INFLAMMATORY FORM OF HISTIOCYTOMA
WITH A MALIGNANT COURSE IN A DOG.
A CASE REPORT

MARCIN NOWAK, JANUSZ A. MADEJ, MARTA GOTOWIECKA1, HIROAKI KANZAWA2, AND PIOTR DZIĘGIEL3

Department of Pathological Anatomy, Pathophysiology, Microbiology, and Forensic Veterinary Medicine, Faculty of Veterinary Medicine, Wroclaw University of Environmental and Life Sciences, 50-375 Wroclaw, Poland
1Student of Faculty of Veterinary Medicine, Wroclaw University of Environmental and Life Sciences, 50-366 Wroclaw, Poland
2Specialistic Hospital for Animals “Kanzawa”, 51-147 Wroclaw, Poland
3Department of Histology and Embryology, Medical University, 50-368 Wroclaw, Poland
marcin.nowak@up.wroc.pl

Received for publication November 12, 2008

Abstract

The aim of this paper is to describe the case of a 10-year-old Siberian husky with a right upper lip neoplastic tumour and a metastasis to a submandibular lymph node. Histopathological examination with application of immunohistochemistry confirmed neoplastic outgrowth with an inflammatory form of histiocytoma and a high proliferative potential. Local progression of the neoplastic disease occurred despite the removal of the primary tumour and neoplastically infiltrated lymph node.

Key words: dog, histiocytoma, histopathology, immunohistochemistry.

Histiocytoma is the most frequently manifested non-malignant tumour originating from histiocytic cells. Theirs precursors are dendritic cells, localised in the skin. The lesion prevalence amounts up to 14% of dermal tumours in dogs and most frequently affects young animals (2, 10, 12). Although commonly it is histologically malignant in character, histiocytoma is not a malignant tumour. Moreover, it used to be perceived as a non-neoplastic lesion, termed the histiocytosis of epidermotropic Langerhans cells (8). A spontaneous regression of the lesions is also described, usually in young individuals (8). Histiocytoma most often affects breeds such as small bulldogs, dachshunds, spaniels, German boarhounds and bullterriers (10, 15). Manifestation of histiocytoma in older animals is associated with much more unfavourable prognosis. In such cases, the process may rapidly undergo malignant transformation with the involvement of sentinel lymph nodes and even with distant metastases (2).

Malignant tumours originating from histiocytic cells, most frequently develop in dogs of moderate or advanced age. Studies carried out by Waters et al. (16) revealed that the average age of individuals with malignant fibrohistiocytoma is nine years. There is no significant difference in the incidence of the tumour between males and females. Moreover, studies of Kerlin et al. (6) proved a higher incidence of malignant fibrohistiocytoma in golden retrievers and rottweilers than in other dog breeds.

Macroscopically MFH is a tumour of a firm consistency, grey-whitish colour, more or less clearly separated from the surrounding tissues, and usually without capsule. Sometimes, fine petechiae and necrotic foci may be noted at a cross-section (7). There are several cell types of mesenchymal origin in the histological texture of the tumour: fibroblasts, mononuclear histiocytes, multinuclear giant cells, macrophages, granulocytes, and lymphocytes.
Reciprocal quantitative ratio of the cell groups determines biological character of the tumour (7). Furthermore, there are often abnormal, mitotic figures in cells of histiocytic fibrosarcoma.

Five morphological types of malignant fibrohistiocytoma afflict humans (pleomorphic, magnocellular, inflammatory, myxomatous, and vascular types), three forms occur in the veterinary medicine: the pleomorphic, inflammatory, and magnocellular types (3, 6, 13, 16).

The pleomorphic type resembles a well-differentiated fibrosarcoma or an extensive anaplasia. There are spindle-like, fibroblast-resembling cells arranged into a typical spiral pattern and spherical, histiocyte-resembling cells with traits of nuclear atypia (karyomegaly, presence of multiple nucleoli), along with polymorphic, multinuclear giant, and inflammatory cells. The inflammatory infiltrate contains lymphocytes, plasma cells, neutrophils, and, sporadically, eosinophils. In some cases, tumour stoma may include regions with a high content of collagen fibres. Such pattern of lesions occurs most frequently in cases of malignant histiocytoma of the skin and inner organs of dogs (7).

The lesion is identified as inflammatory form of MFH when the histological pattern is dominated by inflammatory cells, i.e. lymphocytes, plasma cells, eosinophils, and neutrophils against the background of histiocytic cell texture. Malignant histiocytoma in its inflammatory form occurs seldom and in most cases is localised in the spleen (7).

The magnocellular form consists of multinuclear giant cells above mononuclear histiocytes and fibroblasts. The histological pattern may include inflammatory cells (mainly granulocytes, lymphocytes, and plasma cells) but they are not typical of this form of the tumour.

**Description of the case and Discussion**

The discussed case is an inflammatory form of histiocytoma in a 10-year-old male dog of Siberian husky breed. The thickening on the right upper lip, protruding above the mucosa, located next to the first two premolars was noted (Fig. 1).

The lesion was oval in shape, 14x18 mm in size, of an uneven, depigmented surface with numerous fine petechiae. Palpation failed to disclose regional lymphadenopathy. Thin needle aspiration biopsy of the tumour was performed and the obtained material was used to prepare a smear, stained in a routine way by haematoxylin and eosin (HE). In the histological pattern, the presence of numerous atypical cells as well as individual neutrophilic and acidophilic granulocytes was detected (Fig. 2).

Acting with consent from the owner, it was decided to remove the lesion. The procedure was preceded by morphological and biochemical blood tests, which demonstrated no abnormalities. The lesion was excised together with the surrounding fragment of the lip (Fig. 3) and the tissue was sent for histopathological appraisal.

Fragments of tissue sampled from the neoplastic lesion were fixed for 24 h in a buffered formalin, passed in a routine way to paraffin blocks, cut to 4μm thick sections, then stained with HE. For histopathological evaluation of the preparations, WHO tumour classification was applied.

The microscopic examination allowed classifying the tumour as an inflammatory form of histiocytoma with a high proliferative potential, which was affirmed by numerous histiocytic cells with spherical or oval cell nuclei (Fig. 4).

In some places, the neoplastically transformed histiocytes showed foamy cytoplasm and numerous, mostly abnormal, mitotic figures. A dominant trait of the examined tumour was inflammatory infiltrate, consisting of neutrophilic and acidophilic granulocytes, lymphocytes, and plasma cells. In some regions of the tumour, there were a slight fibrosis and the presence of giant cells (Fig. 5). Bands of neoplastic cells, which penetrated in-between muscle fibres, were present in the peripheral zone. (Fig. 6).

In order to verify results of the standard histopathological staining (HE), the immunohistochemical technique using a panel of monoclonal antibodies was applied. The panel involved three antibodies, including those directed to vimentin (clone V9, dilution 1:100, DakoCytomation), to desmin (clone D33, dilution 1:50, DakoCytomation), and to cytokeratin (clone K, dilution 1:50, DakoCytomation). The reactions proved to yield positive results in the form of fine-granular and brown cytoplasmic deposits (Figs 7-8), which confirmed the preliminary diagnosis. It should be noted that positive reaction for cytokeratin (Fig. 9) was observed only in cells of the epithelium, which covered the lesion; the tumour cells proved to be negative in the test.

Approximately two weeks following the excision of the tumour, an enlargement of the right submandibular lymph node (approximately 40 mm in diameter) was noted. Histopathological examination of the biopsy material sampled from the lymph node displayed the presence of neoplastic cells, similar to those noted in the earlier removed tumour, numerous stimulated lymphocytes, acidophilic granulocytes, and individual neutrophils (Fig. 10).

Chest radiogram in the lateral projection and USG examination of the abdominal cavity demonstrated no significant alterations aside from those typical for the age of the patient (a slightly dilated outline of the heart, insignificant hypertrophy of the prostate gland). These tests let to make the decision to excise the altered lymph node. Histopathological analysis of the removed lymph node demonstrated numerous foci of neoplastically transformed histiocytic cells (Fig. 11).
Fig. 1. Lesion in the right upper lip in the dog of Siberian husky breed.

Fig. 2. Histiocytoma cells in a smear prepared from the tumour. HE, 400x

Fig. 3. Procedure of excision of the lesion together with the margin of healthy tissues.

Fig. 4. Neoplastically transformed histiocytic cells and an abundant inflammatory infiltrate. HE, 200x

Fig. 5. Regions of slight fibrosis in the tumour and presence of giant cells. HE, 200x

Fig. 6. Bands of neoplastic cells penetrating in-between muscle fibres. HE, 200x
Fig. 7. Expression of vimentin in the cytoplasm of histiocytoma cells. 400x

Fig. 8. Expression of desmin in the cytoplasm of histiocytoma cells. 400x

Fig. 9. Expression of cytokeratin in the cytoplasm of epithelial cells, which covered the lesion. 200x

Fig. 10. Histiocytoma cells in the smear of submandibular lymph node. HE, 200x

Fig. 11. Foci of neoplastically transformed histiocytic cells in the submandibular lymph node. HE, 400x
Malignant fibrohistiocytoma represents a neoplastic process, which may manifest itself in two forms: either as an individual tumour located usually in the skin or in the spleen, or as a diffuse process involving several inner organs, including, lungs, liver, kidneys, lymph nodes, and bones (5, 6). Histiocytic fibrosarcoma relatively rapidly yields metastases both by blood and lymphatic vessels, which significantly restricts survival of the affected animals (7). Studies carried out by Waters et al. (16) on 10 dogs with malignant form of histiocytoma showed that the average survival was 61 d from the recognition of the tumour. The regions predisposed to metastases included sentinel lymph nodes and next the lung tissue (7).

In our case, there was a relapse of neoplastic process in submandibular region despite of the removal of the primary focus and submandibular lymph node. The proliferating tumour was classified again as a malignant form of histiocytoma with a very high dynamics of growth, infiltrating laryngeal cartilages and trachea. The described case confirms the hypothesis that in older animals, despite the radical management, histiocytoma may be very malignant and difficult to control the neoplastic process. Imaging studies (radiogram, USG) detected no metastases in inner organs despite the rapid local expansion of the tumour. When the dog started to suffer from intense asphyxia, it was subjected to euthanasia. In addition, the autopsy examination demonstrated no distant metastases. It seems that in this case, similarly to some other tumours in animals, such as mammary carcinoma in bitches, no distant metastases develop despite the histologically clear malignant character of the primary tumour. This is in contrast to the situation in humans. The observation may suggest that in dog’s body there are several mechanisms, which block or restrict metastases. Their recognition and detailed understanding may assist in gaining control over the development of neoplastic diseases in humans.

References