurrence rates of 18%–38% are reported for incompletely excised tumors,[5-9] meaning that neoplastic cells were histologically evident at or within 1 mm of the cut tissue edges. By comparison, local recurrence for completely excised tumors occurred in 3%–11% of cases.[6,7,10,11]

Dogs with incompletely or narrowly excised MCT were reported to have a significantly shorter disease-free interval compared to those with complete histologic margins.[12] Local recurrence is a negative prognostic factor[5,13] and, although there is no uniform consensus, additional local treatment is commonly recommended if histologic margins are narrow or incomplete.[5]

There is no consensus on the definition of complete, narrow, or incomplete margins for canine cutaneous MCT. Current definitions for narrow or close margins vary from >1 mm to 9 mm.[3,9-11,14] Donnelly et al. aimed to establish the smallest width of histologic tumor-free margin associated with long-term local tumor control but found no relationship between margin width and local recurrence.[15] Local recurrence was not seen in low-grade tumors excised with histologic margins of ≤3 mm. However, two low-grade tumors excised with 4 mm and 20 mm histologic margins recurred. High-grade tumors were significantly more likely to recur compared to low-grade tumors, regardless of histologic margin width.[15] The local recurrence rate for incompletely excised Grade II MCT (neoplastic cells extending to the tissue edge) has been reported to be 23.3%, whereas local recurrence was not seen in Grade II MCT excised with 1 mm histologic margins.[9] Based on these results, additional local therapies "may not always be necessary" for all incompletely excised Grade II MCT.[9] Further investigation to determine which subset of this cohort of tumors would benefit from additional treatment was recommended.[9]

Primary re-excision or scar revision surgery has been advocated for incompletely or marginally excised cutaneous mast cell tumors in areas amenable to further surgery.[5] Dogs undergoing scar revision surgery were more likely to be alive at their final follow-up compared to those undergoing no local therapy following incompletely resected MCT.[5] At the authors' institution and elsewhere, scar revision surgery following incomplete or narrow tumor excision is standard of care for establishing complete local tumor control. Several risk factors have been reported to increase risk of local recurrence or disease progression and shorter survival including tumor grade, size, location, and surgical margins;[9,16-18] however, clear guidelines defining which tumors require scar revision surgery currently do not exist. The purpose of this retrospective study was to (1) determine the frequency with which residual neoplastic cells are present within resected scars of incomplete or narrowly excised cutaneous MCT and (2) identify factors associated with local recurrence or disease progression after scar revision surgery. We hypothesized that: (1) high grade or Grade III mast cell tumors would be more likely to have residual neoplastic cells in the scar than low-grade tumors; and (2) high grade or Grade III mast cell tumors would be more likely to have local recurrence or disease progression than low grade or Grade I tumors after primary re-excision.

2 | MATERIALS AND METHODS

Medical records of the Matthew J. Ryan Veterinary Hospital, University of Pennsylvania School of Veterinary Medicine were searched for dogs diagnosed with cutaneous mast cell tumor between January 2000 and April 2013. Dogs were included in the study if they had undergone incomplete or narrow surgical resection of a cutaneous MCT and subsequently underwent scar revision surgery at the Ryan Hospital with the intent of achieving histologically complete margins. Incomplete resection was based either on the initial biopsy report or on the specific referrals for incomplete or narrow tumor excision. Histologic margins from the initial surgery were deemed "incomplete" if tumor was at or within <1 mm of the specimen edges and "narrow" if neoplastic cells were present within ≤3 mm of the specimen edges.

Dogs were excluded if they had a planned incisional biopsy at the initial surgery; tumors located at a mucocutaneous junction; evidence of macroscopic disease at or within 2 cm of the surgery site at the time of scar revision; if the scar revision surgery involved amputation of an appendage (i.e., limb, digit, or tail); or if systemic metastases were documented at the time of the initial evaluation. Dogs treated with radiation therapy prior to scar revision surgery were excluded. Dogs that had concurrent or developed new mast cell tumors in other areas were included in the study. Metastases to regional lymph nodes associated with a de novo tumor at the time of referral presentation were not included as disease progression.

Data collected from medical records included breed, sex, weight, and age at the time of the first surgery.

Additional data gathered from the first surgery included: tumor location, size, histologic grade using the 3-tier Patnaik system,[16] histologic margins, mitotic index, and administration of perioperative chemotherapy. Tumor locations were divided into groups: trunk, proximal limb, distal limb, tail, and head/neck. Tumors distal to the stifle and elbow were grouped into "distal limb," whereas those proximal to these joints were grouped under "proximal limb." Tumors located in the axilla or inguinal region were categorized as "trunk."

Time interval in days was calculated between the initial tumor excision surgery and scar revision surgery. For scar revision procedures, data collected included the width of the surgical margins reported as the smallest dimension, locoregional lymphadenectomy, presence of metastasis at the time of scar revision, presence of neoplastic cells in resected scar or lymph node, tumor grade, mitotic index, and histologic margins. The width of surgical margins at the time of scar revision surgery was not standardized. Surgery was generally of curative intent, but margin width was decided by the individual surgeons based on anatomic location and tissues available for closure.

The submitted tissue samples underwent routine histologic processing. Tissues were fixed in 10% neutral buffered formalin, and the specimen edges and deep margin were inked. The specimens were trimmed using the cross-sectional method (i.e., halves and quarters).[19] The surgical revision site (scar) was bisected along its shortest axis and this center piece was cassetted. Each half of the tissue was then bisected through its long axis and each piece cassetted.[19] All tissues were embedded in paraplast and 5 μm sections were routinely stained with hematoxylin and eosin (HE). All sections were examined by board-certified veterinary pathologists. Margins were considered incomplete if neoplastic cells were present at the tissue edge or within <1 mm of the edge and narrow if neoplastic cells were present ≤3 mm from the tissue edge.[5] Lymph nodes were examined for the presence of neoplastic mast cells and special staining was performed if indicated as deemed by the board-certified veterinary pathologists.

Follow-up information regarding chemotherapy, radiation therapy, or subsequent surgery was recorded. Local recurrence was defined as macroscopic disease at the scar or within 2 cm of the original surgical site.[5] Time calculations to local recurrence or disease progression were performed in days with the scar revision surgery as day zero. Disease progression was defined as either regional metastasis (evidence of mast cell disease in the regional lymph node confirmed by biopsy or cytology) or as systemic metastasis (metastasis to the abdominal viscera or bone marrow). Follow-up information was collected from medical records at the Ryan Hospital.

Statistical analysis was performed using Stata Version 12.1 (StataCorp, College Station, TX). Several factors were investigated for association with local recurrence, regional and systemic metastasis including age, sex, weight, breed, tumor size, tumor location, tumor grade, time interval between primary excision and scar revision, presence of MCT in the resected scar, lymphadenectomy, and follow-up time. For the purpose of statistical analysis, the tumor grades reported for the primary tumor excision were used. Tumors that were recorded to be Grades I and II were categorized as Grade II, tumors that were recorded as Grades II and III were categorized as Grade III. Recurrences were grouped as local (within 2 cm of surgical scar), regional (regional lymph nodes metastasis), locoregional (within 2 cm of scar and/or regional lymph node metastasis), systemic (systemic metastasis), and any disease progression (local, regional and/or systemic disease). For categorical variables, a Fisher's exact test was used. A student's t-test was used for normally distributed continuous variables (age, weight, and tumor size) and the Mann–Whitney rank sum test was used for statistical analysis of all other non-normal continuous variables. A two-tailed value of $p \leq .05$ was considered statistically significant.

3 | RESULTS

A total of 85 dogs with 86 tumors met the inclusion criteria. Mean age ± SD at the time of initial tumor excision was 6.8 ± 2.6 years (range 1.3–12.8 years) and mean weight ± SD was 28.7 ± 10.3 kg (range 4.0–54.9 kg). Forty-three males and 42 females were included in this study of which four were sexually intact (two male, two female). Mixed breed dogs were most commonly presented ($n = 25$) followed by Labrador retrievers ($n = 16$), Golden retrievers ($n = 7$), Boxers ($n = 6$), German shepherds ($n = 4$), Pugs ($n = 4$), American Pitbull terriers ($n = 3$), American Staffordshire terrier, Bassett hound, Cocker spaniel, and German shorthair pointer (two each), and Beagle, Boston terrier, greater Swiss mountain dog, Rhodesian ridgeback, soft coated Wheaten terrier, Shih Tzu, Sharpei, standard Schnauzer, St. Bernard, toy poodle, Hungarian viszla, and Weimaraner (one each). Age, sex, and breed were not significantly associated with local, regional, locoregional, systemic, or any disease progression.

3.1 | Primary tumor excision

Tumors were most commonly located on the trunk (43%), followed by the distal limb (21%), proximal limb (20%), head and neck (15%), and the tail (1%). Tumor size

at the time of initial primary tumor excision was available for 64 tumors with a median size of 2 cm (0.5–8 cm). Tumor location and size were not significantly associated with local, regional, locoregional, systemic, or any tumor recurrence. Two tumors (2.3%) were classified as Grade I, 75 tumors (87.2%) were Grade II, and nine (10.5%) were Grade III. Primary tumor excision was performed at the referring primary veterinarian for 83 tumors and 3 tumors were initially excised at the Ryan Hospital. Mast cell tumor was present at one or more of the margins of the primary tumor excision in 75 cases. Margins for seven cases were within 1 mm of the cut edge and narrow in four cases (within 1–3 mm of the cut edge). Descriptions of the precise location of the tumor positive, incomplete, or narrow margins and the presence or absence of an uninvolved fascial plane were not available. The median time interval between the primary excision and scar revision surgery was 29 days (6–142 days). Reasons for delay in referral for scar revision surgery were not evident from the medical records. Time interval between primary excision and scar revision surgery was not significantly associated with local, regional, locoregional, or systemic

TABLE 1 Distribution of cases with neoplastic mast cells (MCT) present in the resected scar compared to those without MCT in the scar

	MCT in scar ($n = 23$)	No MCT in scar ($n = 63$)
Age (years)	7.3	6.6
Weight (kg)	29.7	28.4
Tumor location		
Head/Neck	4 (17%)	9 (14%)
Trunk	11 (48%)	26 (41%)
Prox. Limb	3 (13%)	14 (22%)
Dist. Limb	5 (22%)	13 (21%)
Tail	0	1 (2%)
Tumor grade	0 Grade 1	2 Grade 1
	21 Grade 2	54 Grade 2
	2 Grade 3	7 Grade 3
Histologic margins of primary excision	Tumor at margins: 21	Tumor at margins: 54
	Incomplete (<1 mm): 1	Incomplete (<1 mm): 6
	Narrow (<3 mm): 1	Narrow (<3 mm): 3
Histologic margins of the scar	16 Complete	63 Complete
	Six incomplete (≤1 mm)	
	One narrow (2 mm)	
Lymphadenectomy	3	11
LN metastasis	One confirmed	Four confirmed
	One questionable	One questionable
Chemotherapy	Four steroids alone Three vinblastine Two vinblastine/cytoxan One vinblastine/CCNU	Seven steroids alone Two vinblastine Two vinblastine/cytoxan One vinblastine/cytoxan/ CCNU One vinblastine/CCNU/palladia
Radiation	1	0
Local recurrence	Three local regrowth (993, 64, 555 d) One regrowth and LN metastasis One regional LN metastasis only (355)	One local regrowth (212 d) One regrowth and LN metastasis One regional LN metastasis only (83 d)
Disease progressions	0	One spleen (1583 d) One bone marrow (354 d) One abdominal LN (69d)[a,b] One abdominal LN, liver, spleen (97d)[a,c]

[a]No cytology to confirm MCT.
[b]Euthanized 103 days after scar revision surgery due to mastocytemia.
[c]Euthanized shortly after last visit 153 days after surgery.

disease progression. Eight dogs were treated with prednisone following primary excision. No other chemotherapy agents were administered between initial tumor excision and scar revision surgery. Forty-four dogs with Grade II tumors and all dogs with Grade III tumors had complete staging performed before scar revision surgery.

3.2 | Scar revision surgery

Surgical margin width for scar excision was available for 81 tumors. The median width was 2 cm (0.5–4 cm) with one facial plane deep where available. Sixty-three (73%) resected scars were free of neoplastic cells and 23 (27%) scars had residual MCT. Twenty-one (91%) of these cases had mast cell tumor present at the margins of the primary excision. One case had incomplete (<1 mm) and one case had narrow (<3 mm) primary excision margins. Three of 8 dogs that received prednisone after the primary excision had residual MCT. The presence of neoplastic cells within the resected scar was not significantly associated with local, regional, locoregional progression, systemic disease, or any disease. A histologic grade was available for all but 2 of these 23 scars. In 18 scars, the histologic grade was in agreement with the grade at the time of primary tumor excision (16 Grade II, 2 Grade III), whereas in three scars, the grades differed. All three of these tumors were determined to be Grade II at the primary tumor excision; however, two were diagnosed as low grade[20] and one was Grade I at the time of scar revision (Table 1).

Following scar revision surgery, complete margins were achieved in all but 7/86 (8%) tumors. Six tumors had margins of ≤1 mm and one had a margin of 2 mm. The incomplete or narrow margin was identified at the deep tissue edge in three (3/7) tumors, at the lateral margin in one (1/7) tumor and in both the deep and lateral margin in three (3/7) tumors. All seven tumors with incomplete margins were Grade II. One dog with an incompletely excised Grade II MCT on the distal limb underwent two additional surgeries, after which histologic margins remained narrow (<1 mm).

Regional lymphadenectomy was performed in 14 cases at the time of scar revision surgery. Metastatic mast cell disease was confirmed on biopsy in 5 of the 14 lymph nodes, three in dogs with Grade III and two in dogs with Grade II tumors. In two additional lymph nodes, metastasis could be neither definitively confirmed nor excluded.

Following scar revision surgery, 12 dogs were treated with prednisone as a single drug protocol; eight of these dogs also received prednisone prior to scar revision. Prednisone and vinblastine were administered in another 12 dogs and additional chemotherapy agents were administered in seven of these dogs: Cytoxan ($n = 4$), CCNU ($n = 2$), and a combination of cytoxan and CCNU ($n = 1$). Palladia was given to one dog in addition to prednisone, vinblastine, and CCNU. One dog underwent radiation therapy for a Grade II axillary tumor that had incomplete deep margins following scar revision.

3.3 | Follow-up

All dogs were discharged from the hospital following scar revision surgery. Follow-up was available for 68 dogs

TABLE 2 Details of 10 dogs with local recurrence and/or disease progression

Grade	Primary excision margins	Surgical re-excision margins	MCT in scar	Histologic margin	Local recurrence	LN metastasis	Systemic metastasis	MCT-related death
2	MCT at margin	2 cm	Yes	10 mm	555 d			Alive 1051 d
2	1 mm	2 cm	Yes	Deep margin dirty	993 d			
2	MCT at margin	1 cm	Yes	5 mm		64 d		Euthanized 100 d
2	MCT at margin	2 cm	No	N/A			1583 d[a]	Euthanized 1669 d
2	3 mm	4 cm	No	N/A		202 d	354 d[a]	Euthanized[c] 354 d
3	MCT at margin	NA	No	N/A			69 d[b]	Euthanized 103 d
3	MCT at margin	2 cm	No	N/A			97 d[b]	Euthanized [c]153d
3	MCT at margin	3 cm	No	N/A	212 d	212 d		
3	MCT at margin	0.5 cm	No	N/A		83 d		
3	3 mm	2 cm	Yes	10 mm		355 d		Alive 1496 d

Abbreviations: MCT, mast cell tumors; N/A: no mast cells in resected specimen.

[a]Metastatic mast cell disease confirmed on cytology.

[b]Abdominal ultrasound suspicious for metastatic mast cell disease.

[c]Discharged with intent to euthanize.

(69 tumors). The median follow-up time from scar revision surgery was 403 days (4–2939 days). MCT recurrence (local, regional and/or systemic) was seen in 10 dogs at a median of 207 days (64–1583 days) postoperatively (Table 2). None of the Grade I tumors had evidence of recurrence. Five Grade II tumors and five Grade III tumors had evidence of recurrence. Local recurrence alone (within 2 cm of the scar) was found in two dogs at 555 and 993 days following scar revision surgery; both were Grade II at the time of primary tumor excision. Regional lymph node metastasis was diagnosed in four cases, two Grade II cases at 64 and 202 days and in two Grade III cases at 83 and 355 days. One dog had both local recurrence and regional metastasis (locoregional) at 212 days. This dog had a Grade III tumor at primary excision, no evidence of MCT in the resected scar, but a metastatic lymph node was removed at the time of scar revision surgery. Systemic disease was definitively diagnosed on cytology in two cases (spleen and bone marrow) 354 and 1583 days after scar revision. Ultrasonographic findings were suggestive of systemic disease progression in two additional cases at 69 and 97 days post scar revision. Cytology was not performed on these two dogs but one of these dogs developed intra-abdominal lymphadenopathy, mastocytemia, and local recurrence at 69 days and was euthanized at 103 days. None of the dogs that developed systemic disease had evidence of metastases on full staging prior to scar resection. In total, three dogs were euthanized at their last visit for MCT-related reasons (100, 103, 1669 days) and two additional dogs were discharged with the intent to euthanize following their last visit (153, 354 days).

No statistically significant factors associated with local tumor recurrence or for systemic disease progression alone were identified. Grade III tumors were more likely to develop regional lymph node metastasis ($p = .004$), locoregional recurrence ($p = .013$) or any disease progression ($p = .001$) than Grade II tumors. Cases that underwent lymphadenectomy at the time of scar revision surgery were more likely to have disease progression ($p = .011$). Margin status and presence of MCT in the resected scar were not associated with recurrence or disease progression.

4 | DISCUSSION

Following incomplete or narrow primary tumor excision, 27% of resected scars had evidence of residual mast cell tumor. Local recurrence after scar revision was seen in only 3 of 69 cases (4%), with a median follow-up time of 403 days. These results differ from those described by Kry and Boston who reported local tumor recurrence in 13% of dogs after scar revision surgery and microscopic disease in 48% of resected scars.[5] Reported recurrence rates for incompletely excised cutaneous mast cell tumors range from 18% to 38%.[5-9] Additional local therapy for incompletely resected tumor such as scar revision surgery and radiation therapy significantly increased survival time compared those without additional local treatment in one study.[5] There was no association between presence of neoplastic cells in the scar and local recurrence, disease progression, or metastatic disease in either the present study or previous reports.[5,9] Tumors with incompletely resected scars did not develop local recurrence or metastatic disease. Margin status and the presence of MCT in the resected scar were not associated with either tumor recurrence or disease progression in the current study. These findings question the necessity for scar revision. However, a large randomized clinical trial (revision vs. no revision) is needed before a well-founded recommendation on scar revision can be made.

High-grade tumors were not statistically more likely to have residual MCT in their resected scar, so we reject our first hypothesis. However, tumor grade was the main factor associated with local recurrence and disease progression. High-grade MCT were more likely to have locoregional recurrence and disease progression than low-grade tumors, substantiating our second hypothesis. The main risk factor for disease recurrence after primary mast cell tumor excision in two previous studies was microscopic disease at the surgical margins.[6,12] Following incomplete primary excision of Grade II MCT, 11%–23.3% recurred locally.[6-8,10,11] In the current study, none of the cases with incomplete scar resection margins developed local recurrence. Locoregional recurrence and disease progression were associated with high tumor grade. High-grade tumors were more likely to recur locally after primary excision with incomplete or narrow margins[7] or complete margins[15] in two previous studies.

Currently, no clear consensus exists in the literature on the definition of a histologically complete margin for canine mast cell tumor. A wide range of histological margin widths are reported as clean or complete margins, ranging from the mere "absence of tumor cells in the submitted surgical margins,"[6] to >1 mm,[9,13] and up to >10 mm[21] from the cut edge. Schultheiss et al. reported that for every 1 mm increase in the deep margin, the odds for the patient not to develop metastasis or local recurrence increased by 1.46 ($p = .024$) and metastases were identified only in cases with lateral margins <10 mm and deep margins <4 mm.[22] It has been suggested that deep surgical margins should not be planned as a specific measurements but rather as the presence of an anatomic barrier such as a fascial plane between the tissue edge and neoplastic cells.[23]

The presence of a fascial barrier was not always specifically stated in the pathology reports and therefore could not be used to assess deep margins. Of the 23 scars with residual MCT in this study, quantitative histologic margins were reported in only 2, and in the remaining scars the margins were stated to be complete or incomplete based on the opinions of the pathologists. The effect of specific margin widths on the risk of local recurrence or disease progression could therefore not be evaluated.

Tumor grade was the main factor significantly associated with local recurrence and disease progression, with Grade III tumors significantly more likely to have any disease progression. This is in concordance with previous reports where Grade III or high-grade tumors were at a higher risk of local recurrence than low-grade tumors.[13,15,16,18,23] For high-grade tumors the width of histologically tumor-free margins was not significantly associated with recurrence.[15,24] In this study, 56% of the nine Grade III tumors developed local recurrence, systemic disease progression, or both, despite scar revision surgery with clean margins. Grade II tumors represent a management challenge as their biological behavior is often unpredictable. Adjuvant therapy has been recommended for incompletely excised Grade II MCT in order to achieve local tumor control and decrease the risk of tumor-related death.[6,25] The reported local recurrence and metastatic rates for incompletely excised grade 2 MCT is 23.3% and 21%, respectively.[9] To overcome this challenge, Kiupel et al. proposed a two-tiered grading system with the intent to improve predictions of biologic behavior.[20] In a study comparing the two grading systems, 85.6% of Grade II tumors (Patnaik) were defined as low grade according to the Kiupel system with a 94% 1-year survival probability. The remaining 14.4% were defined as high grade and had a 46% 1-year survival probability.[26]

The 86 tumors in this study were graded based on the Patnaik 3-tier system with the majority of cases being categorized as Grade II; mitotic index and other biologic markers were not always stated in the histopathology reports so further information regarding biologic characterization of these tumors was not available. This represents a limitation of this retrospective study. The three-tiered system could have influenced our results and may account for the lack of significant difference in local recurrence and systemic disease progression between Grade II and III tumors in this study.

Additional limitations of this study include the retrospective nature, the heterogeneous sample population, and the lack of complete referral and follow-up information for all cases. Grading of tumors was not performed by a single veterinary pathologist and therefore variations in grade may have occurred and affected the results of this study. Interobserver agreement on MCT grades has been reported to be low based on a three-tier system with only 63% agreement on the diagnosis of Grade I and II MCT and 74% agreement on the diagnosis of Grade III tumors.[20] In a group of 10 veterinary pathologists, agreement of histologic grade among all pathologists was seen in less than 7% of mast cell tumors.[27] Over the 13 years during which these cases were retrospectively collected, several advances have been made in the histopathologic interpretation of mast cell tumors and this represents a limitation of this study. In addition to the histopathologic interpretation, samples were prepared by cross sectioning rather than parallel slicing (bread-loafing) or tangential sections (orange-peel) techniques.[19,28] The process of evaluating cross sections is inherently flawed by the fact that a very limited portion of margin tissue is evaluated and the assumption that the mass expands symmetrically in the sample.[19] This technique may lead to a significant number of false negative diagnoses, meaning that tumor cells present at the margins or within the resected scar may be missed and margins erroneously categorized as clean or complete. Margin measurements were also not available for all samples.

Distinguishing normal mast cells, potentially recruited to the surgical site because of inflammation, from neoplastic mast cells can be difficult.[6] In this study, the histopathology reports for the resected scars containing residual disease clearly stated "mast cell tumor" in all but one case where the term "neoplastic mast cells" was used. The criteria used by individual pathologists to make the distinction between neoplastic and inflammation-associated mast cells were not clear, given the retrospective nature of the study. However, given the definitive nature of the pathology reports, we chose to use this terminology.

The intent of the primary tumor excision (curative vs. excisional biopsy) was not clear from the available referral records. The vast majority of primary mast cell tumor excisions (96.5%) were performed at local veterinary practices. For comparison, soft tissue sarcoma excisions in primary care practices were described as "marginal" (around the tumor pseudocapsule) in 41% of cases and "local" (<3 cm margin of normal tissue) in 33.4%. "Wide" or "radical" resections were only performed in 9% of cases.[29]

The effects of different chemotherapy protocols on local recurrence or disease progression could not be determined with this study due to the variable, nonstandardized protocols and follow-up available. The frequency of lymph node and systemic metastasis may have been influenced by the administration of chemotherapy in this study, although a previous report found that chemotherapy did not improve survival or local disease control.[5] Further studies are needed to assess the benefit of chemotherapy following scar revision surgery for incompletely excised cutaneous MCTs.

Lymphadenectomy of regional lymph nodes has been advocated to achieve complete locoregional tumor control but draining lymph nodes are not always correctly identified. Sentinel lymph node mapping showed that 42% of draining lymph nodes differed from the anatomic regional node.[30] In the current study, lymphadenectomy was performed based on anatomic location of the primary surgery site (scar). Metastatic MCT was confirmed in 5 of 14 nodes (36%) and was possible in another 2 nodes. Removal of lymph nodes based on anatomic location may have influenced our results so that regional lymph node metastasis may have already been present at the time of scar revision surgery. In this study, lymphadenectomy was performed in only 16% of cases. Cases that did not undergo lymph node removal at the time of scar revision surgery were significantly less likely to have any disease recurrence. It is possible that the surgeons' selection of cases from which to remove lymph nodes may have contributed to selection bias in these results.

Local recurrence was seen in 4% (3/69) of cases and any disease progression was found in only 14% (10/69) of cases after resection of incompletely excised cutaneous mast cell tumors. Similar to previous reports, tumor grade was the most significant factor associated with local recurrence or disease progression. Neither the presence of residual neoplastic disease in the resected scar nor incompletely resected scars were significantly associated with recurrence or disease progression.

AUTHOR CONTRIBUTION

Georga T. Karbe: Data collection, data analysis, manuscript writing; Elizabeth Davis: Data collection; Jeffrey J. Runge: Study design, data collection, manuscript writing; Dorothy C. Brown: Statistical analysis; David E. Holt: Study concept and design, manuscript writing, and review.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest related to this report.

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