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CLINICAL KNOWLEDGE INSIGHTS

NEOPLASTIC DERMATOSES

MAST CELL TUMORS – CANINE

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CONTENTS

AT A GLANCE

- Mast cell tumors (MCTs) are neoplasms that that typically develop in the skin and subcutaneous tissues, usually on the trunk and limbs of dogs; they represent the second most common tumor found in dogs.
- Breeds of dog predisposed to develop MCT include those of bulldog descent (Boxers, Pugs, etc), Labrador and Golden Retrievers, and Shar-peis.
- MCT exhibit a wide range in biologic behavior from benign disease, that is readily cured with surgical removal, to aggressive tumors that metastasize widely resulting in death of affected dogs.
- While the molecular changes that drive MCT in many dogs are not know, 25-50% of aggressive MCT possess a mutation in a cell surface receptor called KIT that drives the uncontrolled growth of the malignant cells in these tumors.

- There are now several new therapies available to treat aggressive MCT in dogs and long-term outcome has been significantly improved by using a multimodal approach to treatment including surgery, radiation therapy, chemotherapy and small molecule inhibitors that target KIT.

WHAT DOES IT LOOK LIKE?

- MCT most commonly appear as a solitary, haired to hairless cutaneous nodule ranging from 1-3 cm in size *(Pathologic Image Library - Figure 1)*.
- Some dogs will present with multiple (2-3) MCTs although this does not necessarily affect the overall prognosis *(Pathologic Image Library - Figure 2)*.
- Occasionally owners will report that the tumor appears to increase then decrease in size over several days; this change appearance is often secondary to histamine release from the malignant mast cells causing local swelling.
- As the tumors can be pruritic, trauma from scratching or licking can cause ulceration and less commonly secondary infection.
- Mast cells contain a number of mediators including cytokines, chemokines, prostaglandins, proteases as well as histamine and heparain that they may release. Increased circulating levels in histamine can predispose to the development of gastric ulceration, and affected dogs may present with a history of vomiting and/or diarrhea.
- MCTs may remain unchanged in size over many months to years in dogs; typically this indicates a more benign behavior; in contrast, those tumors that grow rapidly tend to exhibit aggressive biologic behavior and result in metastatic disease *(Pathologic Image Library - Figure 3)*.

WHAT ELSE LOOKS LIKE IT?

- MCTs are often termed the great pretenders as they can resemble anything including:
  - → Fibropapilloma/sebaceous adenoma
  - → epidermal inclusion cyst
  - → non-healing wound
  - → lipoma *(Pathologic Image Library - Figure 4)*

HOW DO I DIAGNOSE IT?

- Cytologic evaluation of fine needle aspirates is the easiest method to diagnose a MCT; poorly differentiated MCTs may contain few, if any granules, necessitating special stains. Additionally, sometimes mast cell granules do not stain with Diff-Quick, making the use of a Wright-Geimsa stain necessary for definitive diagnosis.

PATHOLOGIC IMAGE LIBRARY : MAST CELL TUMORS – CANINE

Figure 1. Mast cell tumor (MCT) in the perineal region

Figure 2. Multiple grade 2 MCT on the ventral abdomen.

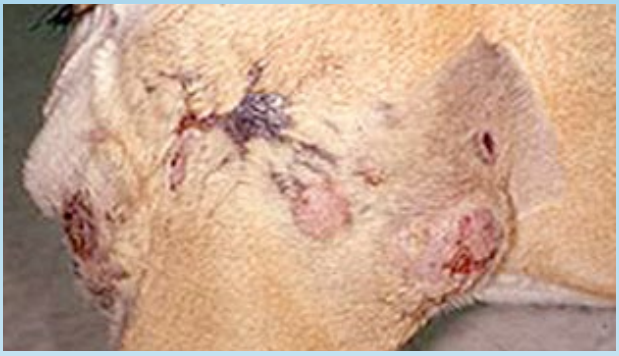

Figure 3. Recurrent grade 3 MCT with satellite cutaneous metastases.

Figure 4. Recurrent "lipoma-like" subcutaneous MCT.

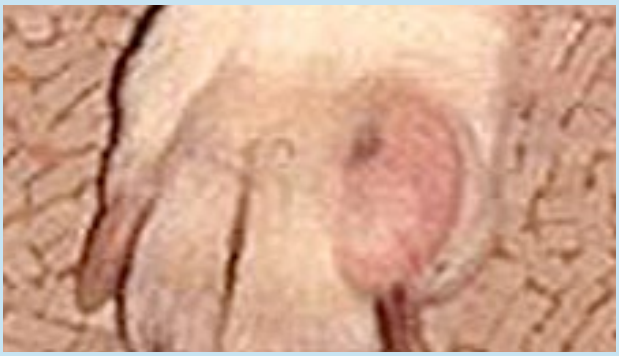

Figure 5. Subungula grade 2 MCT

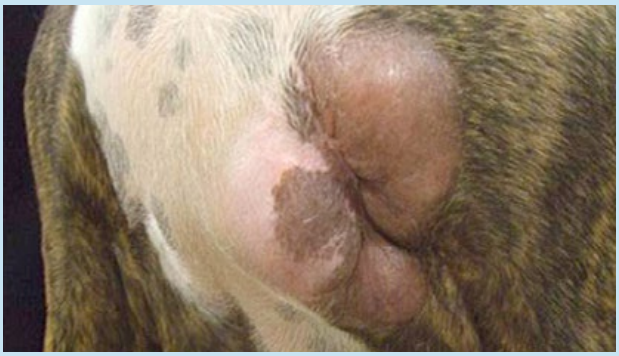

Figure 6. Recurrent grade 2 MCT on the cranial ventral thorax

- If cytologic diagnosis proves difficult, a needle or punch biopsy can be obtained; this is preferred to a larger incisional biopsy as release of mast cell mediators can result in impaired clotting and delayed wound healing.
- Excisional biopsy is required for histologic grading which is based on several features including degree of invasion, mitotic index, cellular atypical, etc.
- Staging of dogs with MCT should include standard tests such as CBC, biochemistry profile, and urinalysis. Additionally, the regional lymph nodes should be evaluated by fine needle aspiration (prior to tumor removal) for evidence of metastasis. Lastly, abdominal ultrasound and thoracic radiographs should be performed in dog whose MCTs exhibit signs of biologically aggressive behavior.
- It is important to note that fine needle aspirates of the liver and spleen should be obtained in all dogs with aggressive MCT as these organs may have a normal ultrasonographic appearance despite the presence of metastatic disease.

DIAGNOSTIC TECHNIQUES VIDEOS: ExcellenceInDermatology.com → Education Library → Videos

DIAGNOSTIC TECHNIQUES SECTIONS: ExcellenceInDermatology.com → Diagnostic Techniques

HOW DO I MANAGE IT?

- There are several prognostic indicators that help to guide the type of therapy for a particular MCT. These include:
  - → Breed: Pugs and Boxers tend to develop benign MCT while Shar-peis tend to develop aggressive MCT
  - → Clinical signs: dogs with vomiting, diarrhea, weakness tend to have a worse prognosis
  - → Growth rate: MCT unchanged in appearance for > 6 months are generally less aggressive
  - → Stage: dogs with multiple independent MCT may not have worse prognosis, but significant lymph node involvement (i.e., enlarged, effaced nodes) and/or abdominal organ involvement indicates aggressive disease.
  - → Location: MCT in the subcutaneous tissues are often less aggressive; those on the muzzle and nail bed (Pathologic Image Library - Figure 5) have a high metastatic rate.
  - → Grade: grade 1 tumors are typically benign, while grade 3 tumors are typically malignant; about 75% of grade 2 tumors (Pathologic Image Library - Figure 6) will behave aggressively. A new tumor grading system (awaiting validation) has been developed to guide decision making, this system separates MCT into low or high grade tumors.
  - → Proliferation markers: mitotic index, Ki67 and others are often helpful in determining the likelihood for a MCT to spread.
  - → KIT mutation: testing is now offered through multiple diagnostic labs; the mutation is associated with a higher risk of local recurrence, metastasis and death.

- The mainstay of MCT treatment is wide surgical excision (2-3 cm lateral margins, 1 fascial plane deep).
- Radiation therapy (RT) is extremely effective at eliminating residual tumor cells following an incomplete excision; recent evidence suggests that RT may also be effective in controlling MCT that are not amenable to surgical removal.
- The use of chemotherapy is indicated following removal of grade 3 MCTs, metastatic MCTs, non-resectable MCT, or for any other MCT with negative prognostic indicators.
  - → Prednisone: this drug has activity against most MCT, with up to 75% decreasing in size following treatment. It is generally included in all treatment protocols as it also helps to decrease mast cell mediator release.
  - → Vinblastine: this is the most commonly used chemotherapy agent for MCTs.
  - → Alkylating agents such as lomustine, chlorambucil and hydroxurea also have activity against MCTs, although these are generally considered to be less effective than that of vinblastine.
- Small molecule inhibitors of KIT, such as toceranib phosphate (Palladia) are indicated for the treatment of recurrent MCT with KIT mutations (70-90% response rate); toceranib may also have activity against MCT without KIT mutation (30% response rate).
- Supportive care including a proton pump inhibitor to decrease gastric acid production and an H1 antagonist to block histamine effects on smooth muscle is indicated in all dogs with aggressive MCT. Sucralfate can also be used if GI ulceration is suspected.

COMMENTS

- The integration of multiple therapeutic approaches (surgery, RT, chemo, and KIT inhibitors) to treat aggressive MCT has substantially improved survival times of affected dogs.
- Given the high response rate of MCTs with KIT mutation to KIT inhibitors such as toceranib, KIT mutation testing should be performed in all dogs with aggressive disease or negative prognostic indicators.

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