Improve Veterinary Education

Mast Cell Tumours

Learning Objectives and Clinical Relevance

This presentation focuses on mast cell tumours, with the primary objectives of understanding their biological behaviour and tumour grading, recognising how grading influences survival, prognosis, and overall clinical outcome, and clarifying the surgical approach and indications for adjunctive management. Effective management also requires familiarity with prognostic factors and appropriate follow-up strategies. Mast cell tumours are among the most common cutaneous tumours in dogs, representing approximately sixteen to twenty-one per cent of all skin tumours. They are most frequently diagnosed in older dogs, although they can occur at any age. In very young dogs, lesions with a similar appearance are more commonly histiocytomas rather than mast cell tumours; however, clinical appearance alone must not be relied upon, and diagnostic testing is required to distinguish tumours that may regress spontaneously from those that require definitive treatment. Lesions may be ulcerated or non-ulcerated, and both their appearance and their anatomical location have prognostic implications.

Breed Predisposition, Location Effects, and Biological Behaviour

Certain breeds are overrepresented, including brachycephalic breeds, Golden Retrievers, Staffies, Boxers, and Pugs, with Shar-Peis also showing a strong breed predilection. Tumour grade varies by breed; some breeds more commonly develop lower-grade tumours, whereas Shar-Peis tend to present with more aggressive, higher-grade disease. Ulceration may reflect rapid tumour growth. Manipulation of the mass may trigger a Darier sign, characterised by a red wheal and local swelling caused by mast cell degranulation and release of mediators such as heparin and histamine. Dogs demonstrating a Darier sign, or a history of wheals or hives associated with handling of the lesion, tend to have a poorer prognosis. Anatomical location is an important prognostic factor. Tumours adjacent to the external genitalia, including peripreputial and perivulvar sites, are associated with poorer prognosis, as are periungual and nail bed tumours. By contrast, tumours located adjacent to the conjunctiva, such as near the lateral or medial canthus, may carry a better prognosis biologically, but their excision is technically challenging because preserving ocular and eyelid function may limit surgical margins. In such cases, electrochemotherapy has been used by some clinicians as an alternative approach, aiming to achieve improved outcomes with reduced morbidity.

Tumour differentiation also influences prognosis. Better differentiated tumours generally have improved outcomes, whereas poorly differentiated tumours carry a worse prognosis. Evidence

of distant metastasis at the time of diagnosis is a negative prognostic indicator. Tumour grade and tumour morphology provide important preoperative prognostic information, and these considerations must be integrated into clinical planning.

Cytological Diagnosis and the Role of Histopathology

Fine needle aspiration provides a clinical diagnosis in approximately ninety-five per cent of mast cell tumour cases. These tumours are round cell tumours and exfoliate readily, allowing high diagnostic yield when sampling technique is appropriate. A good aspirate sample should be cellular, with a well-distributed smear and a feathered edge around the sample. Cytologically, mast cells typically have abundant cytoplasm containing multiple purple-staining granules, with indistinct cell borders and frequent cell clustering. Criteria of malignancy may include nuclear moulding, multiple nucleoli, and nuclear pleomorphism. It is recommended to prepare three to four slides from a single lesion. Because mast cell tumours exfoliate easily, the pin-cushion method is preferred over active aspiration, avoiding excessive negative pressure that may rupture granules; nevertheless, samples with ruptured granules can remain diagnostic. In-house slide assessment is useful to confirm that cellular, representative material has been obtained prior to submission. Diff-Quik does not always highlight mast cell granules reliably, and laboratories may instead use stains such as Wright–Giemsa or toluidine blue to improve visualisation.

Incisional biopsy is not always required for diagnosis, but it provides definitive tumour grading, which is clinically valuable because it influences the surgical plan and the decision-making process regarding postoperative adjuvant chemotherapy or radiation therapy. Knowledge of grade before definitive surgery can therefore be advantageous in selected cases.

Staging, Lymph Node Assessment, and Systemic Evaluation

Lymph node staging is a central component of mast cell tumour assessment. Staging should include aspirates from the sentinel lymph node or adjacent regional lymph nodes, ideally sampling multiple locations within the node. Palpation alone is not sufficient, as lymph nodes can contain metastases yet remain small and non-firm. It is also important to recognise that small numbers of resident mast cells may be present in lymph nodes as part of the normal cell population; metastatic disease is suggested when mast cells show cytological criteria of malignancy.

Abdominal ultrasonography is considered a mainstay of staging because mast cell tumours show tropism for organs including the spleen, liver, and gastrointestinal tract. Ultrasonographic

findings may include tissue thickening and hypoechoic changes, but metastasis may occur even when discrete hypoechoic nodules are not visible. In some cases, diffuse splenic involvement may be present, particularly with systemic mastocytosis. Aspiration of spleen and liver has been suggested regardless of ultrasonographic appearance in patients with a high risk of metastasis, such as those with peripreputial, perivulvar, or periungual tumours. By contrast, in a patient with a single, well-differentiated cutaneous tumour with few granules, histopathology may confirm a low-grade lesion with low metastatic risk, and in that context, splenic aspiration may be considered less essential if the spleen appears uniform. Nonetheless, aspiration is not inappropriate, and the decision must account for sampling limitations and procedural risks. Even with ultrasound guidance, aspirates can result in haemorrhage, and the risks associated with splenic or hepatic aspiration should be discussed with the owner in advance.

Thoracic radiographs are not performed routinely in all cases, but may be indicated when a high-grade tumour is suspected or confirmed, as such cases may metastasise to pulmonary parenchyma and thoracic lymph nodes, including hilar nodes. Historically, complete blood count and blood film evaluation were used more routinely to assess for mastocytaemia or systemic mastocytosis, including examination of the buffy coat. Although this is less commonly performed now, mast cells may occasionally be observed in circulation provided they are not malignant. If mast cells are present in unexpectedly high numbers, or if malignant mast cells are detected in peripheral blood, bone marrow aspiration may be warranted to evaluate for systemic mastocytosis, which carries a very poor prognosis when bone marrow infiltration is present.

Perioperative Medical Management and Adjunctive Therapies

Preoperative administration of antihistamines or H2 antagonists is not routine for all patients. However, in dogs that demonstrate a Darier sign on presentation, or have a history of degranulation-associated wheals or hives after manipulation, antihistamines may be beneficial. In patients with vomiting associated with mast cell tumours, H2 antagonists may be appropriate. Routine prednisolone use is not standard practice, although some surgeons use corticosteroids; prednisolone may be considered postoperatively in selected cases, such as when surgical margins are narrow at approximately one to two millimetres, and this should be discussed with a medical oncologist to determine clinical necessity. Chemotherapeutic agents and other cytotoxic medications may be utilised in appropriate patients following consultation with a medical oncologist.

Principles of Surgical Excision and Tissue Handling

Surgical planning requires the same fundamental decision as for soft tissue sarcomas, namely whether a marginal excision is appropriate or a definitive excision is required. Definitive excision aims to achieve clean margins circumferentially and at depth. For a distal limb mass, such as a lesion on the antebrachium, wide margins are marked preoperatively, typically at least two centimetres and often three centimetres depending on tumour grade. For high-grade tumours, a three-centimetre lateral margin is used, and where possible two fascial planes are included at depth. If two fascial planes are not available in the anatomical region, muscle may need to be excised to achieve an adequate deep margin. For low-grade or intermediate-grade tumours, a two-centimetre margin is typically selected, with consideration of depth and tissue planes. Dissection is often taken to the antebrachial fascia, aiming to preserve essential blood supply for distal limb healing when possible, while sacrificing tissues as required to achieve oncologically appropriate margins.

Because mast cell tumours may degranulate, surgical oncology principles emphasise avoidance of direct tumour manipulation. Minimising contact, avoiding handling of the tumour with gloved fingers, and using meticulous haemostasis reduce the risk of tumour seeding and transplantation of viable tumour cells. A two-instrument approach is recommended, with one set of instruments and gloves used for tumour excision and a separate clean set used for closure after irrigation and tissue preparation, thereby maintaining a clear separation between a “dirty” excision field and a “clean” closure field. Tension-free closure is essential to reduce wound complications such as dehiscence and to mitigate impaired healing that may occur following subclinical degranulation. Halsted’s principles remain applicable. Slowly absorbable sutures are preferred for deeper layers, and intradermal closure may be used provided there is no tension at the wound edges; some clinicians may elect skin sutures depending on wound characteristics.

Reconstructive planning may be required in anatomically challenging sites. An example includes a mast cell tumour on the lateral upper lip, where preoperative planning for a cheek-based rotational flap allows closure of the defect following excision. Tissue hooks or skin hooks may be used to handle flap tissues while protecting the skin edges. The decision to place a drain under a flap is surgeon-dependent; drains are recommended when dead space is present to preserve tissue viability, reduce seroma formation, and improve flap adherence to the recipient bed. Client communication is aided by preoperative discussion using photographs to set expectations regarding cosmetic outcome and potential disfigurement.

Margin Interpretation, Biomarkers, and Grading Systems

Grading systems are validated for cutaneous mast cell tumours, an important limitation because mast cell tumours may also occur in subcutaneous tissues. Subcutaneous tumours are generally considered less aggressive, and grading information from cutaneous tumours is often extrapolated to subcutaneous lesions, although this extrapolation may not be fully accurate. Surgical margin quality remains important. It has been suggested by surgical oncologists that any clean margin for mast cell tumours should be regarded as a clean margin, whether one millimetre or two millimetres, provided no tumour cells are present at the margin. Conversely, the presence of tumour cells at the margin is associated with increased risk of recurrence and poorer prognosis, particularly in high-grade tumours, and potentially also in low-grade tumours.

Lower-grade tumours typically have a better prognosis. In practice, low-grade tumours with incomplete margins may not always be re-excised immediately; instead, a “wait and see” approach may be adopted, with close monitoring and sampling of any subsequent nodular change, followed by re-intervention if recurrence is confirmed.

Additional prognostic information can be obtained through immunohistochemistry and tumour biomarker assessment. Markers such as c-KIT mutations may influence prognosis and response to tyrosine kinase inhibitors, with c-KIT exon 8 mutations generally associated with better prognosis than exon 11 mutations. Proliferation indices including AgNORs and Ki-67 may also guide prognosis and therapeutic planning. The mitotic index is a key parameter; if not included in the pathology report, it should be requested. These additional tests can inform outcome prediction and selection of adjuvant treatment strategies.

Two principal grading systems are in clinical use. The Patnaik grading system is an older three-tier system assigning grade I, II, or III. The Kiupel system is a newer two-tier system classifying tumours as low grade or high grade and is generally considered superior. The Kiupel system effectively groups Patnaik grades I and II into a lower-risk category while distinguishing high-risk disease. Clinically, using both systems in conjunction may provide greater benefit, particularly by helping to stratify the intermediate group more effectively.

Indications for Adjuvant Therapy and Expected Outcomes

Adjuvant chemotherapy is typically considered for known high-grade tumours. There is also a subset of low-grade tumours with high proliferation markers in which adjuvant therapy may offer benefit. Additional indications include low-grade tumours with c-KIT mutations, particularly exon 11, and evidence of metastasis on staging, such as lymph node involvement. In cases with

confirmed nodal metastasis, chemotherapy may be considered to control microscopic disease postoperatively.

Prognostic outcomes vary by grade. Grade I tumours generally have an excellent outcome with complete excision, with a reported recurrence risk of approximately zero per cent. Grade II tumours or low-grade tumours have a recurrence rate in the range of five to eleven per cent with complete excision. Grade II tumours behaving as higher grade may have recurrence rates in the range of five to twenty-three per cent. Grade III tumours have the highest recurrence rates, regardless of completeness of excision.

Management of Recurrence and Non-Surgical Options

When recurrence occurs, the recommended approach is to restart the diagnostic and treatment process. Recurrence should first be confirmed as mast cell tumour using fine needle aspiration as the primary diagnostic method; if diagnosis remains uncertain, incisional biopsy and histopathology are indicated. Once recurrence is confirmed, staging should be repeated to assess for progression to regional or distant metastasis. All available management options, including surgical and medical approaches, should then be discussed with the owner, and a reasonable plan developed. Surgery remains the preferred first-line treatment for recurrence, as excision may include removal of scar tissue as well as recurrent tumour, and the next step generally involves a wider and deeper excision than previously performed.

Non-surgical treatments are available. Mast cell tumours are generally radiosensitive, but the cost of radiotherapy can be prohibitive and should be discussed explicitly with owners. In some cases, medical oncologists may recommend radiotherapy referral depending on tumour location, grade, and biomarker profile, rather than repeating surgery or selecting chemotherapy. Another option is tigilanol tiglate (Stelfonta) for tumours located below the elbow and below the stifle on the extremities, although some clinicians have extended its use to slightly more proximal lesions. Clinical experience with Stelfonta varies; its use may be appropriate where experience supports favourable results. Electrochemotherapy may also be considered, particularly for lesions in challenging anatomical locations.