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Summary of **'Treatment outcomes and prognostic factors of feline splenic mast cell tumours: A multi-institutional retrospective study of 64 cases - B. J. Evans, D. O'Brien, S. D. Allstadt, T. P. Gregor, K. U. Sorenmo.**

Abstract

Mast cell tumours (MCTs) represent a frequent neoplastic condition affecting the feline spleen; however, information regarding therapeutic outcomes for cats diagnosed with this disease remains limited. This retrospective, multi-institutional investigation evaluated treatment responses and survival outcomes in sixty-four cats diagnosed with splenic mast cell tumours. Cats were assigned to one of four treatment categories: splenectomy alone (group A, n = 20), splenectomy combined with chemotherapy (group B, n = 20), chemotherapy as the sole treatment modality (group C, n = 15), or supportive medical management without cytotoxic therapy (group D, n = 9).

Median tumour-specific survival (MTSS) for groups A, B, C, and D was 856, 853, 244, and 365 days, respectively. Statistical analysis did not identify significant survival differences when all four treatment groups were compared directly. In contrast, when cats undergoing splenectomy (groups A and B) were evaluated collectively and compared with cats managed without splenectomy (groups C and D), median tumour-specific survival was significantly longer in the splenectomy cohort (856 days versus 342 days; p = 0.008). None of the evaluated prognostic variables demonstrated a statistically significant association with survival time.

These findings indicate that splenectomy, with or without adjunctive chemotherapy, confers a significant survival advantage for cats with splenic mast cell tumours. The contribution of chemotherapy to outcome remains uncertain.

Keywords

feline, mast cell tumour, mastocytosis, spleen, splenic mast cell tumour

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1 | INTRODUCTION

Mast cell tumour (MCT) is the third most frequently diagnosed neoplasm in cats, surpassed only by lymphoid malignancies and mammary carcinoma.[1] In this species, mast cell neoplasia is typically categorised based on the primary site of involvement into cutaneous, splenic, and intestinal forms, although concurrent involvement of multiple organ systems may occur.[2] Among splenic disorders in cats, mast cell neoplasia represents one of the most

commonly identified tumour types, accounting for approximately fifteen to twenty-seven percent of all splenic diseases.[3,4]

Feline splenic mast cell tumours predominantly affect older animals, with reported mean ages ranging from nine to thirteen years, and no consistent breed or sex predisposition has been documented.[1,2,5–12] Anaemia is frequently observed, with reported prevalence ranging from fourteen to seventy percent of affected cats.[6,10,11] Circulating mast cells are also commonly identified, with mastocytaemia reported in thirty-seven to one hundred percent of cases.[5–7] Notably, resolution of circulating mast cells following splenectomy has been documented months after surgical intervention in individual case reports.[5–7] When mast cells are not readily apparent on routine peripheral blood smears, buffy coat evaluation is recommended to enhance diagnostic sensitivity.[11]

Coagulation abnormalities have been identified in cats with splenic mast cell tumours, with one case series reporting abnormal coagulation profiles in ninety percent of cats assessed prior to surgery (Feinmehl R, personal communication, 20 September 2016).[14] Additionally, up to one-third of affected cats may develop abdominal or pleural effusions that are enriched with eosinophils and mast cells.[1,10]

Previous investigations have suggested that several clinical and laboratory variables may negatively influence prognosis in cats with splenic mast cell tumours undergoing splenectomy, including anorexia, weight loss, anaemia, abdominal lymph node metastasis, mastocytaemia, and peri-operative administration of blood products.[2,10,11] Sabattini et al. further reported improved outcomes in cats with disease confined to the spleen compared with cats exhibiting involvement of additional organs.[12] However, published prognostic factors have been inconsistent between studies, and prior investigations have largely focused exclusively on cats treated surgically.[2,10,11,14]

Despite the absence of standardised treatment protocols, splenectomy is generally regarded as the treatment of choice for feline splenic mast cell tumours, including in cats with evidence of systemic disease. Reported median survival times for cats treated with splenectomy alone range from eleven to nineteen months.[6,10,11,14] The effectiveness of adjuvant chemotherapy or corticosteroid therapy remains poorly defined. One study identified no significant survival difference between cats receiving prednisolone following splenectomy and those managed with splenectomy alone or splenectomy combined with supportive care.[14] Another investigation observed improved outcomes in cats that responded to chemotherapy; however, no overall survival advantage was demonstrated for cats receiving adjuvant chemotherapy compared with those that did not.[10] Cytotoxic agents and targeted therapies, including vinblastine, lomustine, chlorambucil, corticosteroids, and tyrosine kinase inhibitors, are frequently administered to cats with systemic involvement, although their efficacy has not been clearly established.[10,12,13]

Although splenic mast cell tumours represent a common splenic disorder in cats, the overall prevalence remains low, and existing literature consists largely of isolated case reports and small case series.[1–9] A larger retrospective dataset has been presented previously in abstract form but was never fully published.[14] More recently, a case series evaluating thirty-six cats undergoing splenectomy was reported; however, because all cats received surgical treatment, the independent effects of surgery and chemotherapy could not be determined.[10] The primary objective of the present study was therefore to assess the impact of different treatment modalities on survival time and to identify prognostic factors in cats undergoing splenectomy and/or receiving chemotherapy for splenic mast cell tumours.

2 | MATERIALS AND METHODS

Medical records were retrospectively reviewed for client-owned cats diagnosed with splenic mast cell tumours that were evaluated for diagnosis and treatment at three academic veterinary institutions: the Matthew J. Ryan Veterinary Hospital of the University of Pennsylvania, the University of Tennessee Veterinary Medical Center, and the William R. Pritchard Veterinary Medical Teaching Hospital at the University of California–Davis. Cases were identified from electronic medical record databases spanning January 2000 through December 2013. Database searches were conducted using the following terms: splenic mast cell tumour, splenic mastocytosis, mastocytosis, spleen AND mast cell, and mastocytemia.

Cats were considered eligible for inclusion if a diagnosis of splenic mast cell tumour had been established either by histopathologic examination of splenic tissue following splenectomy or by definitive cytologic assessment. Cytologic diagnoses were required to be made by a board-certified clinical pathologist and were based on identification of clusters or aggregates of mast cells. Cats with concurrent cutaneous mast cell tumours were classified as having primary splenic mast cell disease provided that no regional lymph node involvement associated with the cutaneous lesion was documented. Cats with involvement of additional visceral organs were classified as having primary splenic mast cell tumours with metastatic spread.

Cases were excluded if cats were euthanised at initial presentation without receiving treatment or if follow-up information could not be obtained. Cats that died or were euthanised during the immediate peri-operative period prior to hospital discharge were also excluded from analysis.

For each included case, the following data were extracted from the medical record: age, breed, sex, neuter status, body weight, date of initial diagnosis, and presenting clinical signs, including vomiting, anorexia, weight loss, and lethargy. Physical examination findings such as palpable splenomegaly and the presence of concurrent cutaneous mast cell tumours were recorded. Information obtained from clinical staging was documented, including the

presence of anaemia, eosinophilia, mastocytaemia identified on complete blood count (CBC) and/or buffy coat analysis, coagulation abnormalities, and evidence of involvement of other organs based on ultrasonography, cytology, or histopathology.

Treatment-related variables were also recorded, including the date and type of therapy administered, specifically surgery, chemotherapy, supportive care, or combinations thereof. When mastocytaemia was present, its degree was subjectively graded by the reviewing clinical pathologist as mild, moderate, or marked, based on blood smear and buffy coat evaluation; no objective quantification criteria were available for this assessment. Resolution of mastocytaemia was defined strictly as the complete absence of circulating mast cells on follow-up blood smears and/or buffy coat analysis, when performed. Cases with partial improvement were not recorded as responders.

For cats with positive buffy coat analyses, follow-up buffy coat results were compared with pre-treatment findings to assess response. For cats in which mastocytaemia was identified on CBC, follow-up CBCs with or without concurrent buffy coat analysis were compared to baseline results. Only complete resolution of mastocytaemia was classified as a treatment response.

Response of concurrent cutaneous mast cell tumours was evaluated based on physical examination and visual inspection, as documented by the treating veterinarian. Responses were categorised as complete resolution, partial response, or stable disease according to the medical record description.

For analytical purposes, chemotherapy protocols were categorised into the following groups: corticosteroids alone; vinblastine; alkylating agents, defined as chlorambucil or lomustine; tyrosine kinase inhibitors, including imatinib, toceranib, or masitinib; and combination chemotherapy, defined as any of the aforementioned agents administered concurrently with corticosteroids.

Cats were assigned to one of four treatment groups: splenectomy alone (group A); splenectomy with adjuvant chemotherapy (group B); chemotherapy without splenectomy (group C); or supportive care only (group D). Cats receiving corticosteroids were included within the chemotherapy groups. Supportive care was defined as treatment with histamine H1 or H2 receptor antagonists and/or proton pump inhibitors in the absence of corticosteroid therapy.

When follow-up information was incomplete or unavailable in the medical record, additional data were obtained through telephone communication with referring veterinarians and/or cat owners.

2.1 | Statistical methods

Continuous non-survival variables were summarised using means with standard deviations, while categorical variables were expressed as frequencies and percentages. The primary outcome measure was tumour-specific survival (TSS), defined as the interval from the date of initial cytologic or histologic diagnosis to the date of death. Median tumour-specific survival (MTSS) was calculated using Kaplan–Meier survival analysis.

Cats that were alive at the time of last follow-up, lost to follow-up, or that died from causes unrelated to mast cell disease were censored at the corresponding time point. In cases where the cause of death was unknown, death was attributed to mast cell disease for the purposes of analysis. Kaplan–Meier curves were generated to estimate the proportion of cats surviving or dying from mast cell disease over time.

Comparisons of tumour-specific survival between treatment groups (groups A, B, C, and D, as well as combined splenectomy groups A/B versus non-splenectomy groups C/D) and between categories of potential prognostic variables were performed using the log-rank test. Evaluated prognostic variables included body weight, weight loss, anorexia, age, anaemia, mastocytaemia, and hepatic or lymph node metastasis.

Chi-square analysis was used to compare the distribution of previously reported and potential prognostic factors between cats that underwent splenectomy (groups A and B) and those that did not (groups C and D). Statistical significance was defined as a P value less than 0.05. All statistical analyses were conducted using SigmaPlot statistical software for Windows, version 12.0 (Systat Software, Inc.).

3 | RESULTS

3.1 | Patient population

Sixty-four cats satisfied the inclusion criteria for this study. Of these, twenty-three cases originated from the University of California–Davis, twenty-nine from the University of Pennsylvania, and twelve from the University of Tennessee. The median age at diagnosis was thirteen years, with a range spanning from four to twenty-one years. Median body weight was 4.6 kilograms, with recorded weights ranging from 2.3 to 8.8 kilograms.

Thirty-one cats (forty-eight percent) were spayed females, and thirty-three cats (fifty-two percent) were castrated males. Domestic short-haired cats comprised the majority of the study population (forty-seven cats). Additional breeds included six domestic long-haired cats, two Ragdolls, two Siamese cats, and one each of Burmese, Devon Rex, domestic medium-haired, Maine Coon, Norwegian Forest Cat, Ocicat, and Persian.

3.2 | Clinical signs

Clinical signs were documented in fifty-nine cats (ninety-two percent). The most frequently reported presenting complaint was weight loss, observed in thirty-six cats (fifty-six percent), followed by anorexia in thirty-one cats (forty-eight percent), vomiting in twenty-nine cats (forty-five percent), and lethargy in twenty-seven cats (forty-two percent).

Palpable splenomegaly was identified on physical examination in twenty-eight cats (forty-four percent). Concurrent cutaneous mast cell tumours were recorded in nineteen cats (thirty percent). Detailed information regarding the number and anatomic distribution of cutaneous lesions was available for twelve of these cats. Three cats had a single cutaneous mast cell tumour, located beneath the right eye, within the left inguinal region, or on the ventral abdomen. Three cats were noted to have three concurrent cutaneous tumours, while six cats had multiple (greater than four) or disseminated cutaneous lesions. Among cats with disseminated disease, two exhibited raised ulcerated nodules and one displayed small scabbed papules. For the remaining cats with cutaneous involvement, lesion characteristics were not described in the medical record.

3.3 | Clinical staging

Blood work was unavailable for one cat. Anaemia, defined as a haematocrit below the institutional reference interval, was identified in thirty of the sixty-three cats evaluated (forty-seven percent). Eosinophilia was present in six of sixty-three cats (ten percent). Mastocytaemia was detected in twenty-two of sixty-three cats (thirty-five percent) based on evaluation of peripheral blood smears and/or buffy coat preparations.

Thirty-one cats underwent buffy coat analysis, of which sixteen were mastocytaemic. Among mastocytaemic cats, the degree of mastocytaemia was classified as mild in fifteen cats (sixty-eight percent) and moderate in seven cats (thirty-two percent). Marked mastocytaemia was not documented in this cohort.

Coagulation profiles were available for fourteen cats, with abnormalities identified in four of these cases (twenty-nine percent).

Abdominal ultrasonography findings were recorded for forty-nine cats. The remaining fifteen cats either underwent surgery based on findings from abdominal palpation alone or had no documented ultrasonographic report. Splenomegaly was identified ultrasonographically in twenty-six of forty-nine cats. Four cats had spleens of normal size, and one cat exhibited mild splenic thickening. Splenic size was not specified in the medical records of eighteen cats.

Cytologic or histologic evaluation of the liver was performed in fifty-two cats, of which twenty-seven (fifty-two percent) demonstrated evidence of mast cell tumour metastasis.



Abdominal lymph node involvement was identified in twenty-one of fifty-two cats (forty percent) assessed by ultrasonography or laparotomy. The remaining thirty-one cats had lymph nodes described as ultrasonographically or grossly normal, and these nodes were not sampled.

Intestinal involvement was documented in three cats. Two cats underwent splenectomy and had incisional biopsies of the intestines confirming metastatic mast cell tumour. One cat did not undergo splenectomy and was diagnosed with intestinal mast cell tumour based on fine-needle aspiration of a thickened jejunal segment.

3.4 | Treatment groups

Treatment group allocation resulted in twenty cats each in groups A (splenectomy alone) and B (splenectomy with chemotherapy), fifteen cats in group C (chemotherapy alone), and nine cats in group D (supportive care).

Among cats receiving chemotherapy, thirteen were treated with corticosteroids alone, ten received an alkylating agent, four were administered a tyrosine kinase inhibitor, and eight received combination chemotherapy consisting of vinblastine and/or an alkylating agent combined with corticosteroids.

Within group B, eight cats received corticosteroids alone, five received an alkylating agent alone, two received a tyrosine kinase inhibitor alone, and five were treated with combination chemotherapy. Within group C, five cats received corticosteroids alone, five received an alkylating agent alone, two received a tyrosine kinase inhibitor alone, and three received combination chemotherapy.

Comparative analysis of previously reported and potential prognostic variables between cats undergoing splenectomy (groups A and B) and those managed without splenectomy (groups C and D) demonstrated no statistically significant differences in distribution between these cohorts.

3.5 | Response to treatment

Among nineteen cats with concurrent cutaneous mast cell tumours, documented regression of skin lesions occurred in four cases. Three cats achieved complete resolution of cutaneous disease, while one exhibited a partial response. Two of the cats with complete resolution underwent splenectomy without adjuvant chemotherapy, and one cat received adjuvant lomustine. The interval to cutaneous tumour remission could not be determined from available records.

Of the twenty-two cats with mastocytaemia, ten demonstrated complete resolution of circulating mast cells following treatment. Time to complete remission of mastocytaemia ranged from twenty-nine to one hundred and eighty-nine days, with a median of fifty-eight days. Among seven cats in group B achieving mastocytaemia remission, three received corticosteroids alone and four received combination therapy, consisting of chlorambucil or lomustine combined with prednisolone. Two cats in group A also experienced complete resolution of mastocytaemia. One cat in group D demonstrated apparent resolution based on comparison of pre- and post-treatment complete blood counts.

3.6 | Survival analysis

Median tumour-specific survival for the entire study population was 647 days, with survival times ranging from three to 2,113 days. Twenty-seven cats were censored from survival analysis. Seven cats were alive at the conclusion of data collection, with a median follow-up duration of 703 days (range: 485–1,432 days). Nineteen cats died from causes unrelated to mast cell disease, with a median follow-up of 339 days (range: 12–1,180 days). One cat was lost to follow-up six days after splenectomy.

Among cats that died from non-tumour-related causes, thirteen died or were euthanised due to other malignancies, including lymphoma (five cats), pulmonary neoplasia (three cats), carcinomatosis (two cats), squamous cell carcinoma (two cats), and a primary bone tumour (one cat). Two cats died from progressive renal failure, while others succumbed to severe pancreatitis, congestive heart failure, cholangitis, or progressive pulmonary disease.

Median tumour-specific survival times for treatment groups A, B, C, and D were 856 days (range: 3–1,647 days), 853 days (range: 54–2,113 days), 244 days (range: 5–1,096 days), and 365 days (range: 7–1,155 days), respectively. Direct pairwise comparisons among the four treatment groups did not identify statistically significant differences in survival.

When cats that underwent splenectomy (groups A and B) were compared with cats that did not (groups C and D), median tumour-specific survival was significantly longer in the splenectomy cohort at 856 days, compared with 342 days for cats managed without splenectomy ($P = 0.008$). At 1,674 days, twenty-five percent of cats in the splenectomy group remained alive, compared with 780 days for the non-splenectomy group.

Univariate analysis of potential prognostic variables, including body weight, weight loss, anorexia, age, anaemia, mastocytaemia, and hepatic or lymph node metastasis, did not identify any variable that significantly influenced tumour-specific survival. Analysis of these variables within combined treatment groups (splenectomy versus non-splenectomy) similarly failed to demonstrate significant associations with survival outcome.

4 | DISCUSSION

To the authors' knowledge, this investigation represents the first study to examine the impact of chemotherapy and supportive medical management in cats with splenic mast cell tumours both in the presence and absence of surgical intervention. Within this cohort, cats that underwent splenectomy as part of their treatment experienced significantly prolonged median tumour-specific survival compared with cats managed without surgery. Survival outcomes for cats treated surgically were favourable, with median survival exceeding two years. In contrast, the addition of chemotherapy did not result in further survival prolongation, leaving the therapeutic value of chemotherapy in this disease uncertain. These findings are consistent with previously published data evaluating cats undergoing splenectomy for splenic mast cell tumours.[10]

In the present study, twenty-two cats received adjuvant chemotherapy following splenectomy, and survival did not differ significantly between these cats and those treated surgically without chemotherapy. Similarly, earlier work by Rassnick et al. described six cats that received chemotherapy for concurrent cutaneous mast cell tumours following splenectomy for splenic disease, none of which demonstrated a measurable clinical benefit.[13] Nevertheless, it is noteworthy that the majority of cats in the current cohort—approximately seventy percent—died as a consequence of tumour-related disease. This observation suggests that splenic mast cell tumours may represent a biologically aggressive condition and that systemic therapy could still have a role in selected cases, despite the lack of demonstrated benefit in this retrospective analysis.

Consistent with previous reports, splenic mast cell tumours were primarily diagnosed in older cats, with a median age of thirteen years and no apparent breed or sex predisposition.[1,2,5–12] The predominance of domestic breeds and equal sex distribution observed in this study aligns with earlier literature. Most cats presented with vague, non-specific gastrointestinal signs, reinforcing prior observations that clinical manifestations of splenic mast cell disease are often subtle and nonspecific.[1,2,6,10]

Historically, several variables—including anorexia, weight loss, anaemia, abdominal lymph node metastasis, mastocytaemia, and peri-operative blood product administration—have been reported as negative prognostic indicators in cats undergoing splenectomy for splenic mast cell tumours.[2,8–10,14] In contrast, the present study did not confirm these associations. Although anaemic cats exhibited numerically shorter tumour-specific survival than non-anaemic cats, this difference did not reach statistical significance. The absence of a demonstrable effect may reflect limited sample size. These findings are consistent with more recent work that also failed to identify anaemia as a negative prognostic factor.[10] It is important to note that several historically cited prognostic variables originate from unpublished data, which may contribute to inconsistencies among studies.[14]

Sabattini et al. reported improved outcomes in cats with disease confined to the spleen compared with those exhibiting multi-organ involvement.[12] However, that study included follow-up data for only a small number of cats, and the impact of specific organ involvement on survival was not analysed in detail. In the current study, neither mastocytaemia nor hepatic or lymph node metastasis was associated with reduced survival, supporting the conclusion that cats with systemic disease can still derive substantial benefit from splenectomy.

Reported prevalence of mastocytaemia in cats with splenic mast cell tumours ranges widely from thirty-seven to one hundred percent.[5–9] In the present cohort, mastocytaemia was identified in thirty percent of cats. Because buffy coat analysis was performed in fewer than half of the cats, the true prevalence of mastocytaemia may have been underestimated. Previous studies have demonstrated that buffy coat examination is more sensitive than routine blood smear evaluation for detection of circulating mast cells.[11] Persistence of mast cells in buffy coat preparations despite apparent resolution on peripheral blood smears has also been documented, highlighting the importance of buffy coat analysis in both diagnosis and monitoring.[11]

Resolution of mastocytaemia and cutaneous mast cell lesions following splenectomy has been reported previously.[5–7] In the current study, a high proportion of cats receiving splenectomy with chemotherapy achieved remission of mastocytaemia, while fewer cats undergoing splenectomy alone had documented follow-up blood work. This discrepancy likely reflects differences in monitoring intensity rather than true differences in biological response. The single cat in the supportive-care group with apparent resolution of mastocytaemia was assessed using a peripheral blood smear rather than buffy coat analysis, limiting confidence in this finding.

Concurrent cutaneous mast cell tumours were frequently observed in cats with splenic disease, a phenomenon that remains poorly understood.[1,2,13] The coexistence of cutaneous and splenic mast cell tumours complicates determination of the primary disease site, as it is often impossible to establish whether the spleen or skin represents the origin of neoplasia. To minimise misclassification, cats with cutaneous tumours accompanied by regional lymph node involvement were excluded, as visceral disease in these cases could represent metastatic spread from the skin. Although visceral involvement poses similar challenges, the inclusion and exclusion criteria employed were considered sufficient to support classification of included cases as primary splenic disease.

Several limitations of this study stem from its retrospective design. Treatment allocation was not randomised, and cats perceived as more clinically compromised may have been less likely to undergo splenectomy or, alternatively, more likely to receive adjuvant chemotherapy. Although distributions of measured prognostic variables did not differ

significantly between treatment groups, unmeasured confounders may still have influenced outcomes. Additionally, chemotherapy protocols varied substantially among institutions and clinicians, preventing meaningful comparison of individual regimens. Follow-up intensity and restaging were inconsistent, limiting assessment of treatment response in some cases.

Despite these limitations, this study represents the largest reported case series of cats with splenic mast cell tumours. The findings confirm that splenectomy is associated with significantly improved survival and should be regarded as the treatment of choice when feasible. Although splenectomy in cats with advanced mastocytosis or mastocytaemia may be perceived as high risk, previously reported peri-operative mortality rates of approximately eight percent suggest that the potential benefits outweigh the risks for most cats.[10] The role of chemotherapy remains undefined, and clinical judgement remains essential when considering adjuvant treatment following surgery. Given the low incidence of this disease, future progress will likely require multi-institutional, prospective, randomised clinical trials to clarify the contribution of systemic therapy in cats with splenic mast cell tumours.

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