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What is This?

Canine Cutaneous Mast Cell Tumor: Morphologic Grading and Survival Time in 83 Dogs

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Abstract. Eighty-three cutaneous mast cell tumors in the dog were classified morphologically into three grades. The neoplasms were excised surgically, and the dogs were followed for 1500 days. Comparison of morphologic grade of tumor with survival time revealed significant differences among the three groups (p < 0.00010). Comparison of sex and age (above and below ten years) with morphologic grade of tumor revealed no significant differences.

Cutaneous mast cell tumors comprise 7 to 20% of the neoplasms affecting the skin of dogs.[1,2,5] The average patient age varies from 8.2 years to 10.5 years. Most studies report no sex predisposition, but certain breeds such as the boxer, Boston terrier, bull terrier, and Labrador retriever are reportedly more prone to mast cell tumors than other breeds.[1–4,10]

Mast cell tumors are graded histologically as anaplastic, intermediate, or mature based on cellular differentiation and variation in the rate and sites of metastasis.[1,3–6,8,9] In one study, histologic grading correlated well with survival time. It was observed that the survival rate for dogs with the lowest grade was six and two times that of the highest and intermediate grades, respectively.[1]

The 83 mast cell tumors were divided into three grades based on described histomorphologic features. Survival time for each group is compared to the grade of mast cell tumor, and to the sex and age of the dogs.

Materials and Methods

The records of 83 dogs with cutaneous mast cell tumors at various sites were reviewed retrospectively. The 83 dogs were selected for inclusion in the study based on the following criteria: the neoplasms had been surgically resected with wide margins; the dogs were clinically free of mast cell tumor immediately following surgery; and no treatment other than surgery was administered. Dogs were followed for 1500 days after surgery; this time-period was chosen because in one of the groups all but one dog had died or been killed at 1500 days.

Multiple sections from surgical biopsy specimens of the neoplasms were fixed in 10% formalin, routinely processed, and stained with hematoxylin and eosin. All slides were examined and graded by one author (A.K.P.) with no information regarding the dogs. Neoplasms were grouped into three categories using the following histomorphologic features: extent of involvement, cellularity and cellular morphology, mitotic index, and stromal reaction. Grade I was the most benign.

The survival data were analyzed using the Kaplan-Meier method,[7] and the logrank test[11] was used to compare two or more survival patterns. This test also was used to correlate the survival times of the three groups with age and sex of the dogs. All p values reported refer to two-sided tests. The survival data for individual breeds of dog were not analyzed because of the large number of breeds involved, and the inadequate number of dogs in each breed for statistical analysis.

Results

The median age of the 83 dogs with mast cell tumor was nine years (range, 2 to 19 years). There were almost equal numbers of males (43) and females (40). Twenty-eight dog breeds were recorded; mixed breed (24%), boxer (14%), schnauzer (10%), poodle (7%), and cocker spaniel (5%) were the most common.

At 1500 days, 46% (38/83) of the dogs had died or were killed because of mast cell tumor. The survival rate was 54% (45/83).

Grade I. Grade I mast cell tumor was diagnosed in 36% (30/83) of the dogs. Lesions in these neoplasms were confined to the dermis and interfollicular spaces. Well-differentiated mast cells were arranged in rows or small groups, separated by mature collagen fibers of the dermis (figs. 1, 2). Cells were round and monomorphic with ample cytoplasm; most had distinct cytoplasmic
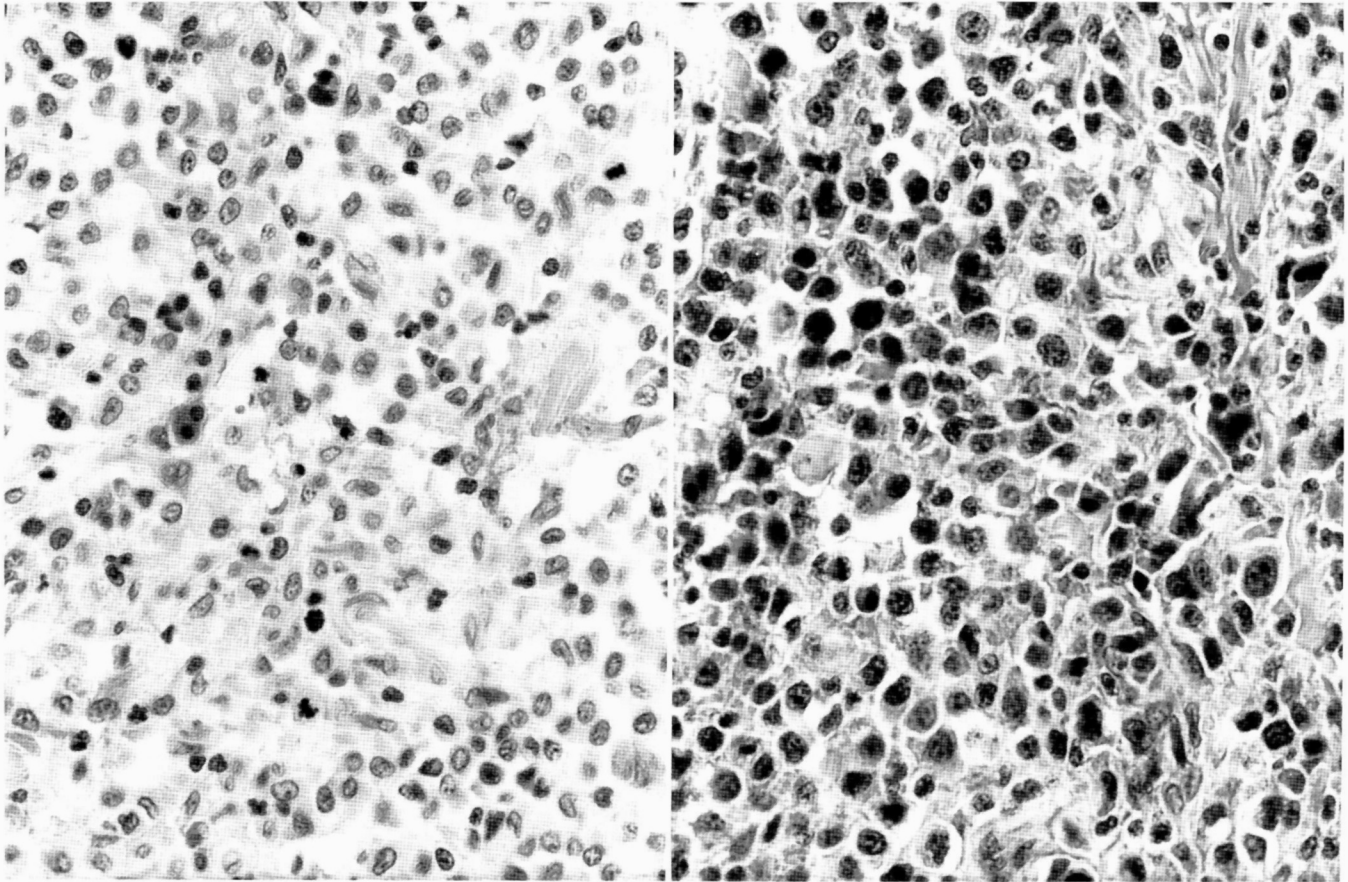
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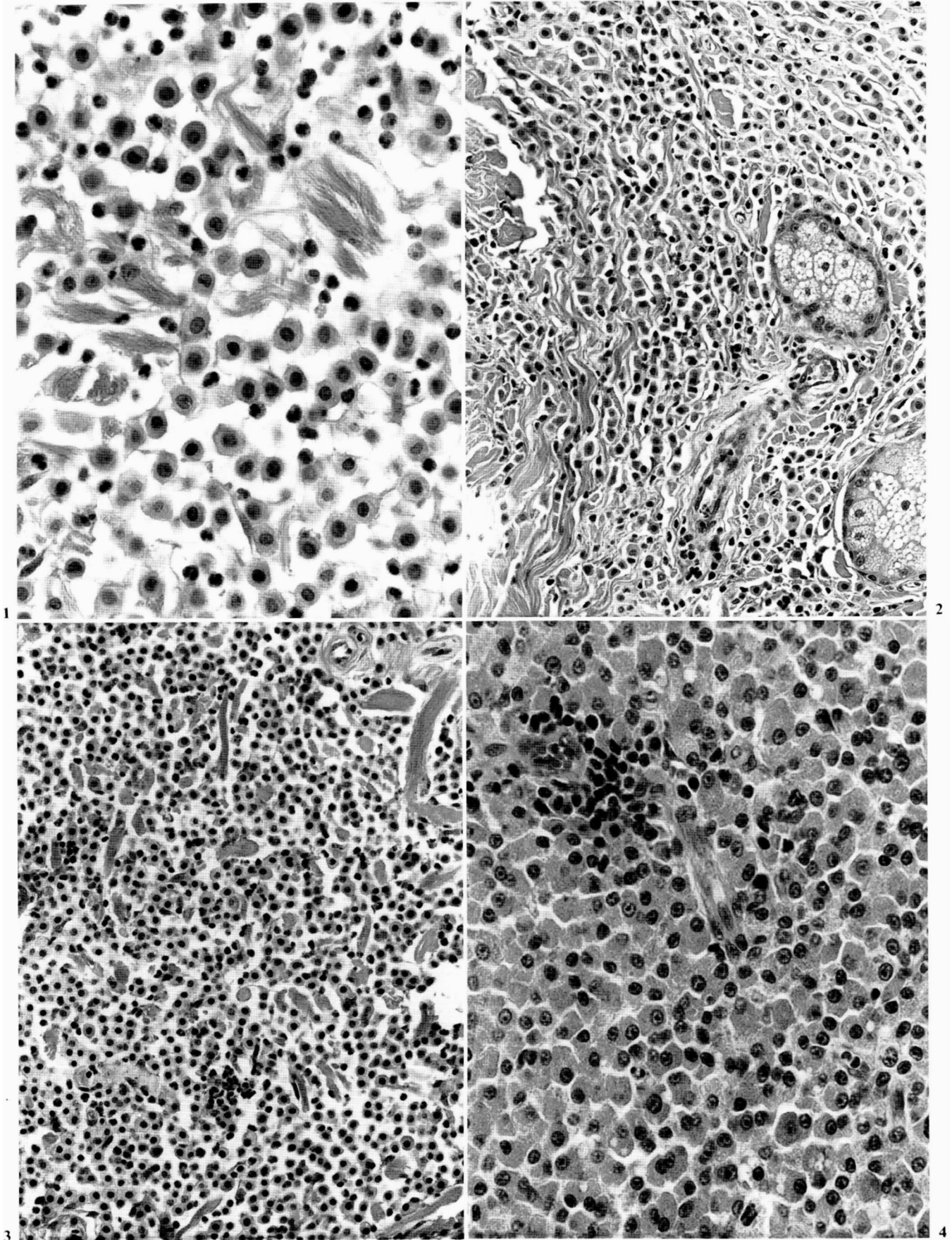
Fig. 5: Grade III mast cell tumor. Highly cellular, indistinct cytoplasm, moderate pleomorphism, large, vesiculated nuclei, distinct and sometimes prominent nucleoli, many mitotic cells.

Fig. 6: Grade III mast cell tumor. Highly pleomorphic cells, hyperchromatic nuclei, prominent nucleoli, many mitotic cells.

boundaries and medium-sized, intracytoplasmic granules. Nuclei were round with condensed chromatin. Mitotic cells were absent. There was minimal edema and necrosis in the neoplasms that had been traumatized.

Grade II. Grade II mast cell tumor was diagnosed in 43% (36/83) of the dogs. These neoplasms were moderately to highly cellular, and the neoplastic cells infiltrated or replaced the lower dermal and subcutaneous tissue. Some tumors extended to the skeletal muscles or surrounding tissues. Moderately pleomorphic cells were arranged in groups with thin, fibrovascular stroma (figs. 3, 4). In some places the stroma was thick and

fibrocollagenous with areas of hyalinization. The neoplastic cells were round to ovoid and there were scattered spindle and giant cells. Most cells had distinct cytoplasm with fine, intracytoplasmic granules; however, the cytoplasm in some was indistinct and the granules were large and hyperchromatic. Nuclei were round to indented with scattered chromatin and single nucleoli; occasional cells had double nuclei. Mitotic cells were rare, ranging from 0 to 2 per high power field. There were areas of diffuse edema and necrosis.

Grade III. Grade III mast cell tumor was diagnosed in 20% (17/83) of the dogs. These neoplasms were cellular and pleomorphic, and neoplastic tissue replaced

Fig. 1: Grade I mast cell tumor. Well-differentiated mast cells arranged in rows separated by dermal collagen. Ample, distinct, granular cytoplasm. Condensed nuclear chromatin. No distinct nucleoli or mitotic cells.

Fig. 2: Grade I mast cell tumor. More cellular than specimen in fig. 1; otherwise, the same.

Fig. 3: Grade II mast cell tumor. Cellularity increased above grade I, well-differentiated cells, ample, distinct cytoplasm, slight pleomorphism, and some vesiculated nuclei with distinct nucleoli.

Fig. 4: Grade II mast cell tumor. Cellular, indistinct cytoplasm, moderate pleomorphism, vesiculated nuclei with small nucleoli, moderate number of mitotic cells. Cells less well-differentiated than specimen in fig. 3.

the subcutaneous and deep tissues (figs. 5, 6). The pleomorphic, medium-sized, round, ovoid, or spindle-shaped neoplastic cells were arranged in closely packed sheets. The cytoplasm was indistinct with fine, intra-cytoplasmic granules or granules that were not obvious. The stroma was fibrovascular or thick and fibrocolla-genous with areas of hyalinization. The indented to round vesiculated nuclei had one or more prominent nucleoli. Binucleated cells were common. There were many giant cells and scattered multinucleated cells. Mitotic cells were also common, ranging from 3 to 6 cells per high power field. Edema, hemorrhage, and necrosis were common.

The survival rates at 1500 days for each of the three groups of dogs with mast cell tumors are given in table I, and the survival curves for the three groups are given in fig. 7. Of the 30 dogs with grade I mast cell tumor, 93% (28 dogs) survived longer than 1500 days; of the 36 dogs with grade II mast cell tumor, 47% (16 dogs) survived longer than 1500 days; and of the 17 dogs with grade III mast cell tumor, 6% (1 dog) survived longer

Table I. Grading of tumor compared to mortality and survival rates in 83 dogs with mast cell tumor

	Grade I Num-ber (%)	Grade II Num-ber (%)	Grade III Num-ber (%)	Total Num-ber (%)
Dogs with mast cell tumor	30 (36)	36 (43)	17 (20)	83 (100)
Dogs dead or killed because of mast cell tumor	2 (7)	20 (56)	16 (94)	38 (46)
Dogs surviving at least 1500 days	28 (83)	16 (44)	1 (6)	45 (54)

than 1500 days. The differences in survival among the three groups were statistically significant (p < 0.00001). The estimated proportional survival curves for male vs. female and dogs under ten years vs. dogs over ten years of age are given in figs. 8 and 9, respectively. Analysis revealed that the sex of the dogs with mast cell tumor was not related to survival (p = 0.27); after adjusting

CANINE MALIGNANT MAST CELL TUMOR
SURVIVAL BY GRADE

□ Grade III   (17 Pts.,   1 Alive)
× Grade II   (36 Pts., 16 Alive)
△ Grade I   (30 Pts., 28 Alive)

Tick Mark (I) Indicates Last Follow-up

CANINE MALIGNANT MAST CELL TUMOR
SURVIVAL BY SEX

□ Male   (43 Pts., 21 Alive)
× Female   (40 Pts., 24 Alive)
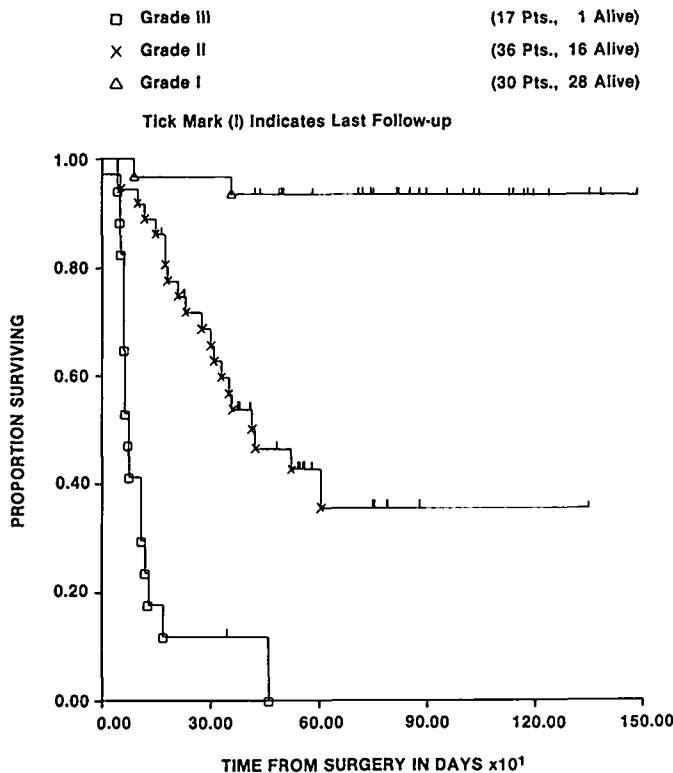
Tick Mark (I) Indicates Last Follow-up

Fig. 7: Graph showing survival curves of 83 dogs by the three grades of mast cell tumor. Note statistically significant (p > 0.0001) differences. Pts. = dogs.
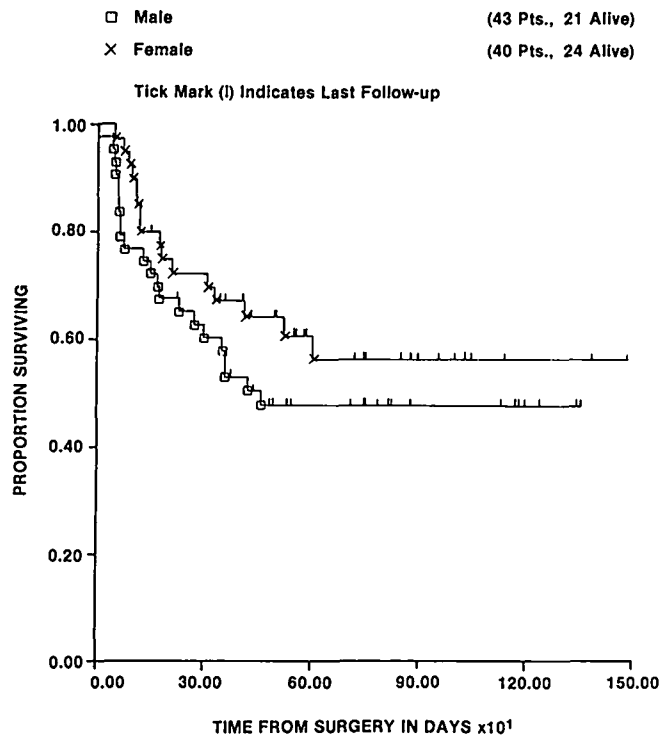
Fig. 8: Graph showing comparison of survival time by sex (male vs. female) in 83 dogs with mast cell tumor. Differences are not statistically significant (p < 0.27). Pts. = dogs.

CANINE MALIGNANT MAST CELL TUMOR SURVIVAL BY AGE

□ Age < 10 Yrs. (43 Pts., 26 Alive)

× Age ≥ 10 Yrs. (40 Pts., 19 Alive)

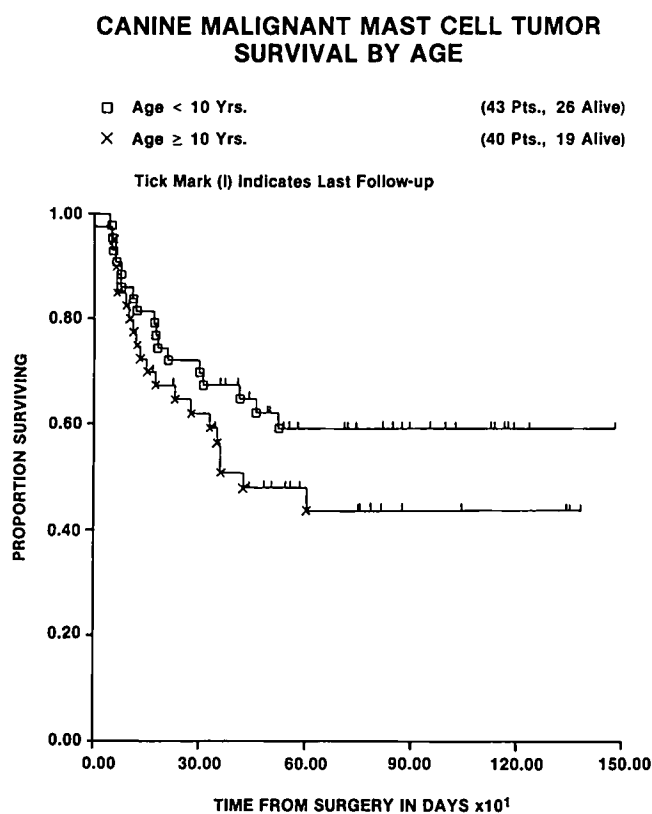Tick Mark (I) Indicates Last Follow-up

Fig. 9: Graph showing comparison of survival time and age (above and below 10 years) in 83 dogs with mast cell tumor. Differences are not statistically significant (p = 0.21). Pts. = dogs.

for grade of disease the p value was 0.06. The difference in survival rates between young and older dogs also was not significant (p = 0.21); after adjusting for grade of neoplasm the p value was 0.52.

Discussion

Mast cell tumors in the dog have been associated in the past with low mortality and minimal effect in regard to shortening the life span.[2,3,5] In one study, however, 39% of the dogs with mast cell tumor were dead or killed because of the neoplasm, and the mortality rate varied from 23 to 87% according to the degree of malignancy within a follow-up period of 30 weeks.[1] In our study, 46% (38/83) of the dogs were dead or killed within 1500 days. Both of these studies indicate that mast cell tumor is not a benign disease, and, like other malignancies, survival time depends on the degree of cellular differentiation of the tumors.

In our study, histomorphologic grading was done with no information regarding the dog or clinical stage of disease. After a 1500-day follow-up period, it was observed that 93% (28/30) of the dogs with grade I mast cell tumor had survived, while only 44% (16/30) and 6% (1/17) of those with grades II and III mast cell tumors, respectively, were still alive (table I). The number of dogs surviving with grade I tumors was two and 16 times the number of dogs that survived with grade II and grade III tumors, respectively. The survival rate of the dogs with grade II tumors was five times the number of dogs with grade III tumors. It was also observed that the overall differences in the survival times of the three groups was highly significant. In a previous study that used a reverse grading system based on cell morphology and morphometry, the survival rate for the group with benign mast cell tumor was six times greater than that for the group with malignant tumors, and two times greater than that of the group graded intermediate.[1]

The median age (9 years) and sex distribution (approximately equal) of the 83 dogs of this report agree with previous findings.[1,2,4,9,10] Age and sex were not significantly associated with survival times in our dogs.

The histomorphologic grading system presented here will be useful in evaluating dogs with mast cell tumors prior to initiation of treatment. It will also be helpful in evaluating the effectiveness of different treatment modalities. This report may stimulate further evaluation of the grading system of mast cell tumors and of its usefulness in treating one of the most common cutaneous neoplasms in the dog.

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