Undifferentiated Pleomorphic Sarcoma (Malignant Fibrous Histiocytoma) of the Head in a Dog

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ABSTRACT. A six year-old intact female miniature poodle was presented with a soft mass of the forehead region. Computed tomography identified generalized frontal bone loss and a large extracranial mass, which had a low attenuation area of hemorrhagic necrosis with septation and enhancement of solid components. In magnetic resonance imaging, the mass was isointense in T1-weighted images except its fluid parts and hyperintense in T2-weighted images with lobulated by low-signal septa. Surgery was performed to remove the mass, and histopathologic examination revealed that the mass was consistent with undifferentiated pleomorphic sarcoma (malignant fibrous histiocytoma). The dog died from the rapidly recurrent mass and severe pulmonary metastasis.
KEY WORDS: canine, CT, malignant fibrous histiocytoma, MRI, undifferentiated pleomorphic sarcoma.

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Malignant fibrous histiocytoma (MFH) is a group of tumors with histologic characteristics resembling histiocytes and fibroblasts [1, 4] and is considered to be a synonym for undifferentiated pleomorphic sarcoma according to the latest World Health Organization classification of soft tissue tumors [2]. MFH has been reported in small animals and appears most commonly in the subcutis of the trunk or hind limbs in both dogs and cats, but in the dog, it is considered to be more common in spleen [1]. MFHs of head origin have been rarely reported in humans and small animals. Moreover, veterinary reports with an emphasis on the imaging features of MFH are limited. This report describes the imaging characteristics and immunohistochemistry results in a dog with undifferentiated pleomorphic sarcoma (MFH).

A six-year-old intact female miniature black poodle weighing 2.8 kg was presented to an local animal hospital with a small subcutaneous mass on the forehead. The veterinarian surgically removed the mass without histological examination. The mass recurred in the same region and contained bloody exudates on fine needle aspiration. The dog showed anorexia and depression with a dramatically enlarged forehead mass for one week. The dog was referred to the Veterinary Teaching Hospital of the Chungnam National University for further examinations one month after initial presentation.

The dog had an approximately 5 × 4 × 3-cm sized tender and non-painful mass on the left frontal region on physical examination. The mass kept growing from the frontal region to the left eyelid in the 4 days after admission. Despite this condition, the dog's rectal temperature, respiratory rate and pulse were within the normal ranges. There

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were no remarkable findings on neurological and blood and serum biochemical examinations.

Skull and thoracic radiography and ultrasonography of the mass were performed. Radiography of the skull revealed a large soft tissue density mass in the forehead. The frontal bone appeared intact in lateral radiography. Thoracic radiographs showed small round soft tissue opacity in the left cranial lung lobe and 7–10th rib fractures as old trauma. Ultrasonography (Sonoace 8800, Medison, Seoul, Korea) showed the mass consisted of two parts, an oval hyperechoic lesion and irregularly septated anechoic areas with variable sizes and shapes. Fine needle aspiration was performed with ultrasonographic guidance. Thick bloody exudates were obtained.

CT examination was performed to evaluate the relationship between the mass and skull bone, and to evaluate lung metastasis. CT images were obtained with a third-generation whole body scanner (CT Max®, GE, Milwaukee, WI, U.S.A.). The dog was positioned in sternal recumbency, and contiguous transverse 2-mm-thick images of the skull were obtained. CT scans showed a large extracranial mass generally involving the left frontal bone. The mass had a lobulated low-attenuation area with a fluid-cell interface and irregularly enhancing solid parts and septa (Fig. 1). There was no evidence of calcification. Extensive lytic changes of the frontal bone and temporal bone were seen in bone window images (Fig. 1C). Enhanced images showed a definite margin of the mass, and the tumor did not appear to invade the brain, although there was mild compression in the frontal and temporal lobes of the brain (Fig. 1B). A thoracic CT scan was also performed and showed a small soft tissue attenuating nodule in size of 1 × 1-cm size in the left cranial lung lobe.

MRI of the brain was performed with a 0.2-T permanent magnet (VetMR®, Esaote, Genoa, Italy) using a standard
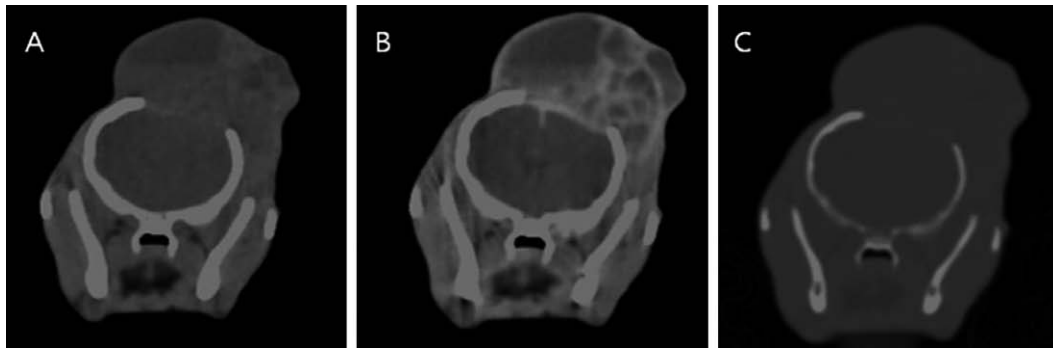
Fig. 1.   Soft tissue window (A), contrast enhanced (B) and bone window (C) transverse CT images at the level of the frontal lobe. There is a large lobulated mass with contrast enhancing septa (A, B). Hemorrhagic contents are shown as hypodense fluid at the non-dependent part and slightly hyperdense cellular sediments at the ventral dependent part. The lytic change of the left frontal bone was marked in the bone window CT image (C).
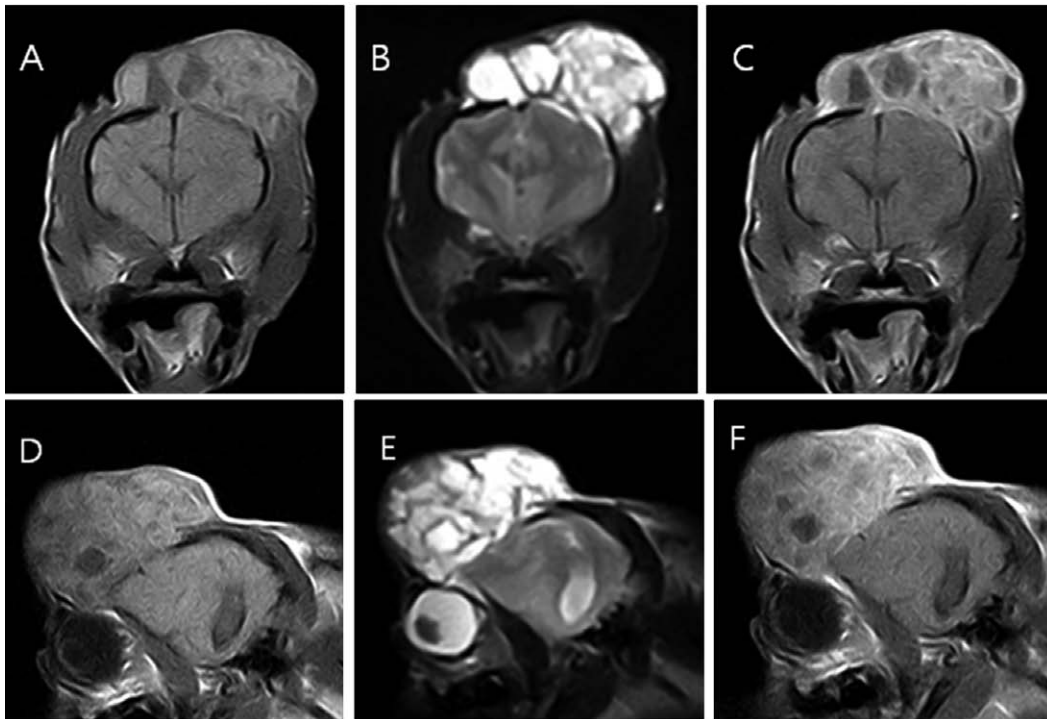

Fig. 2.   Transverse magnetic resonance images at the level of frontal lobe (A, B, C) and sagittal images at the level of left eye (D, E, F). The mass is isointense with hypointense fluid parts in T1WI (A, D) and hyperintense with hypointense septa in T2WI (B, E). Hemorrhagic contents settled down to the dependent portion, which formed a fluid-cell level. Mild contrast enhancement is shown in contrast T1WI (C, F).

small animal coil. The dog was positioned in right lateral recumbency. Sagittal, transverse and dorsal images were obtained through the head by T2-weighted imaging (T2WI, TR/TE/slice thickness=3,800 ms/90 ms/5 mm), T1-weighted images (T1WI, TR/TE/slice thickness = 540 ms/ 26 ms/5 mm) and contrast enhanced T1-weighted imaging. The MR images of the mass were very similar to the CT images. The main signal intensity of the mass was isointense in the T1 weighted images (Fig. 2A and 2D) and hyperintense in the T2-weighted images (Fig. 2B and 2E)

compared with the brain parenchyma, except the fluid parts of the mass. Also, mild heterogenous enhancement was found and the meninges adjacent to the mass were enhanced after intravenous injection of gadolinium (Fig. 2C and 2F). The mass had low-signal-intensity septa that were especially prominent in T2WI. MRI did not show brain parenchymal abnormality.

The dog underwent surgical resection at the cranial mass for client's request despite pulmonary metastasis, but extensive resection along with normal tissue was difficult because

the mass was in contact with the brain. Approximately 80–90% of the mass was removed by surgery, and temporalis muscle flap was performed to cover the large defect. Histopathologic examination of the mass sectioned by surgery was performed. Grossly, the mass consisted of cystic structures containing bloody materials. Histopathological samples of the cranial mass were examined with hematoxylin and eosin (HE) staining. Selected sections of the mass were also stained with immunohistochemical antibodies such as vimentin (3B4, DAKO), CD18 (H20A, VMRD), major histocompatibility (MHC) class II (TAL.1B5, DAKO), vWF (2F2-A9, BD Biosciences), smooth muscle actin (1A4, DAKO), S-100 (DAKO), lysozyme (DAKO), glial fibrillary acidic protein (DAKO) and neuron-specific enolase (DAKO). Histopathologically, severe multifocal hemorrhagic foci and accumulation of neoplastic cells were scattered in the mass. Inner numerous multinucleated giant tumor cells and outer ovoid to spindle tumor cells were accumulated in adjacent areas of hemorrhage (Fig. 3A). These neoplastic tumor cell foci were separated by fibrous bands. Giant tumor cells had multiple vesicular nuclei with prominent nucleoli and abundant eosinophilic or amphophilic cytoplasm, and many abnormal mitotic figures were observed. Ovoid or polygonal cells showed characteristic histicytic appearances such as vesicular nuclei and abundant vacuolated cytoplasm. Many tumor cells had a strong tendency to invade adjacent fibrous tissues and were some-

times lodged in blood vessels. Both neoplastic mononuclear cells and giant cells, as well as spindle cells, showed a strong positive reaction for vimentin (Fig. 3B). Actin expression was restricted to fibroblasts-like spindle cells. In contrast, tumor cells did not show immunoreactivity for CD18, MHC class II, vWF, lysozyme, S-100, GFAP and NSE. Because of the negative results for neural markers including GFAP and NSE, this cranial mass did not originate from nervous tissues. On the basis of the prominent histopathologic features and immunohistochemical characters, this mass was diagnosed as an undifferentiated pleomorphic sarcoma with giant cells (giant cell variant of MFH).

The patient was followed one month after the operation, and the recurrent mass was found to be causing exophthalmos of the left eye. Thoracic radiography demonstrated that the metastatic nodule was dramatically enlarged and that a new metastatic nodule had developed at the left caudal lung lobe. A MRI examination was performed to monitor the recurrent mass. There was no significant change in the findings of MR imaging compared with the first MR examination, but the mass compressed the left eye and invaded the left retrobulbar region (Fig. 4). The dog died at 3 months after the operation, and a necropsy was not permitted.

Malignant fibrous histiocytoma (MFH) has been believed to be the most common soft tissue malignant tumor in human medicine. With the advent of electron microscopy
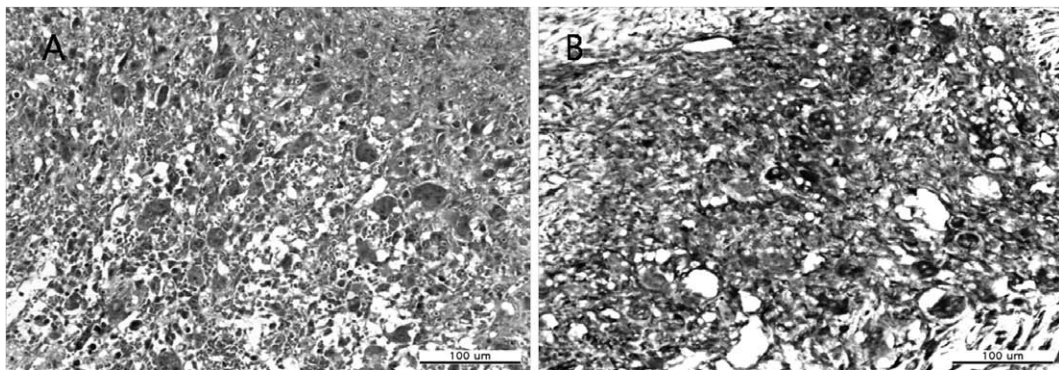

Fig. 3. Undifferentiated pleomorphic sarcoma showing numerous multinucleated giant cells among pleomorphic mononuclear cells (A). HE. Bar=100 μm. Vimentin-positive reactions were detected for both giant cells and histiocytic cells (B). ABC. Bar=100 μm.
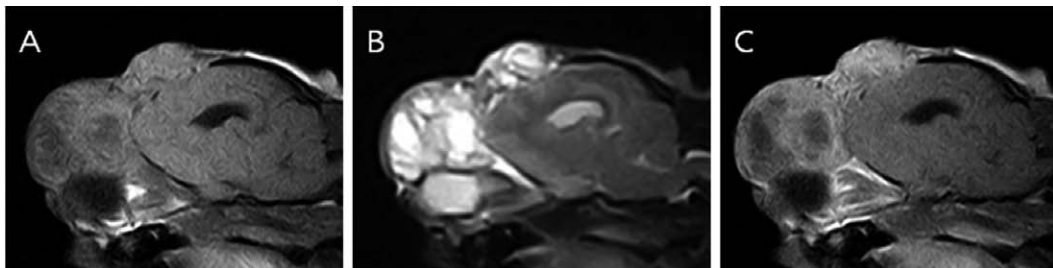

Fig. 4. Sagittal T1- (A) and T2-weighted (B) and contrast T1-weighted MR images at the level of left eye 4 weeks after surgery. The mass recurred and invaded the left retrobulbar region. The imaging characteristics of the mass are similar to those of the initial examination.

and immunohistochemistry, it has recently been proven that the term "fibrohistiocytic" is a misnomer. The World Health Organization suggested a the new classification of soft tissue tumors in which MFH is an obsolete term, and really represents undifferentiated pleomorphic sarcoma [10]. Since the first reports of MFH in two dogs in 1979, it has increasingly been diagnosed in veterinary medicine [4]. Because the appropriate staining patterns of immunohistochemical analysis have not been established in dogs and both terms may be used synonymously, we also used the term MFH with undifferentiated pleomorphic sarcoma in this case report.

Dogs with MFH are middle aged to older, and flat-coated retrievers [14], rottweilers and golden retrievers are overpresented [19], although it is unknown if there is any specific breed predilection. There is no definite predilection for sex, but seven female dogs were reported in a study of 10 dogs with giant cell variants-MFH [19]. MFH rarely occurs in the head, both in humans and dogs. There are only two MFH cases in the head region, except nasal tumors, in the veterinary literature; one case was in the salivary gland in a 12-year-old male boxer [16] and the other was retrobulbar MFH in a 12-year-old castrated male Keeshond [9]. The latter case had CT findings of a heterogenous soft tissue mass without bone lysis adjacent to it. Following contrast medium administration, there was moderate patchy diffuse enhancement of the mass [9].

MFH in the head is also rare in human medicine [5, 15, 22]. Temporal bone, parietal bone, frontotemporal bone, occipitotemporal bone, frontoparietosphenoidal bone and the clivus have been affected by MFH in a small number of human patients. Bone destruction with various degrees and characteristics were presented in most cases, and the masses with inward extension appeared as meningiomas at CT and MR imaging, whereas others showed extracranial bulging with massive osteolysis [5, 15, 22].

Many reports in humans have described imaging characteristics of MFH of various organs, while the majority of the veterinary reports about MFH have focused on the histopathological findings. In human medicine, MFH has been shown to be a large lobulated inhomogeneous hypo- to isodense mass with inhomogeneous enhancement with or without calcification on CT images [18, 23, 24]. Hypodense regions on CT images could suggest hemorrhage, tumor necrosis or myxomatous changes often occurred in MFH. The MR imaging characteristics of MFH have been well described, and hypo- to isointensity on T1WI with inhomogeneous enhancement and hyperintensity with hypointense areas on T2WI have been reported in the liver, temporal bone, thigh, leg, elbow, chest and pancreas in many human reports [12, 15, 18, 23]. In one report, hypointensity septa were shown in all 13 MFHs of soft tissue on T2WI [13]. Septa were not seen in two lesions on T1WI because they could not be distinguished by the isointensity of the lesion itself. The septa suggest fibrous bands or acellular streaks and can be either thin or thick. These low-signal septa were marked in T2-weighted MR images due to increased soft tissue contrast. Unfortunately, these low-signal-intensity septa are not a pathognomonic sign of MFH [7, 11], having been described in liposarcomas, synovial sarcomas and other less common soft tissue sarcomas and in occasional benign tumors such as atypical lipoma and intramuscular myxoma [6–8, 11, 17]. However, some reports have suggested that these low-signal-intensity septa strongly suggest a malignant rather than benign process [6].

In our patient, tumors possibly originating from the skull, such as osteosarcoma, osteoma, osteochondroma, multilobular osteochondrosarcoma (MLO) and metastasis, were included in the differential diagnosis after loss of frontal and temporal bone was revealed in the radiographic and CT findings. However, osteosarcoma and MLO were less likely in our dog due to the different imaging characteristics, such as limited osteolysis and extensive calicification [3].

Four histologic subtypes of MFH have been described, storiform-pleomorphic, myxoid, giant cell and inflammatory. Although definitive immunohistochemical staining patterns have not been clearly identified for MFH in veterinary medicine, MFH has been reported to exhibit a vimentin-positive, CD 18-negative phenotype [14]. The MFH in the dog described here is most consistent with undifferentiated pleomorphic sarcoma with giant cells (giant cell variant of MFH) based on the histopathologic examination results. The histologic subtype of MFH affects prognosis in human and veterinary MFH. The giant cell variant of MFH in human beings is associated with a higher local recurrence rate than storiform/pleomorphic MFH and a higher metastasis rate than inflammatory MFH [20]. In a report about 10 dogs with the giant cell variant of MFH, the tumor was highly metastatic to subcutaneous tissues, lymph nodes, liver and lungs, and the median survival time was only 61 days [19]. The present case also showed rapid and very aggressive metastatic behavior and local recurrence.

In conclusion, we present a case of a middle aged, small breed dog with extensive skull bone lysis caused by undifferentiated pleomorphic sarcoma (MFH). Although the definitive diagnosis of undifferentiated pleomorphic sarcoma by imaging findings is not possible, CT and MRI findings could help to make a differential diagnosis of undifferentiated pleomorphic sarcoma in dogs.

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