

CLINICAL AND PATHOLOGICAL ASPECTS IN 2 CASES OF CANINE MASTOCYTOMA

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Summary

Mast cells are well known for their neoplastic transformation in solitary and multiple cutaneous mast cell tumours, as well as visceral and systemic mastocytosis. In this paper we are presenting 2 cases brought in our Emergency Clinic for consultation, which were diagnosed with canine mastocytoma. In both of the patients, the tumor started as a single nodule. They were diagnosed with grade 3 mastocytoma using cytological and histopathological exam. Combined therapy of vinblastine and prednisolon has proven poor efficiency. Survival times, after the diagnosis, were 35 days (patient 1) and 22 days respectively (patient 2).

Key words: mast cell tumor, mastocytoma, dog

Mastocytoma is a tumor of the subcutaneous connective tissue, but it can also be found in internal organs, in submucosae and the hematopoietic system. The term mastocytoma defines a neoplastic process, as it is known that there is a local reaction with mast cell agglomerations (oedema, allergic reactions etc.), when the term mastocytosis is used (1).

The constitutive cell of mastocytoma is rich in bioactive substances (histamine, heparin, enzymes, prostaglandins, chemotactic factor for eosinophils etc.) is susceptible to spontaneous degranulation and to act on long distance targets (paraneoplastic gastro-duodenal ulcers) (3).

Dogs have a unique risk of developing cutaneous mast cells tumours (MCT), with an unknown aetiology, which is probably multifactorial (6). Important prognostic information can be gained from histological grading and assessment of surgical margins. Surgical excision is indicated if the tumor is solitary and is the treatment of choice for grade 1 and 2 MCT. Grade 3 or metastatic MCT are best treated by chemotherapy and/or palliative therapy. Active chemotherapy agents include vinblastine and lomustine. Recent identifications of mutations in tyrosine kinase receptors on MCT cells imply an exciting new therapeutic role for drugs that target these receptors (4).

It is uncommon to diagnose MCTs without skin involvement in dogs. Mast cells tumours vary greatly in appearance and no estimate of their malignancy or prediction of their behaviour can be made on clinical appearance alone. Some

MCTs may be present for months to years before rapidly disseminating; others act aggressively from the beginning (4).

Occasionally, mechanical manipulation during examination of this tumor causes degranulation of mast cells, producing erythema and wheal formations, phenomenon which is considered of diagnostic significance. Clinical appearance of MCTs may vary widely but diagnosis is relatively easy using aspiration cytology. However, excisional biopsy is required for accurate histological grading of the tumour.

Histopathologic grading of the tumour has been correlated with both recurrence and survival. All dogs with MCTs should be staged to determine the extent of their disease.

Materials and methods

The biological material of this case report was represented by two dogs brought in our Emergency Clinic for consultation. The first one was a Collie, female, aged 12 years (patient no. 1); physical examination revealed lethargy, weight loss over the past month; she also presented a subcutaneous mass on the extern angle of the left eye, which had retroorbital extensions. The mass had grown, by the owner's opinion, in the last month.

The second dog was an Alaskan Malamute, male, aged 7 years (patient no. 2). Clinical findings were anorexia and occasionally vomiting, moderate oedema of the right front limb, moderate oedema of the right thoracic wall. On this patient, an ultrasonography exam was also performed.

We sampled blood from both of the patients and we made a complete blood count and a routine biochemical screening (urea, creatinine, ALT, Alp). Urine was also sampled and we performed a microscopic exam and urine test (with test strips Combi 11- Medi-Test).

Cytological examination of fine-needle aspirate was performed in the Pathology department using rapid Dia Quick staining.

Tissue biopsies from both dogs were examined using the usual hematoxylin - eosin stain (HE).

The histopathological exam from the tumor mass samples was processed by paraffin technique and the slides were stained both using Tricrom Masson (TM) technique and haematoxilin –eosin technique.

Results and discussions

Clinical findings

We found general symptoms such as lethargy, losing weight (in patient no. 1), anorexia and occasionally vomiting (in patient no. 2).

Patient no. 1 had a single subcutaneous nodule on the head region, peri- and retroorbital. Involvement of regional lymph nodes, liver, or spleen was not observed.

Patient no. 2 presented in the first phase oedema of the right front limb and moderate oedema of the right thoracic wall. Later he developed oedema of the right rear limb, and generalized oedema of the right side of the body, pain at palpation and also at sitting down and getting up. Concerning lymph node status, he presented involvement of right regional lymph nodes. Local ultrasonography revealed fluid accumulation and also an abnormal subcutaneous tissue (4-5 cm in diameter). The owner explained that 2 months earlier, he went with him to another clinic and there the dog was sterilized. At that time the patient had a small cutaneous nodule (1 cm in diameter) on the right thoracic wall, behind the olecranon, which was also removed surgically, without making a histopathological exam.

Biochemistry/urinalysis

Blood hematology revealed in both patients anemia and thrombocytopenia; values of the biochemical parameters were found in the normal range and the urinalysis was also normal.

Diagnosis

The diagnostic was based on cytological examination of fine-needle aspirates. Fine needle cytology revealed the presence of pleomorphism, anisocytosis, anisokaryosis, and fewer cytoplasmic granules that are small in size. Cytoplasmic granules were also observed outside the cells, following the destruction of some mast cells during aspiration. The cells had a bizarre appearance, with a predominance of round and oval cells, poorly differentiated with an increase mitotic activity.

Histologic exams were performed from biopsy samples and from the tumor mass following either surgery or necropsy exams. The histopathological exam revealed important cellularity, marked cellular pleiomorfism, with anisocytosis and anisokaryosis (picture number 1), increased mitotic index (picture number 2 and 3), and the presence of eosinophils in the tumor mass. Eosinophils are present because of eosinophil chemotaxis to histamine release by the mast cells (picture number 2). Cytoplasm granules are present, but they are small in size, compared with grade 1 or 2 tumors.

Grading of mast cell tumors historically has been based upon cellular pleomorphism. Typical characteristics have included anisocytosis, anisokaryosis, vesicular nuclei with prominent nucleoli, degree of cytoplasmic granulation, and mitotic activity (2). The current classification according to Patnik, divides mast cell tumors in 3 grades, grading representing an important prognostic factor in these tumors (3). Both our cases were diagnosed with grade 3 mast cell tumor, which is more likely to be incompletely excised, more likely to metastasize and nearly 4 times more likely to lead towards death than tumors of lower grades (4).

Surviving rate for dogs with grade 3 tumors is of 6% at 1500 days, compared with grade 2 tumors where there is a 45% surviving rate at the same period and 93% in the case of grade 1 tumors (3).

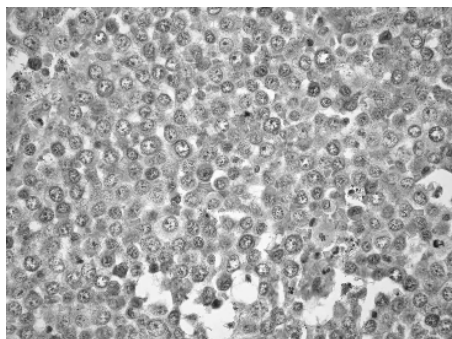


Fig. 1: Poorly differentiated mast cells, cutaneous neoplasm - patient no. 2. The mast cells are round to oval, they exhibit anisocytosis, anisokaryosis with sparse cytoplasmic granulation (HE x 200)

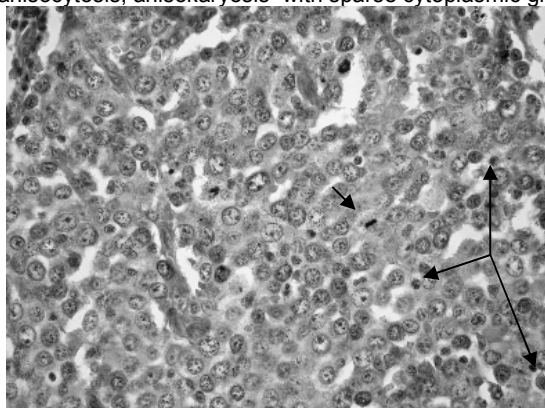


Fig. 2. Neoplastic mast cells present an increased mitotic index (single arrow) and we note the presence of eosinophils (triple arrow) (HE x 200)

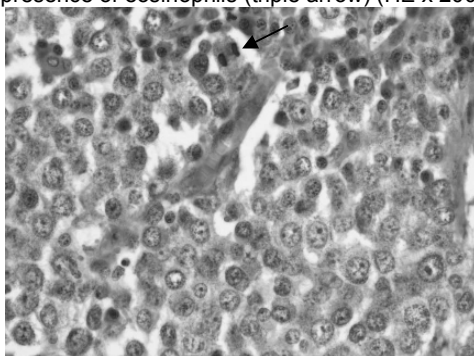


Fig. 3: Poorly differentiated mast cells, with few cytoplasmic granules, small in size, and mitoses (arrow) (HE x 400)

Treatment

In both of the patients the treatment was based on surgical excision and was completed with daily oral prednisone (1 mg/kg PO q24h) and injectable vinblastine (2–3 mg/m² IV; administered on day 1 of each 21-day cycle) (5) as adjuvant therapy to incomplete surgical resection. Also, they received analgesic medication, cimetidine (10 mg/kg q8h), and fluid therapy when needed.

Dogs with lower grade tumors seem to respond better to therapy. Dogs older than 8 years are nearly 3 times more likely to die of their disease after treatment for MCTs. Cytological exam from the excision margins or from the local lymph nodes aspirates were not performed, as it is recommended (3, 4).

Evolution

Response to therapy was poor. In patient no. 1 the owner decided on euthanasia 35 days after the initiation of chemotherapy. Patient no. 2 died suddenly after 22 days of therapy.

Conclusions

The tumor started in both of the patients, in the first phase as a single nodule.

Survival times, after the diagnosis of grade 3 mastocytoma for the two patients, were 35 days (patient 1) and 22 days respectively (patient 2).

The tumor in both patients had a poor prognosis, which proves once again that mast cells tumors in dogs are very aggressive.

All mast cell tumors should be submitted for both cytology and biopsy, as both exams are complementary and could be correlated with the prognostic.

Combined therapy of vinblastine and prednisolon had only poor efficiency in both cases.

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