Initial work up of a mast cell tumor (MCT) will involve diagnosis by FNA and staging. The initial staging performed will depend on the index of suspicion that the mass is a grade II or III MCT and clinician’s preference. Cytology is generally diagnostic for MCT. However, an incisional biopsy to determine grade is recommended in some cases. The histological grade may be important to determine in some cases, where the surgical approach may be altered by the grade of the tumor.

The World Health Organization (WHO) classification scheme for canine mast cell tumours divides them into four stages according to the clinical presentation. Stage I – One tumour confined to the dermis without regional lymph node involvement (Ia – Without systemic signs, Ib – With systemic signs); Stage II – One tumour confined to the dermis with regional lymph node involvement (IIa – Without systemic signs, IIb – With systemic signs); Stage III – Multiple dermal tumours or one large infiltrating tumour with or without regional lymph node involvement (IIIA – Without systemic signs, IIb – With systemic signs); and Stage IV – Any tumour with distant metastasis or a recurrence with metastasis (including blood and/or bone marrow involvement). Locoregional staging and evaluation for visceral metastasis (to spleen and liver) are the areas that are most important to evaluate when staging canine patients with MCT.

Lymph node staging will involve palpation, FNA for cytology and biopsy for histopathology in some cases. One pitfall with cytological evaluation of the lymph nodes is that it can be difficult to differentiate between neoplastic mast cells and normal mast cells that are at the site due to chemotaxis. Krick et al attempted to define the cytological staging of lymph nodes to create consistency in the literature. In that study they defined:

Normal – No mast cells seen
Reactive lymphoid hyperplasia - Reactive node +/- rare individual mast cells
Possible metastasis – 2-3 mast cell aggregates of 2-3 cells
Probably metastasis - >3 foci of mast cell aggregates of 2-3 cells and/or 2-5 aggregates of >3 mast cells
Certain metastasis - Effacement of lymphoid tissue by mast cells and/or presence of aggregated, poorly differentiated MC with pleomorphism, anisocytosis, anisokaryosis, and/or decreased or variable granulation, and or >5 aggregates of >3 MC

Although this definition is helpful and may lead to the ability to predict prognosis in future studies, it still creates a clinical problem of what to do with cases that are determined to have possible or probably metastasis. In Krick’s study, 152 dogs with MCT had lymph node evaluation. 63.8% of dogs were considered stage I and 36.2% were considered stage II. In that study, stage II dogs had a shorter survival time and dogs with grade III MCT were more likely to have stage II disease. In cases with enlarged locoregional lymph nodes with questionable or certain metastasis, removal of the affected lymph node at the time of surgery for histopathology and cytoreduction is recommended.

Abdominal ultrasound is also recommended for staging MCT in dogs, with ultrasound-guided FNA of the spleen and liver if they appear abnormal. This can also raise questions of true metastasis versus normal mast cells. Recently Stefanello et al evaluated 52 dogs with MCT that had ultrasound guided aspirates of the liver and spleen. 10/52 (19%) dogs had abnormalities of the spleen or liver on cytology and all 10 of these cases had abnormalities noted on ultrasound.
An additional 21/42 dogs with normal cytology had abnormalities on ultrasound. Although it is somewhat controversial, this study suggests that cytology should be performed in cases with ultrasound abnormalities of the liver or spleen. This study also found that dogs with cytological evidence of visceral metastasis had a significantly shorter survival time than dogs with normal cytology. (34 days vs 733 days)

Thoracic radiographs are often taken as part of a work up for mast cell tumors. However, this is a low yield test. A recent retrospective study evaluating the prevalence of gross lung metastasis on three view thoracic radiographs in 115 dogs with mast cell tumors yielded 1/115 (0.87%) dog that was positive for gross metastasis. (Fung & Boston, unpublished data) Three-view thoracic radiographs can be considered as part of a baseline data base for older dogs, in cases with respiratory signs and in cases with high grade tumors with metastasis to other sites.

Staging with bone marrow aspirate or biopsy has also been shown to be a relatively low yield test. However, some would argue that it is worthwhile because the prognosis is significantly altered with a positive bone marrow. Endicott et al evaluated the bone marrow of 157 dogs with MCT. In that study, they found that 2.8% of cases were positive at initial evaluation, with 4.5% positive overall. 3/18 dogs were positive after recurrence or progression of clinical signs, suggesting that bone marrow is not indicated for routine staging, but may be considered in cases with progressive disease or when indicated based on CBC. Another study by Marconato et al evaluated the prognosis in 14 dogs that were positive on bone marrow evaluation. The MST in these cases was 43 days and most cases had concurrent metastasis to the lymph nodes or visceral metastasis, with 3 cases that had evidence of pulmonary metastasis.

Although dogs with multiple mast cell tumor are classified as Stage III, recent evidence suggests that these are separate events, with mast cells developing de novo in dogs that are predisposed to mast cell tumors, rather than metastatic events. Stage III is likely a misnomer for the predicted behavior of dogs with multiple mast cell tumors. The survival time of dogs with multiple mast cell tumors was not found to be significantly different than dogs with solitary mast cell tumors. This suggests that for dogs with multiple mast cell tumors, each tumor should be treated as a separate event. (Murphy et al 2006; Mullin et al 2006)

Surgery remains the mainstay of treatment for canine mast cell tumors. The completeness of surgical excision has been shown to have a significant effect on prognosis of mast cell tumors. (Mullins et al 2006; Murphy et al 2004). Although the dogma has been that malignant tumors should be removed with 3cm margins and one fascial plane deep, this has recently been critically evaluated. Simpson et al prospectively evaluated margins of grade I and II MCT of 1, 2 and 3cm. A total of 23 MCT were evaluated in this study. They found that the grade I MCT were all completely excised at all margins, suggesting that 1cm may be adequate for low grade tumors. For the grade II tumors, 75% were considered clean at 1cm margin and 100% were considered clear at 2cm margins. A follow up of this study by Fulcher et al evaluated the margins of grade I and II MCT that were excised using 2cm lateral margins. They had 16 dogs with 23 MCT in this study. 4/23 were grade I MCT and all of these had clean margins. 19 of the tumors were grade II and 2 of these were considered to have dirty margins. In light of the fact that 10% of the margins were considered dirty for grade II MCT that were cut with 2cm margins, this recommendation should be considered with caution. The author continues to use 3cm lateral margins for grade II and III MCT when this is possible.

Seguin et al evaluated the outcome of dogs with grade II MCT that were treated with surgery alone. 55 dogs with 60 tumors were evaluated retrospectively. Only one case had dirty histological margins. 3 cases (5%) recurred locally and the same number developed metastasis.
6 cases (11%) developed a MCT at another site. 84% of cases were free of MCT for the duration of follow up (median follow up 540 days). The authors of this paper concluded that additional therapy may not be necessary for grade II MCT with complete excision and no evidence of metastasis. Seguin later evaluated the recurrence, outcome and proliferation indices in cases of MCT after incomplete excision. 28 dogs were evaluated with 30 MCT. 7 (23.3%) of the cases recurred locally and this was found to be a negative prognostic indicator for survival. Ki-67 and PCNA were also found to be prognostic for local recurrence.

Predicting the behavior of grade I and grade III is straightforward. However, the common grade II MCT continues to be difficult to predict behavior. Indices of proliferation have been assessed to try to determine between “good” and “bad” grade II MCT. Mitotic index (MI) appears to be the most straightforward and promising method of separating out the good and bad grade II MCT. Recently, Romansik et al evaluated the MI for 148 MCT and found that MI correlated with tumor grade. As well the median survival time for dogs with a MI of 0-5 was 70 months, and was significantly longer than dog with a MI of >5 (MST of 2 months). Similarly, a new two-tier grading scheme has been recently proposed by Kiupel et al. This scheme attempts to separate the mast cells into high-grade or low grade. High grade tumors were those with: at least 7 mitotic figures in 10 high-power fields (hpf); at least 3 multinucleated (3 or more nuclei) cells in 10 hpf; at least 3 bizarre nuclei in 10 hpf; karyomegaly. Fields with the highest mitotic activity or with the highest degree of anisokaryosis were selected to assess the different parameters. According to the novel grading system, high-grade MCTs were significantly associated with shorter time to metastasis or new tumor development, and with shorter survival time. The median survival time was less than 4 months for high-grade MCTs but more than 2 years for low-grade MCTs. This new grading scheme may help to guide therapy and predict behavior of mast cell tumors in the future.

Although a complete excision of a mast cell tumor should always be the goal of surgical treatment. This is not always feasible or achieved. Dogs with an incompletely excised mast cell tumor will continue to require local control of their disease. If possible, a staging recut should be performed using 2-3 cm margins around the previous excision scar and one fascial plane deep. If this is not feasible, radiation therapy to the site is recommended.

For tumors where complete excision is not feasible due to the extent of disease, the approach will depend on the owners treatment goals and on full staging. In these cases, full staging including an incisional biopsy to determine the tumor grade is recommended preoperatively. In cases where palliation is the goal, pretreatment with either chemotherapy or corticosteroids can be considered prior to cytoreductive surgery. However, caution should be exercised in using corticosteroids to shrink mast cell tumors if a curative intent surgery is to be performed. A recent article by Gilson et al evaluated the use of neoadjuvant prednisone in cases of MCT that were treated with surgery. This study was a combined retrospective and prospective study. Dogs received 0.5-2.2mg/kg, with no control group, a median of 9 days prior to surgery. The overall objective response rate was 70% and prospectively the maximal diameter reduction was 42.5% and the reduction in tumor volume was 80%. The authors concluded that neoadjuvant prednisone useful for inducting reduction of MCTs and may facilitate resection when adequate surgical margins cannot be confidently attained because of mass location or size or both. However, despite the fact that 89% of the cases in this study had histologically complete margins, the overall local recurrent rate was 23.8% and the local recurrence rate for cases with “complete” excision was 17.6%. This suggests that pretreatment with corticosteroids may decrease the tumor size and facilitate resection, but that there may be islands of malignant mast cells that are left in
the periphery that may be left behind after resection. Pretreatment corticosteroids is appropriate in some situations, such as when a curative intent surgery is not possible, when the intent is palliation and cytoreduction, or when cytoreduction followed by radiation is part of the treatment plan.
References


11. Recurrence Rate, Clinical Outcome, and Cellular Proliferation Indices as Prognostic Indicators after Incomplete Surgical Excision of Cutaneous Grade II Mast Cell Tumors:
