Case Report

A case of hepatic leiomyosarcoma with osteosarcomatous differentiation (malignant mesenchymoma) in a dog

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Abstract: A rare spontaneous hepatic leiomyosarcoma with osteosarcomatous differentiation was observed in a female beagle dog and its morphological and immunohistochemical characteristics were examined. Upon necropsy, an endoceliac mass originating from the liver was detected, which was composed of hematoid fluid-filled cysts and white to grayish solid tissue. There were no macroscopic findings in other organ systems. Histopathologically, the hepatic mass consisted of two different mesenchymal components. One form was spindle cells arranged in interlacing fascicles immunohistochemically positive for smooth muscle actin (SMA) and smoothelin, indicating leiomyosarcomatous differentiation. The other form was composed of short spindle cells positive for S-100 and was producing various amounts of eosinophilic osteoid and trabecula-like matrices positive for osteocalcin, indicating osteosarcomatous differentiation. In addition, invasive growth in the hepatic parenchyma and cell atypia were observed. Based on these findings, the mass was diagnosed as hepatic leiomyosarcoma with osteosarcomatous differentiation (malignant mesenchymoma), which might be derived from undifferentiated mesenchymal cells. (DOI: 10.1293/tox.2019-0065; J Toxicol Pathol 2020; 33: 33–37)

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was observed in hepatic tissue (Fig. 2). The tumor partly showed invasive growth into the hepatic parenchyma, and the adjacent hepatic tissue was atrophied. Neither intrahepatic nor pulmonary metastases were observed. In the central area of the tumor tissue including the macroscopically cystic area, multifocal necrosis and hemorrhage were observed. The mass consisted of two different mesenchymal components (Fig. 2). One component was spindle cells with oval to spindle nuclei and eosinophilic cytoplasm arranged in interlacing fascicles that were immunohistochemically positive for vimentin, smooth muscle actin (SMA) and smoothelin, and negative for S-100 and Schwann cells, indicating leiomyosarcomatous differentiation (Fig. 3). The other component was intricately observed in the leiomyosarcomatous area and mainly located in the macroscopically gritty area. Proliferative cells contained round nuclei and short spindle basophilic cytoplasm, which were often embedded in various amounts of eosinophilic osteoid-like and bone-like matrices, indicating differentiation to osteoblasts and bone tissue (Fig. 4). The tumor cells in this area were positive for vimentin and S-100, which could be consistent with osteosarcoma, and negative for SMA, smoothelin, and Schwann cells (Fig. 4). The osteoid-like and bone-like matrices were positive for osteocalcin (Fig. 4). Osteoclast-like multinucleated cells, which were immunohistochemically positive only for vimentin, were sporadically observed in this area. These histopathological and immunohistochemical characteristics were indicative of osteosarcomatous differentiation. In total, the area of leiomyosarcomatous lesion was more predominant than the osteosarcomatous area. Furthermore, apparent sequential histopathology was not observed between the two components. Mild anisokaryosis of tumor cells was observed in both proliferative components. Based on these findings, the mass was diagnosed as a hepatic leiomyosarcoma with osteosarcomatous differentiation (malignant mesenchymoma).

The term “malignant mesenchymoma” has been applied to sarcomas that exhibit two or more lines of differentiation; however, there is a clear difference between humans and animals in the World Health Organization...
Classification of Tumors. In humans, descriptive diagnosis such as leiomyosarcoma with osteosarcomatous differentiation is preferred instead of the usage of malignant mesenchymoma. On the contrary, malignant mesenchymoma is the terminology currently used for the classification of animal tumors. Based on these criteria, this case can be categorized as malignant mesenchymoma, but descriptive terminology modification such as leiomyosarcomatous and osteosarcomatous would be ideal as a diagnosis.

Canine malignant mesenchymomas are rare. Several cases were reported in various organs such as the heart, spleen, abdominal cavity, bone, and submandibular tissue. In the liver, only one case has been reported, which showed rhabdomyosarcomatous and hemangiosarcomatous phenotypes. In addition, primary hepatic bone or smooth muscle tumors are rare. Therefore, the present case was the second hepatic malignant mesenchymoma reported in dogs with relatively rare histological phenotypes such as leiomyosarcomatous and osteosarcomatous differentiation.

The malignant mesenchymomas might be derived from undifferentiated cells which have pluripotent property such as mesenchymal stem cells (MSCs) mentioned in other cases of mesenchymomas in dogs. Moreover, MSCs and MSC-like cells have been found to harbor in various organs, which supports the hypothesis that mesenchymomas are derived from MSCs.

Fig. 3. Histopathological features of leiomyosarcomatous area. Proliferation of spindle cells arranged in interlacing fascicles was observed in hematoxylin and cosin (H&E) section (A). Cytoplasm of tumor cells were immunohistochemically positive for vimentin (B), smooth muscle actin (SMA) (C) and smoothelin (D), and negative for S-100 (E) and Schwann cell (F). Bar=100 μm.
Especially in the hepatic mesenchymomas, hepatic stellate cell (HSC) progenitor cells could be the origin as we suspect in the present case. HSC progenitor cells are derived from mesothelial and submesothelial cells during liver development, or from bone marrow cells of adult animals\(^{15}\). The HSC progenitor cells have the capacity to differentiate into osteoblast- and adipocyte-like cells, providing evidence of their multipotent nature\(^{16},^{17}\). In addition, fibroblasts derived from bone marrow, which could contribute to liver fibrosis\(^{18}\), also have pluripotency\(^{19}\). It has also been reported that there are MSCs in pericytes, which can differentiate into bone, cartilage, and adipose tissue\(^{20}\). Therefore, the origin of the tumor cells of the present case might be the cells possessing the phenotype of MSCs such as HSC progenitor cells, fibroblasts or pericytes.

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\[\text{Fig. 4. Histopathological features of osteosarcomatous area. Proliferative cells were intricately observed in the leiomyosarcomatous area and contained polygonal cytoplasms, around which various amounts of eosinophilic osteoid-like and bone-like matrices were observed in hematoxylin and eosin (H&E) section (A). Cytoplasm of tumor cells were immunohistochemically positive for vimentin (B) and S-100 (C), and osteoid-like and bone-like matrices around the tumor cells were positive for osteocalcin (D). On the other hand, the cytoplasm of tumor cells is negative for smooth muscle actin (SMA) (E), smoothelin (F), and Schwann cells (G). Bar=100 μm.}\]
References


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