

PALPEBRAL MAST CELL TUMOUR IN A DOG. A CASE REPORT

MASTOCITOM CU LOCALIZARE PALPEBRALĂ LA UN CÂINE. RAPORT DE CAZ

Diana Mihaela ALEXANDRU^{1),*}, Maria CRIVINEANU¹⁾,
Inmaculada MORALES²⁾, Otilia FERRER QUINTANA²⁾

ABSTRACT | REZUMAT

Mast cell tumour (MCT) is a common cancer in dogs, this type of tumour has a variable biological behaviour which is why the chosen therapeutic management will be different depending on the case.

The aim of this case report is to describe the evolution of a canine mast cell tumour and its response to the treatment. The patient, a half breed dog of 13 years old, had an eyelid tumour (histopathological evaluation showed a mastocytoma) surgically excised which shortly recurred. The administration of toceranib (tyrosine kinase inhibitor) resulted in significant remission of the tumour, but due to the onset of side effects the treatment had to be stopped. In one month without treatment, the tumour recurred with much larger dimensions, metastases appeared, and the patient's condition worsened. Palliative treatment was recommended in order to improve the quality of life of the patient.

Choosing a therapeutic protocol in veterinary oncology is sometimes difficult because it is influenced by so many factors and must be constantly adapted to the patient. In this case, therapeutic management included early excision of the tumour and chemotherapy, but the results depended of the patient's tolerance and the tumour's characteristics. The patient was constantly monitored and the systemic therapy was modified every time it was needed to achieve maximum therapeutic effect with minimal adverse reactions.

Key words: cancer, mast cell tumour, toceranib, tyrosine kinase inhibitor

Mastocitomul este un tip de cancer des întâlnit la câini, această tumoare prezintă un comportament biologic variabil, motiv pentru care managementul terapeutic ales va fi diferit în funcție de caz.

Scopul acestui raport de caz este de a descrie evoluția unei mastocitom și răspunsul acestuia la tratament. Pacientul, un câine, metis, în vârstă de 13 ani, a avut o tumoare palpebrală (evaluarea histopatologică a arătat un mastocitom) excizată chirurgical, care a recidivat la scurt timp. Administrarea de toceranib (inhibitor de tirozinază) a dus la o remisie considerabilă a tumorii, dar din cauza debutului efectelor secundare tratamentul a fost oprit. Într-o lună fără tratament, tumora a recidivat, având dimensiuni mult mai mari, au apărut metastaze și starea pacientului s-a agravat. S-a recomandat tratament paliativ pentru a îmbunătăți calitatea vieții pacientului.

Alegerea unui protocol terapeutic în oncologia veterinară este uneori dificilă, deoarece este influențată de foarte mulți factori și trebuie adaptată în mod constant pacientului. În acest caz, managementul terapeutic a inclus excizia precoce a tumorii și chimioterapia, dar rezultatele au depins de toleranța pacientului și de caracteristicile tumorii. Pacientul a fost monitorizat constant și terapia sistemică a fost modificată de fiecare dată când a fost nevoie pentru a obține efectul terapeutic maxim cu reacții adverse minime.

Cuvinte cheie: cancer, mastocitom, toceranib, inhibitori de tirozinază

Mast cell tumours (MCTs) are the most common types of cutaneous cancer in dogs, representing about 7% to 21% of all dog skin tumours and 11% to 27% of malignant skin tumours (3, 9). The majority of canine MCTs appear as solitary tumours but multiple tumours can be also encountered (1). MCTs can affect dogs of any age but generally occur in dogs over the age of 9 years old, there is no predisposition for sex, some breeds such as Boxer, Pugs, Terriers, Retrievers pre-

sent a risk by up to 8 times higher than the rest of the breeds (8, 11). Some studies shown that breed predilections are based on genetic causes. Mutations in the c-kit tyrosine kinase receptor, which can lead to malignant transformation of mast cells, are found in up to 50% of intermediate to high-grade tumours (5, 13). The KIT receptor promotes the malignant process when it has a mutation (4). These mutations result in continuous activation of c-kit and unregulated cell growth (13).

Canine MCTs treatment differs depending on many factors such as tumour grade and stage, growth rate, MI (mitotic index), tumour location, animal status and it involves surgery, chemotherapy, radiation therapy, used either individually or in combination (6, 7).

1) University of Agronomic Sciences and Veterinary Medicine, Faculty of Veterinary Medicine, Bucharest, Romania

2) University of Las Palmas de Gran Canaria, Faculty of Veterinary Medicine, Veterinary Hospital

*) Corresponding author: albu.dm@gmail.com

Surgical removal is the treatment of choice for canine MCTs, when is reasonable, taking into account patient and tumour factors. Complete excision is the most important for local tumour control, the most of low grade MCTs can be controlled long-term with wide margin surgical excision (2-3 cm laterally and a fascial plane deep) (2, 3, 4). Systemic therapy (chemotherapy, TKI - tyrosine kinase inhibitor therapy) is considered in dogs with poor prognostic indicators (e.g. high grade and MI, metastasis), for non-excisable tumours, as adjuvant, neoadjuvant or palliative therapy (corticosteroids) (6). Various chemotherapeutic agents can be used alone or in combination in the treatment of canine MCTs, with ORR (overall response rates) between 20–60% (1). The most commonly used are Vinblastine + Prednisone and Lomustine (10). Tyrosine kinase inhibitors like toceranib and masitinib are used successfully in MCTs therapy, studies show that in dogs with an activating mutation in the c-kit gene the ORR have increased up to 69% (1). Generally, mast cell tumours with c-Kit mutations have a greater response to toceranib, but some recent studies shown that tumours without mutations can also respond to toceranib (with an ORR around 30%) (6, 8, 12). Toceranib have both direct antitumour and anti-angiogenic activity, so it controls cell division by killing tumour cells and also by cutting off the blood supply to the tumour. The favourable evolution and response to the treatment with tyrosine kinase inhibitors results from the presentation of the following case report. There are also shown the adverse reactions occurred following treatment and the aggressive evolution of the mast cell tumour in a dog.

MATERIAL AND METHODS

A 13 years old, male, half-breed dog was presented at the clinic for evaluation because it had a mass at the eyelid of the left eye. The owners noticed that the palpebral mass appeared three months ago and since then tears are more intense. At the clinical examination no other changes were noticed. The fine-needle aspiration from the mass and the cytological examination were performed, indicating highly granulated mast cells with moderate numbers of eosinophils, following which the diagnosis of canine mastocytoma was made.

Abdominal ultrasound, thoracic and abdominal radiographs were performed in order to see if the mast cell tumour spread systemically, and as a result, the presence of metastases was not detected. The blood tests were performed (complete blood count - CBC and serum chemistry) and they revealed no significant abnormalities so the patient was scheduled for surgical intervention. The mass was removed (Fig. 1) and sent for histopathological evaluation.



Fig. 1. In figure A is the patient before the surgery, it has an eyelid mass of 1 cm and in figure B is the patient after the surgery

The neoplastic cells corresponded to well differentiated mast cells, with scarce mitosis (1 per field of 400 magnifications), which infiltrate the collagen fibers, glandular epithelium and muscle fibers. Accompanying the process, acanthosis, interstitial oedema, collagen hyalinization and infiltration of few eosinophilic polymorphonuclear leukocytes can be seen. Following the histopathological examination, the diagnosis of well differentiated palpebral mastocytoma (grade II) was established. Postoperative management included fluid therapy, analgesia, appropriate nutritional support, systemic treatment with corticosteroids (Prednisone for three weeks, after the first week the dose was halved) and locally was used Tobrex ointment.

After the surgery the patient's recovery was rapid but after four months he returned at the clinic with a palpebral tumour on the left side (3.8 × 2.5 cm) and with severe ipsilateral lymphadenopathy (Fig. 2).

Upon examination, it was observed that the patient was lethargic, it had inappetence, 40°C temperature and the mass was ulcerated.

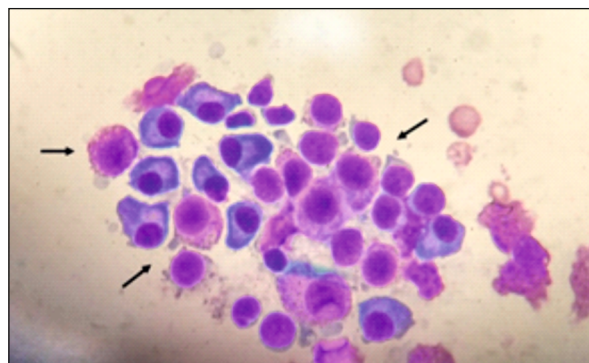


Fig. 2. Cytology of fine needle aspirate from the lymph node. The arrows show granulated mast cells. Diff-Quik ×100

At the cytology examination, were observed cells with multiple basophile granules, compatible with mast

cells. Systemic treatment with antibiotics (amoxicillin and clavulanic acid), tyrosine kinase inhibitors (toceranib) in combination with corticosteroids (prednisone) was instituted. For gastric protection was recommended omeprazole.

RESULTS AND DISCUSSIONS

Improvements were observed immediately after the administration of chemotherapy. The action of tyrosine kinase inhibitors was favourable and rapid, after 2 weeks of treatment the decrease in size of the tumour could be observed. The evolution was unexpectedly good, leading to the significant remission of the tumour (Fig. 3).

Unfortunately, after one month the treatment was stopped because of the adverse reactions. The dog was apathetic, shown lack of appetite, vomiting and diarrhoea. Gastrointestinal complications are most common in therapy with toceranib and the specialty literature recommends stopping therapy and treating symptoms. After stabilizing the patient, toceranib therapy was resumed but this time the dose was reduced from 3.25 mg/kg to 2.2 mg/kg. Although the dog received gastric protection and the dose was low (2.2 mg/kg), gastrointestinal complications recurred, so the treatment had to be stopped again.

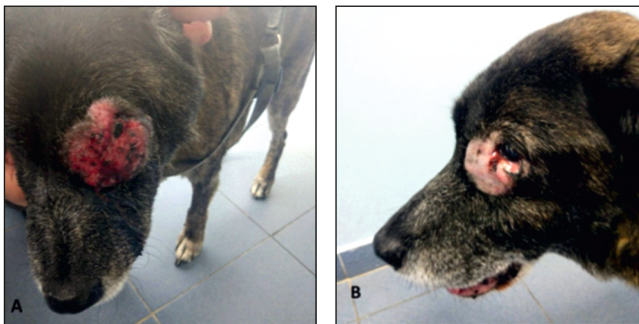


Fig. 3. In figure A is the patient before the treatment, it has an ulcerated mass of 3.8×2.5 cm and in figure B is the patient after treatment with toceranib

After stopping the treatment with toceranib, the gastrointestinal symptoms diminished, but soon the patient's condition worsened. It became lethargic and a gradual weakening was observed. In just one month without treatment the tumour recurred, having a much larger dimension than initially (Fig. 4).

The blood tests highlighted severe anaemia and a CT scan was performed, after which we observed that the tumour had a greater dimension than we expected, and it was extending retrobulbar (Fig. 5). The CT scan also revealed the appearance of metastases in the liver. Considering the aggressiveness of the tumour and the patient's condition, palliative treatment

was recommended to maintain the patient comfort. Euthanasia was also recommended when the quality of life of the animal decreases.



Fig. 4. The recurred tumour (an ulcerated mass of 4×3.5 cm covering the left eye), after one month without treatment



Fig. 5. Axial CT scan of the retrobulbar mass

CONCLUSIONS

Canine mast cell tumours represent a challenge because they can have an unexpected and aggressive evolution. Predictions for their behaviour are difficult to make and the prognosis is influenced by many factors. When they have a poor localization and the excision at 2-3 cm from the tumour edge can't be obtained, there is a high probability of recurrence.

In these cases, chemotherapy provides good results, but the patient should be monitored permanently because the side effects are common.

The administration of tyrosine kinase inhibitors can have remarkable results because a significant percentage of canine MCTs possess an activating mutation in the c-kit gene.

This case report highlights that during the administration of toceranib the tumour had a considerable remission. It is also shown that when treatment is discontinued the tumour growth is very rapid and the patient's condition deteriorates.

REFERENCES

1. Britton Brooke M., (2019), Mast Cell Tumors. Clinician's Brief, December 2019, 31-37. Available at: <https://www.cliniciansbrief.com/article/mast-cell-tumors> (Accessed: May 15, 2020)
2. Cahalane A.K., Payne S., Barber L.G., Duda L.E., Henry C.J., Mauldin G.E., Frimberger A.E., Cotter S.M., Moore A.S., (2004). Prognostic factors for survival of dogs with inguinal and perineal mast cell tumors treated surgically with or without adjunctive treatment: 68 cases (1994-2002). *J Am Vet Med Assoc*, 225(3):401-408
3. Fan T.M., Lorimier L.P., (2005), Treatment options for canine cutaneous mast cell tumors. *Veterinary Medicine*, 100:272-284
4. Fournier Q., Cazzini P., Bavcar S., Pecceu E., Ballber C., Elders R., (2018), Investigation of the utility of lymph node fine-needle aspiration cytology for the staging of malignant solid tumors in dogs. *Veterinary Clinical Pathology*, 47 (3):489-500
5. Garrett L., (2014), Canine mast cell tumors: diagnosis, treatment, and prognosis. *Veterinary Medicine: Research and Reports*, 5:49-58
6. Horta R.S., Lavalle G.E., Monteiro L.N., Souza M.C.C., Cassali G.D., Araújo R.B., (2018). Assessment of Canine Mast Cell Tumor Mortality Risk Based on Clinical, Histologic, Immunohistochemical, and Molecular Features. *Vet Pathol*, 55 (2):212-223
7. Kiupel M., Camus M., (2019), Diagnosis and Prognosis of Canine Cutaneous Mast Cell Tumors. *Vet Clin North Am Small Anim Pract*, 49(5):819-836
8. Moore A.S., Frimberger A.E., (2009), Mast Cell Tumor in dogs. Chapt. 27, (Ed.) Blackwell Publishing, USA
9. Newman S.J., Mrkonjich L., Walker K.K., Rohrbach B.W., (2007), Canine subcutaneous mast cell tumour: diagnosis and prognosis. *J Comp Pathol*. 136 (4):231-239
10. Olsen J.A., Thomson M., O'Connell K., Wyatt K., (2018), Combination vinblastine, prednisolone and toceranib phosphate for treatment of grade II and III mast cell tumours in dogs. *Vet Med Sci*, 4(3): 237-251
11. Smiech A., Lopuszynski W., Slaska B., Bulak K., Jasik A., (2019), Occurrence and Distribution of Canine Cutaneous Mast Cell Tumour Characteristics Among Predisposed Breeds. *J Vet Res*, 63(1): 141-148
12. Weishaar K.M., Ehrhart E.J., Avery A.C., Charles J.B., Elmslie R.E., Vail D.M., London C.A., Clifford C.A., Eickhoff J.C., Thamm D.H., (2018), c-Kit Mutation and Localization Status as Response Predictors in Mast Cell Tumors in Dogs Treated with Prednisone and Toceranib or Vinblastine. *J Vet Intern Med*, 32(1):394-405
13. Willmann M., Hadzijušufovic E., Hermine O., Dacasto M., Marconato L., Bauer K., Peter B., Gamperl S., Eisenwort G., Jensen-Jarolim E., Müller M., Arock M., Vail D.M., Valent P., (2019), Comparative oncology: The paradigmatic example of canine and human mast cell neoplasms. *Veterinary and comparative oncology*, 17(1):1-10.