Simultaneous Aortic Body Tumor and Pulmonary Histiocytic Sarcoma in a Flat-Coated Retriever

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ABSTRACT. A case of multiple primary tumors observed in the heart base and in the lung of a 7-year-old intact female, flat-coated retriever was reported. Morphological differences between both tumors and detailed immunohistochemical study revealed that the cardiac neoplasm was as a malignant aortic body tumor and the lung tumor was a pulmonary histiocytic sarcoma. The occurrence of aortic body tumor with other primary neoplasms has been previously reported in animals suggesting that this might be a common presentation in dogs.

Key Words: aortic body tumor, canine, multiple tumor, pulmonary histiocytic sarcoma.

Multiple primary tumors (MPTs) were defined as multiple autonomously originating tumors in an individual patient by Warren and Gates [18]. The occurrence of more than 1 primary cancer in an animal, previously only a medical curiosity, has now become a worldwide problem; however, there are few studies on this interesting entity in veterinary literature [8, 9, 16]. The present paper describes the histopathological and immunohistochemical findings of a malignant aortic body chemodectoma and pulmonary histiocytic sarcoma (PHS) in a flat-coated retriever.

A 7-year-old intact female, flat-coated retriever was admitted to the Veterinary Hospital, Gifu University, Japan, with severe dyspnea. Thoracic X-ray images revealed severe pleural effusion and a large heart-base tumor. At needle thoracocentesis an opaque, red-whitish (chylous effusion) fluid was observed. A sample of the pleural effusion was collected for cytology, which demonstrated mesothelial cells, macrophages, and lymphocytes, suggestive of modified transudate. Neoplastic cells were not observed. Despite symptomatic treatment, in early July, she showed severe subcutaneous edema and dyspnea and died during hospitalization.

Necropsy revealed 2 hard, encapsulated, reddish, coalescent masses (8 × 7 × 6 cm and 3 × 3 × 2 cm) arising at the heart base, around the ascending aorta (Fig. 1a). Moreover, a large (7 × 5 cm) whitish mass with an irregular surface was observed in the right caudal pulmonary lobe (Fig. 1a). The thoracic cavity contained approximately 2.5 l of an opaque, red-whitish fluid (chylous effusion) with a moderate amount of fibrin, hydropericardium, concentric hypertrophy of the left ventricle, and ascites. On the other organs, abnormality was not seen.

In microscopic observation, the cardiac neoplasm was comprised of multiple lobules separated by fine connective tissue septa. The tumor cells were cuboidal to polygonal with lightly basophilic granular cytoplasm and prominent round nuclei (Fig. 1b). Mitotic figures were frequent, and some blood vessels showed neoplastic invasion. In the lung, round to polygonal tumor cells arranged in a solid pattern were observed to replace the pulmonary parenchyma, while there were areas preserving normal alveolar and bronchiolar architecture. These cells had ample eosinophilic cytoplasm and round to oval nuclei (Fig. 2b). Binucleated and multinucleated giant cells, a small number of lymphocytes, and a few neutrophils were also observed; mitotic figures were frequent. Moreover, extensive and coalescent areas of necrosis, multiple foci of cholesterol clefts, and mineralization were observed. Immunohistochemical analyses using a variety of antibodies and the streptavidin-biotin peroxidase method showed that the tumor cells in the heart were faintly positive for chromogranin A (diluted 1:50, Dako Cytomation, Denmark, Fig. 1c) and synaptophysin (SY38, diluted 1:50, Dako Cytomation) but negative for cytokeratin (AE1/AE3, ready-to-use, Dako Cytomation), thyroglobulin (diluted 1:10,000, Dako Cytomation), and calcitonin (ready-to-use, Dako Cytomation). In the lung, some tumor cells stained strongly for vimentin (V9, ready-to-use, Dako Cytomation); all the cells were positive for CD18 (CA16.3C10, diluted 1:100, provided by Dr. Moore, PF, Davis, Califor-nia; Fig. 2c); and most were also positive for HLA-DR (TAL.1B5, diluted 1:100, Dako Cytomation). The lung lesions showed negative periodic acid-Schiff staining for specific pathogens including fungus.

Based on morphological and immunohistochemical findings, the diagnosis was malignant aortic body tumor and
PHS, which is similar to previous descriptions of these tumors in dogs [1–5, 7]. The expression of chromogranin A and synaptophysin in the heart base tumor was low; this might indicate malignancy, since it has been reported that concentration of secretory granules of chromogranin is diminished in malignant tumors [2]. Even without metastasis to remote organs or lymph nodes, another important sign of malignancy for aortic chemodectoma was the microscopic evidence of frequent mitotic figures and local vasculature infiltration. Cytokeratin, thyroglobulin, and calcitonin were used to differentiate chemodectoma from ectopic thyroid tumor, in which the tumor cells would have stained positive for the above mentioned antibodies [14]. CD18 and HLA-DR confirmed the histiocytic origin of the lung tumor. In addition, CD3, CD79a, CD20, and cytokeratin immunoreactivities were helpful in differentiating histiocytic sarcoma from other pulmonary tumors with a similar histological pattern, such as large cell carcinomas, lymphomatoid granulomatosis, and granulomatous inflammation [19].

Considering the size and general tendency of slow growth of aortic chemodectoma reported previously [5], it is more likely that the aortic body tumor observed here is a chronic neoplasm. The chemoreceptor tissue is found at several sites in the body of animals, and, mainly, tumors arising in
the aortic and carotic bodies have been reported [5, 9, 15]. In accordance with this case, aortic chemodectomas (non-chromaffin paragangliomas) are the most commonly reported chemoreceptor tumors in dogs [5, 9, 15]. Male dogs and brachycephalic breeds are believed to be predisposed to aortic body chemodectomas, and chronic hypoxia caused by nasopharyngeal conformation in these breeds have been suggested as a possible cause for this overexpression [9, 15]. Although the latter observations for canine chemodectomas were not consistent with this case, the primary location of the present histiocytic sarcoma was in accordance with other demographic findings of canine histiocytic proliferative disorders [1, 7]. The association with chemodectoma has been previously reported in 16% to 60% of MPS in dogs [13, 15]. Despite the differences between the multiple endocrine neoplasia (MEN) syndrome in humans and animals (especially in relation to the autosomal-dominant etiology, classification of the disorder, and combination of neoplasms in humans), paragangliomas may occur as a MEN syndrome or associated with other endocrine tumors in both species [6, 9, 10, 12, 15, 17]. In humans, paragangliomas are usually combined with medullary thyroid gland carcinoma, and, facultatively, pheochromocytoma [12]. In dogs, it has been described to occur in association with other endocrine tumors, such as insulinoma, thyroid carcinomas, endocrine tumors of the testis, and adrenocortical adenocarcinomas [9, 10, 15, 20]. Although extensive studies have reported high synchronous occurrences of chemodectomas with pulmonary neoplasms [15] and other non-endocrine tumors such as mastocytoma, malignant melanoma, lymphoma, and hemangiosarcoma [9, 13, 16, 20], to the best of the author’s knowledge, this is the first description of the simultaneous occurrence of canine malignant aortic body chemodectoma and PHS.

Compared with individuals with no cancer, individuals with 1 malignant neoplasm have an increased risk of developing an additional primary tumor [11], but the relationship between multiple cancers is as yet poorly understood. The study of MPTs is important since an association of certain malignancies may facilitate the investigation of germ line mutations or genetic alterations and assessment of patient prognosis, and may require specific treatments.

REFERENCES