**CASE REPORT**

**Diagnosis and treatment of a feline oral mast cell tumor**

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A cat was diagnosed with an oral mast cell tumor following incisional biopsy. The location of the tumor, possible metastasis, financial restraint and patient disposition severely limited therapeutic options. The patient was treated with six doses of 1-(2-chloroethyl)3-cyclohexyl-1-nitrosurea (CCNU) and methylprednisolone acetate. Complete remission was obtained after the third dosing regimen. This is the first documented case of feline oral mast cell tumor and one of a small group of cats with various cancers to be responsive to CCNU treatment.

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A 9-year-old, male neutered domestic medium hair cat presented for generalized lethargy, mild anorexia, sporadic gagging and dysphagia. Initial evaluation revealed a fractious patient who required sedation for a physical examination. The patient had severe periodontal disease and was mildly underweight with a body condition score of 2/5. Other findings included bilateral submandibular lymphadenopathy and bilateral purulent ocular discharge. Initial diagnostic testing included a complete blood count which revealed a mild lymphopenia (1152/µl, reference range 1500–7000/µl). In house ELISA tests for feline leukemia virus (FeLV) antigen and feline immunodeficiency virus (FIV) antibodies were negative. A serum biochemistry panel and urinalysis revealed no significant findings.

Stage tests performed included a buffy coat smear (which was negative). Cytologic evaluation of the fine needle aspirates of both submandibular lymph nodes reported reactive lymphoid hyperplasia with one mast cell per 10 high power fields (hpf). Abdominal ultrasonography revealed a mildly enlarged but diffusely homogenous spleen. Fine needle aspirates of both the spleen and liver were normal and no mast cells were noted. Bone marrow aspiration was declined. A severe yeast infection in the left ear and moderate infection in the right ear were confirmed on cytology. Therapy consisting of neomycin 0.25%, triamcinolone 0.1%, and...
thiabendazole 4% (Tresaderm, Merial, Inc, Duluth, GA, USA) was started in both ears. The patient received 10 mg of 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosurea (CCNU) given at a dose of 50 mg/m² (CeeNU, Bristol-Meyers Squibb Co, Princeton, NJ, USA). Twenty milligrams of methylprednisolone acetate was also administered subcutaneously to treat both the underlying eosinophilic complex and the MCT. Prednisone was not used due to the owner’s inability to give oral medications to the patient. A complete blood count, 7 days post chemotherapy, was within normal limits. The patient had improved clinically with the exception of a 0.2 lb weight loss. Fourteen days following treatment, the patient was re-evaluated. His owner reported a noticeable improvement in overall health and clinical signs. Physical examination revealed an improved, but persistent, right submandibular lymphadenopathy (0.4 cm × 0.4 cm × 0.35 cm) and less severe otitis. The sublingual lesion had undergone a partial response (>50% reduced in size). A complete blood count revealed leukopenia (1900/μl, reference range of 3500–16000/μl), and neutropenia (760/μl, reference range 2500–8500/μl). The patient was placed on prophylactic enrofloxacin (Baytril, Bayer Corp, Shawnee Mission, KS, USA) at 5 mg/kg PO q24h for 2 weeks, received a single dose of subcutaneous fluids (150 ml lactated Ringers solution) and was discharged.

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Four weeks (day 28) after treatment his owner reported that the cat appeared to be in overall good health. The right submandibular lymph node was stable in size (0.3 cm × 0.4 cm × 0.30 cm). Oral examination revealed gross resolution of the mast cell tumor. A complete blood count was within normal limits. The patient received a second dose of CCNU at a lower dosage of 7.5 mg PO (25% standard dose reduction) and a second dose (20 mg) of methylprednisolone acetate subcutaneously. Fourteen days later, a complete blood count was within normal limits. There was no evidence of myelosuppression. The patient returned 1 month after chemotherapy for a recheck. A complete blood count and serum biochemistry were performed revealing a lymphopenia (858/μl, reference range of 1200–8000/μl) but was otherwise within normal limits. The patient continued to return at 28 day intervals for further assessment, laboratory work and treatment. Three months post diagnosis there was no gross evidence of disease and the patient was deemed to be in remission (Fig 2). After six doses of CCNU and methylprednisolone, the patient remained in clinical remission. Consequently, all treatment was discontinued. Periodic rechecks every 3 months was recommended. Nine months since discontinuation of therapy, the patient continues to remain in complete remission.

Feline mast cell tumors account for 2–20% of all feline neoplasms. More specifically, MCTs are the second most common cutaneous tumor in cats and show a clear male sex predilection of 2:1 (Garner and Lingeman 1970, Macy 1986, 286 ZM Wright and JD Chretin

Fig 1. A 0.5 cm pedunculated mass at the base of the tongue. Photo taken at initial presentation for referral.

Fig 2. Follow up photograph taken 4 months later. No evidence of original lesion. The tumor is in perceived remission.
Feline mast cell tumors can occur cutaneously, viscerally and systemically. Upwards of 50% of all mast cell disease in felines are cutaneous in nature with 50% of these lesions located on the head and neck (Ogilvie 1996, Rogers 1996). Other cutaneous sites include the limbs and body wall (Ogilvie 1996). There are rare cases of ulcerative lip lesions being diagnosed as feline mast cell disease as well as the sporadic report of oral involvement in dogs (Macy 1986, Guerger and Scott 1987). However, to the author’s knowledge, there are no documented reports of feline oral mast cell tumors.

Intestinal MCT is the third most common gastrointestinal neoplasm of the cat (Thamm and Vail 2001). Recent literature suggests that lymphoma and MCT, which occur with similar frequency, are the two most prevalent neoplastic diseases associated with the feline spleen (Hanson et al 2001). Furthermore, both splenic and bone marrow infiltration commonly occur with systemic mastocytosis. It is important to note that feline systemic mastocytosis can routinely develop independent of cutaneous lesions (Rogers 1996).

Histological grading of feline mast cell tumors is far more complex and significantly less prognostic than the canine grading system (Guerger and Scott 1987, Molander-McCary et al 1998, Johnson et al 2002). In dogs, grade I describes well-differentiated dermal lesions. Grade II describes intermediate differentiation with indistinct cellular borders and infiltration. Grade III describes a highly mitotic, undifferentiated tumor (Patnaik et al 1984). This grading system has proved effective in predicting outcome in dogs but it has failed to accurately predict prognostic outcome in feline patients. Consequently, a simplified and more prognostic feline grading system divides MCT into two primary categories. The cutaneous histiocytic form is markedly lymphoid and eosinophilic in nature, most common in Siamese cats less than 4 years of age, and imitates granulomatous inflammation because of the eosinophilic infiltration and its tendency to be non-encapsulated (Wilcock et al 1986, Molander-McCary et al 1998). The mastocytic form contains cells that morphologically resemble mast cells, and is further subdivided into compact (well-differentiated) and diffuse (anaplastic) lesions. The diffuse form, while accounting for only 10% of feline MCT, is classically anaplastic and infiltrative, with marked anisocytosis, giant cells, and eosinophils (Wilcock et al 1986, Molander-McCary et al 1998, Thamm and Vail 2001). The presence of high mitotic activity in the diffuse form is associated with a high rate of metastasis and a subsequently poorer prognosis (Rogers 1996, Johnson et al 2002). Numerous studies have shown that the well-differentiated compact MCT (representing up to 90% of all feline mast cell tumors) generally behave in a more benign fashion with a relatively low metastatic rate of between 0 and 14% (Macy 1986, Wilcock et al 1986, Molander-McCary et al 1998, Thamm and Vail 2001, Johnson et al 2002).

Historically, the difficulty in grading feline MCT results in a greater difficulty of predicting prognosis. The histiocytic lesions found in young Siamese cats have a tendency to regress spontaneously (Guerger and Scott 1987). Recent literature suggests compact cutaneous MCT, even with marked pleomorphism, routinely exhibit benign characteristics and can consequently justify a good prognosis (Guerger and Scott 1987, Molander-McCary et al 1998, Johnson et al 2002). A high mitotic rate found only with the diffuse form of cutaneous MCT appears to be the only definitive predictor for a poor prognosis (Johnson et al 2002). With systemic and/or visceral disease, metastasis is common. Furthermore, paraneoplastic syndromes with systemic involvement are common justifications for a guarded prognosis. These syndromes, include but are not limited to, delayed wound healing, gastric ulceration, hypotensive shock and coagulation abnormalities (Rogers 1996).

Surgery remains the primary option for both non-metastatic cutaneous tumors and visceral disease. It is interesting to note that splenectomy in cats with systemic mastocytosis may result in greater than 1 year of stable disease (Feinmehl et al 1992). Likewise, resection and anastomosis is the treatment of choice for non-metastatic intestinal MCT. However, due to the high metastatic rate and local invasiveness of intestinal MCT, surgery may only offer short-term palliation. Therefore, adjunctive chemotherapy may
be warranted. Multiple studies have shown that incomplete excision of benign cutaneous mast cell tumors does not negatively affect prognosis (Wilcock et al 1986, Molander-McCary et al 1998, Thamm and Vail 2001). The oral lesion in question was not excised due to location, possible regional lymph node metastasis, and because of the fractious nature of the patient.

Older studies advocated the use of corticosteroids as both a systemic and intrallesional therapy for canine and feline MCT (Macy 1986, Ogilvie 1996, Rogers 1996), however, no recent literature supports this claim. Anecdotally, feline MCT appears less responsive to corticosteroids than the canine counterpart, but this question has not been carefully investigated. It is this lack of scientific evidence, which prompted the authors’ use of CCNU in conjunction with methylprednisolone.

Radiation therapy is now a common treatment modality in dogs. Multiple studies indicate that greater than 85% of canines with stage 0 (residual microscopic disease) grade II MCT treated with radiation have a reported 3 year disease free interval (Al-Sarraf et al 1996, Frimberger et al 1997). However, the indications and benefits of radiation therapy are still being evaluated in cats. Numerous factors, including multiple anesthetics and cost, may make radiation an unattractive option for owners.

Chemotherapy, either alone or as an adjunct to other treatment modalities, is primarily advocated when systemic or metastatic disease is present. The recent literature suggests CCNU (1-(2-chloroethyl)3-cyclohexyl-1-nitrosurea) is a viable treatment option for cutaneous mast cell disease. Rassnick et al (1999) showed a partial response rate of 37% in dogs, defined as a greater than 50% reduction of tumor mass. Furthermore, 32% of cases resulted in stable disease. There was no correlation, however, between response rate and histological grade (Rassnick et al 1999).

A phase I clinical trial of CCNU in cats with various end stage neoplasms resulted in a partial response in one cat with cutaneous MCT and a stable disease response in the another with cutaneous MCT (Rassnick et al 2001). The standard dosage of 50–60 mg/m² used on our patient was developed from that clinical trial. As observed, the neutropenic nadir occurred in the reported time frame of 7–28 days post therapy (Rassnick et al 2001). The dose limiting side effect of CCNU in cats appears to be the duration of the neutropenic nadir which can last up to 14 days. However, no cats in the previous study developed clinical signs of infection during that period (Rassnick et al 2001). Furthermore, no organ toxicity beyond myelosuppression was noted in any of the 25 feline patients treated with CCNU (Rassnick et al 2001). This information, in conjunction with the Rassnick canine study (Rassnick et al 1999), indicates that CCNU is a viable option for the treatment of non-surgical and/or metastatic feline MCT.

Our patient was selected for treatment with CCNU for several reasons. First, as previously stated, there is no current literature reporting on the incidence or behavior of oral MCT in a cat. Histopathology suggested the tumor displayed characteristics of both the compact (well differentiated and low mitotic index) and diffuse (invasiveness and presence of eosinophilia) forms of feline mastocytic MCT. Consequently, prognosis, behavior and response to therapy were all relatively unknown. Secondly, radiation treatment was not financially feasible for this patient, yet therapy was needed to alleviate the clinical signs of gagging and dysphagia. Furthermore, submandibular lymphadenopathy, in conjunction with occasional (1 per 10 hpf) well-differentiated mast cells within the lymph node was suggestive of, (but not diagnostic for), regional metastasis. It is important to note that the inflammatory response secondary to the primary tumor could also be responsible for the lymphadenopathy as the lymph node cytology as a whole was consistent with reactive lymphoid hyperplasia. Finally, the choice of CCNU was based upon the positive, although minimal, data of both of the Rassnick studies regarding the use of CCNU in the treatment of cutaneous MCT in different species. Based upon the successful outcome of this patient (given the initial presentation of clinical signs and metastasis), CCNU may offer palliation to cats presenting with similar clinical findings. Additionally, based on the information presented in this case study, feline oral MCT may carry a fair prognosis if clinical signs can be alleviated. This case supports the need for a carefully designed prospective study looking at the efficacy of CCNU in feline MCT disease as well as documenting incidence and a more exact grading scale for feline oral MCT.

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References


