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NEOPLASTIC DISEASE

Mixed Form of Pericardial Mesothelioma with Osseous Differentiation in a Dog

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Summary

An 8-year-old female Yorkshire terrier was referred for evaluation and treatment of recurrent pericardial effusion. Echocardiographic examination revealed a markedly and irregularly thickened pericardial sac with frequent hyperechoic areas with acoustic shadows. Pericardiocentesis produced only a small amount of thick serosanguineous fluid. The dog underwent subtotal pericardiectomy, but died during surgery. At necropsy examination, the heart was encased by voluminous, grey–white to red–tan, soft to firm proliferative tissue arising from the pericardial sac. The pericardial cavity was obliterated. Microscopically, the tissue was predominantly sarcomatoid with osseous differentiation and epithelioid elements were admixed with bundles of spindle cells. Immunohistochemically, the constituent cells, especially those that were epithelioid, co-expressed cytokeratin and vimentin. A diagnosis of mixed form pericardial mesothelioma with osseous differentiation was made. This appears to be the first report of such a tumour in a dog.

Keywords: dog; mesothelioma; osseous differentiation; pericardium

Mesotheliomas are rare tumours that arise from the mesothelial lining of a serosal cavity and account for <0.2% of all tumours occurring in dogs (Head *et al.*, 2002; Wilson and Dungworth, 2002). Pleural, peritoneal and pericardial sites are most often affected, but the tumours can also affect the scrotum and tunica vaginalis (Wilson and Dungworth, 2002). There is a strong association between pleural mesothelioma and asbestosis in man (Ikede *et al.*, 1980; Mutsaers, 2004), but causative factors related to canine mesothelioma remain unknown (Ikede *et al.*, 1980; Harbison and Godleski, 1983). Microscopically, three kinds of mesothelioma can be distinguished: epithelioid, sarcomatoid and mixed (biphasic) (Head *et al.*, 2002). This pleomorphism has been attributed to the pluripotentiality of the mesothelium itself (Yousem and Hochholzer, 1987; Lansley *et al.*, 2011). Mesotheliomas are also capable of differentiating into other mesenchymal elements and sporadic reports have described such differentiation in human mesotheliomas (Goldstein, 1979; Yousem and Hochholzer, 1987; Kiyozuka *et al.*, 1999; Demirag *et al.*, 2007). To our knowledge, few reports have documented canine mesotheliomas accompanied by differentiation of other mesenchymal elements (Avakian *et al.*, 2008).

An 8-year-old female Yorkshire terrier was presented to a referring veterinarian with a 3-week history of anorexia. Clinical signs included those associated with right-sided heart failure (ascites and distended jugular veins). Echocardiographic examination revealed pericardial effusion; the pericardial fluid was hyperechoic, consistent with blood, but no discrete masses arising from the heart were seen. The dog was referred to the Animal Medical Centre of Tokyo University of Agriculture and Technology for further evaluation and treatment. Echocardiography revealed moderate pericardial effusion, with collapse of the right ventricle in expiration and a markedly and irregularly thickened pericardium that exhibited frequent hyperechoic areas with acoustic shadows. Pericardiocentesis was performed to reduce the pericardial effusion, but only 20 ml of thick

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serosanguineous fluid was withdrawn. Cytological examination of the fluid revealed clusters of neoplastic epithelioid cells (possibly mesothelial cells), neutrophils and red blood cells. On the same day, the dog underwent median sternotomy for exploration of the thoracic cavity and subtotal pericardiectomy, but died during surgery.

A complete necropsy examination was performed. On gross examination, both lungs were congested and oedematous with cranioventral segmental and subsegmental areas of collapse. The bronchial and mediastinal lymph nodes were normal. Thin, turbid, serosanguineous fluid (50 ml) was found in the thoracic cavity. The heart was encased by voluminous, grey–white to red–tan, soft to firm proliferative tissue arising from the pericardial sac. Transverse sections of the heart revealed a markedly and irregularly thickened pericardial sac that had been completely replaced by neoplastic tissue and had a roughened inner surface. The proliferative lesions consisted of multiple and frequently confluent tumour nodules and masses of varying size on the visceral and parietal pericardium and often filling the pericardial cavity (Fig. 1). The tissue invaded contiguous structures of the heart locally or superficially. The abdominal cavity contained 670 ml of straw-coloured fluid with a few gelatinous fibrin clots. The liver was slightly enlarged and firm with a 'nutmeg' appearance on the cut surface. Gross examination of all the abdominal and thoracic viscera revealed no evidence of metastatic spread or any other primary tumours.

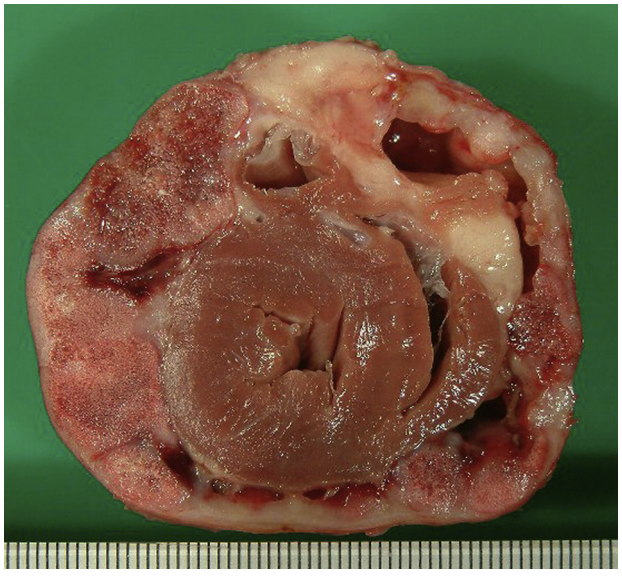

Fig. 1. Transverse section of the heart. The heart is encased by voluminous, grey–white to red–tan, soft to firm proliferative tissue arising from the pericardial sac. Scale, 1 mm.

Tissue samples collected from the pericardial sac, heart, lungs and mediastinal and tracheobronchial lymph nodes were fixed in 10% neutral buffered formalin and processed routinely. Sections (5 μm) were stained with haematoxylin and eosin (HE). Immunohistochemistry (IHC) was performed for identification of cytokeratin (MNF 116; Dako Corp., Santa Barbara, California, USA), vimentin (V9; Dako) and α-smooth muscle actin (1A4; Dako). Antigen retrieval was performed with citrate buffer (10 mM citric acid, 0.05% Tween 20, pH 6.0). Clone MNF 116 detects an epitope common to a wide range of cytokeratins corresponding to Moll's numbers 5, 6, 8, 17 and probably 19 (Moll *et al.*, 1982). The avidin–biotin–peroxidase method (Vectastain; Vector Laboratories, Burlingame, California, USA) was used for detection of immunoreactivity, with haematoxylin as a counterstain.

Microscopically, the neoplastic tissue was characterized by cellular irregularity and histological variability, but was predominantly sarcomatoid with osseous differentiation (Fig. 2). This pattern consisted of bundles of spindle cells arranged in an interlacing or whorled pattern or occasionally a herringbone pattern, resembling a fibrosarcoma. Collagen fibres were present between the tumour cells and were occasionally abundant and hyalinized. The spindle cells showed mild to moderate anisocytosis and anisokaryosis with indistinct cell borders and a scant amount of weakly eosinophilic cytoplasm. The nuclei were oval to elongated, centrally located and contained one or two prominent nucleoli (Fig. 3A). There were 1–2 mitoses per ×400 field. In these areas there were frequent foci of osseous differentiation, where

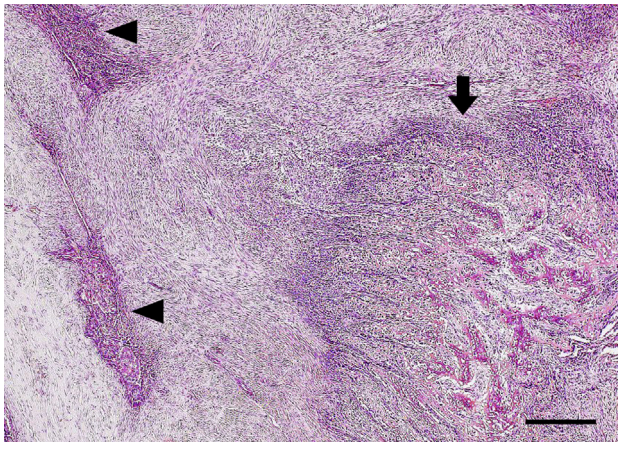

Fig. 2. The neoplastic tissue is predominantly sarcomatoid with frequent foci of epithelioid elements (arrowheads) and osseous differentiation (arrow). The sarcomatoid pattern consists of bundles of spindle-shaped tumour cells arranged in an interlacing or whorled pattern. HE. Bar, 200 μm.