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Case Report

Two different types of malignant fibrous histiocytomas from pet dogs

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We describe 2 cases of malignant fibrous histiocytomas (MFHs) that spontaneously developed in young pet dogs. To classify these tumors, we applied a panel of antibodies (vimentin, desmin, α-SMA, and ED1) and Azan staining for collagen. The MFHs were most consistent with osteoclast-like giant and inflammatory cell types. The first case had positive staining for ED1 and vimentin, and given the osteoclast-like giant cells, calcification sites accompanying peripheral giant cell infiltrates. The latter case, the inflammatory cell type, exhibited a storiform-pleomorphic variant of neoplastic cells, including an ossifying matrix. MFHs are among the most highly aggressive tumors occurring in soft tissue sarcomas in elderly dogs; however, MFHs have been poorly studied from a diagnostic point of view. Herein, we describe the histologic and immunohistologic features of MFHs in detail, thus classifying the subtypes of these tumors.

Keywords: dog, inflammatory, malignant fibrous histiocytoma, osteoclast-like giant cell

Malignant fibrous histiocytomas (MFHs) are mesenchymal tumors frequently occurring in skeletal muscles and cutaneous regions in elderly humans; the visceral form is most common in young immunodepressed humans [6,7,10]. Based on histologic and immunohistologic studies, most of the tumors have been shown to originate from fibroblasts and/or myofibroblasts, presumably from undifferentiated mesenchymal cells [2,3,5]. MFHs have been diagnostic dilemmas because of the histologic variation from plexiform fibrohistiocytic to infiltrative subcutaneous fibroblast-like spindle cell types [7,10].

The neoplasm is characterized by a mixture of neoplastic fibroblasts, histiocytes, and multi-nucleated giant cells that interlace in tight bundles [8]. Large giant cells that resemble osteoclasts are generally present [1]. The primary tumor cells are pleomorphic, vary in appearance from fusiform-to-round, and have a nucleus with one or two prominent and irregular nucleoli [8]. Extracellular amorphous eosinophilic material may be prominent and likely represents reactive collagen production by the neoplastic cells [8].

The osteoclast-like giant cell type of MFH is rare. The characteristic features of the osteoclast-like giant cell type have not been described in detail in domestic animals. Thus, we studied the histopathologic features of osteoclast-like giant cell type MFH with calcifications in a young healthy dog and compared of the findings to another case of inflammatory MFH.

A two-month old female Shih-tzu was brought to a local veterinary clinic with a raised subcutaneous mass in the left dorsal region. Because of the rapid growth of the mass, the veterinarian performed a surgical excision. The mass was 2.5 cm in diameter and had well-defined boundaries without involving the surrounding tissues. The tumor was circumscribed with an incomplete capsule, was firm and gritty, and included focal calcifications of dense portions.

The second case involved a 6-year old male Pointer. The dog had a history of a mass at the same site 3 years earlier with a red-to-brown blood-filled nodule, approximately 2 cm in diameter, in the left ultimate costa. The clinical examination revealed that the nodule extended into the muscle layer.

Biopsies from each dog were submitted to Kyungpook National University for pathologic evaluation. The masses were fixed in 10% neutral-buffered formalin, and paraffin-embedded tissues were sectioned at 4 μm and stained with hematoxylin and eosin (H&E) and Azan for collagen activity in the neoplastic cells. Immunohistochemical evaluation was performed using commercially available antibodies. The source and dilution of the primary antibodies were as follows: anti-vimentin (clone V9, 1 : 100; DAKO, USA), anti-desmin (clone D33, 1:100; DAKO), anti-α-smooth muscle actin (α-SMA: clone 1A4, 1:800; Sigma, St. Louis, MO, USA), and anti-monocytes/macrophages antibody (clone ED-1, 1 : 100; Chemicon, USA). Histologically, the two masses extended from the subcutaneous tissue into the dermis. The first mass was

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composed of spindle-shaped neoplastic cells with a storiform pattern intermixed with blood vessels and a few inflammatory cells. Giant cells were scattered throughout the lesion, especially around the calcification site, and resembled normal osteoclasts (Fig. 1A). In addition, peripheral giant cells were seen in association with epitheloid cells, which is a common feature in giant cell type MFH. Multinucleated giant cells engulfed calcifying material at the site of calcification. Areas of necrosis and hemorrhage were seen in the adjacent fat and muscle tissue. The tumor cells were positive for vimentin (Fig. 1B), and negative for desmin (Fig. 1C) and α-SMA (Fig. 1D). The osteoclast-like giant cells, the majority of giant cells in this case, were positive for ED1 on immunohistochemical staining (Fig. 1E). The histologic appearance of this lesion was a salient feature of the osteoclast-like giant cell type of MFH. The animal was very young compared to most animals in which such tumors have been reported.

The tumor consisted of neoplastic histiocytes, hyperplastic fibroblasts, and an ossifying matrix, including spindle cell areas showing an occasional storiform pattern in the second case. The undifferentiated sarcoma was diagnosed as an inflammatory cell type of MFH because of mixed cellularity with a heavy infiltration of lymphocytes, plasma cells, and neutrophils (Fig. 1F). An ossifying matrix was also detected as the result of continuous and reactive hyperplasia of fibroblasts (Fig. 1G). At the center of the tumor, areas of osteocentral fibrous histiocytomas, characterized by bone matrix formation, were present (Fig. 1H). The neoplasm also included neovascularization, necrosis of affected muscle cells, and involvement of the surrounding tissue.

MFH is one of the most common soft tissue sarcomas in elderly humans and animals in which the cells have morphologic features of both fibroblasts and histiocytes. Generally, the storiform-pleomorphic type of MFH exhibits a cartwheel (storiform) pattern of fibroblast-like cells and histiocytoid cells. Inflammatory-type tumors showed bizzare histiocytoid cells concealed by inflammatory cells, including

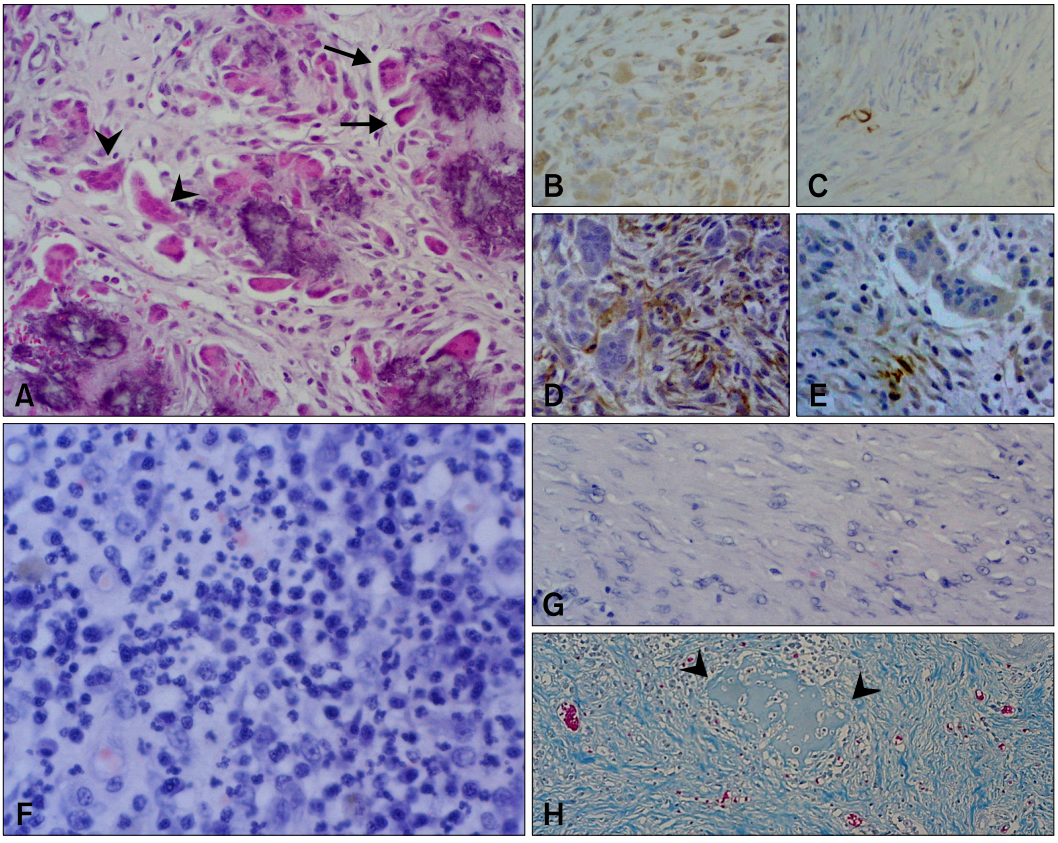

Fig. 1. Malignant fibrous histiocytoma (MFH), subtype osteoclast-like giant cell type (A-E). Osteoclast-like giant cells (arrow head) resembling normal osteoclast are scattered throughout the lesion, especially around the calcification sites. In addition to these features, peripheral giant cells (arrow) appeared (A). Immunostaining for vimentin, desmin, α-SMA, and ED1, respectively (B-E). Tumor cells were positive for vimentin (B), and negative for α-SMA (D) and ED1 (E). Note the strong positive for desmin of smooth muscle cells of blood vessels vs. negative staining of tumor cells (C). Osteoclast-like giant cells showed positive for ED1 (E). Inflammatory cell type of MFH (F-H). This type of MHF was characterized by infiltration of various inflammatory cells (F) and ossifying matrix (G). Note the bone matrix surrounding the neoplastic fibroblasts (H). A, F and G: H&E stain, B, C, D and E: ABC method counterstained with hematoxylin, H: Azan stain. A-E: ×66, F and G: ×132, H: ×33.

lymphocytes, plasma cells, eosinophils, and neutrophils. Tumors of the giant type had multi-nucleated giant cells, spindle cells, and mononuclear histiocytic cells. Human MFHs have been classified into 5 subtypes based on the pattern and predominance of the cell types: storiform-pleomorphic, inflammatory, giant cell, myxoid, and angiomatoid, but only the first three types have been reported in non-human animals [2,5].

The origin of histiocyte-like cells in MFH remains controversial. In some reports, three possible cells have been proposed: 1) facultative histiocytic cells that are able to differentiate into fibroblasts, 2) fibroblasts, and 3) primitive mesenchymal cells that are able to differentiate into fibroblasts and histiocytes [1,4]. In most cases of MFH, immunohistochemical studies have not supported the hypothesis that these tumor cells are derived from true histiocytes [8,9]. Several other studies have suggested that the immunohistologic heterogenity of MFH tumor cells indicate that these tumors are indeed from a primitive cell type or are the end result of "differentiation" of several different types of sarcomas [4,8]. The undifferentiated mesenchymal cell-origin tumors in which giant cells are usually present have also been described as fascial sarcomas, epithelioid sarcomas, malignant histiocytomas, reticulum cell sarcomas, and giant cell tumors [8].

The specimens of the first case included the osteoclast- like giant cell type of MFH, a rare case in non-human animals, with large numbers of osteoclast-like giant cells and multi-nucleated giant cells engulfing calcified materials. This tumor had immunoreactivity for vimentin. However, the tumor showed no immunoreactivity for desmin and α-SMA. The osteoclast-like giant cell type of MFH rarely occurs in young animals. In addition, the second case showed typical findings of the inflammatory cell type of MFH with an ossifying matrix resulting from continuous fibroblast reactive hyperplasia and bone matrix surrounding neoplastic fibroblasts in the central region of the lesion.

The current report may be important in identifying MFHs based on histologic and immunohistologic findings and classifying the subtypes of these tumors that have atypical features occurring in pet dogs.

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