Pericardial mesothelioma in a German Shepherd dog: a case report

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ABSTRACT: In this case report, a diagnosis of pericardial mesothelioma in a four year old male German shepherd dog is described. The dog, which had anorexia, bloody diarrhoea, dehydration and depression and, died on day 10 of therapy, was systematically necropsied. At necropsy, approximately 1.5 litres of cloudy and bloody exudate were detected in the thoracic cavity. The parietal lamina of the pericardium was covered with multilobular nodular masses related with each other, 1 to 5 cm in diameter and grey-yellow in colour. There were proliferations characterised with grey-yellow colour and approximately 1 to 5 mm in length on visceral pleura. The presence of abscess foci with liquefied-centrum was observed when examining a section surface of the lung. The appearance of the oesophageal serosa, thoracic aorta and the thoracic section of the diaphragm were similar to pleura. A thickening was microscopically determined in the parietal lamina of the pleura and pericardium due to papillary proliferations consisting of cells similar to cubic or cylindrical epithelium. Severe lymphocyte and plasma cell infiltrations were observed in the pleural sections next to the lung. Neoplastic cells had nuclei with large eosinophilic granular cytoplasms and large vesicular and single nucleoli. Some neoplastic cells were determined to include intracytoplasmic vacuoles. The neoplastic cells contained some mitotic figures. It was observed that some tumour cells contributed to giant cell formation through integration. In periodic acid Schiff-haematoxylin (PAS-H) examinations it was determined that the pleural basal membrane maintained its integrity. Immunohistochemically, the tumour gave a weak positive reaction with anti-pancytokeratin staining while giving intense reaction with anti-vimentin staining.

Keywords: dog; mesothelioma; pericardium

Mesothelioma is a rare tumour which either covers surfaces including the pericardium, pleura and peritoneum, or originates from the mesothelial cells in the tunica vaginalis of the testes (Head et al. 2002; Caswell and Wiliams 2007). The prevalence of this tumour has been reported as one in every 1000 dogs (Garrett 2007). Although the tumour is mostly observed in dogs aged four to thirteen years old (Head et al. 2002), juvenile mesothelioma and epitheloid mesothelioma in a nine-month puppy have previously been described (Kim et al. 2002; Vural et al. 2007). The tumour is observed in males more frequently than females and no breed predisposition has been reported up to now (Ledecka et al. 2010). The most prominent and reliable clinical finding in mesothelioma is respiratory distress caused by pleural exudation or abdominal distention due to peritoneal fluid accumulation. Also typical are excess effusions in cavities caused by exudation and infiltration on tumourous surfaces or lymphatic vessels under the pressure of tumourous tissues (Harbison and Godleski 1983; Ogilvie and Moore 2006). Classical mesotheliomas are diffuse nodular multifocal masses that cover the body cavities (Head et al. 2002). The primary sites of tumour development in dogs as well as in humans have been reported to be the pleura, followed by the pericardium and the peritoneum (Garrett 2007). Histologically, three main types of mesothelioma have been defined: epitheloid, sarcomatoid and biphasic or mixed in domestic animals (Head et al. 2002; Caswell and Wiliams 2007).

In this report we describe a case of epitheloid-type pericardial mesothelioma with macroscopic, microscopic and immunohistochemical findings in a German shepherd used as a security tracking dog.

Case description

A four-year-old male German shepherd dog, which had died on the tenth day of antibiotic and vitamin treatment because of anorexia, bloody diarrhoea, dehydration and depression, was admitted to the pathology department for diagnosis. Following necropsy, collected tissue samples were fixed in 10% neutral buffered formalin, embedded in paraffin, and cross sections were stained with haematoxylin and eosin (HE) and periodic acid Schiff-haematoxylin (PAS-H). The sections were also immunohistochemically stained utilising the avidin-biotin-peroxidase complex method for pan-cytokeratin and vimentin antibodies (Bourne 1985). Mouse anti-human vimentin and pancytokeratin kits (Dako Corp, Carpinteria, CA) that were used as primary antibodies were diluted to 1 : 100. Skin sections were used as positive and negative controls for vimentin and pan-cytokeratin. The epidermal layer was the positive control for pancytokeratin, while the dermal layer was the positive control for vimentin. Immune complexes were stained with diaminobenzidine tetrahydrochloride, and counterstained with Mayer's haematoxylin (MH).

Macroscopically, approximately 1500 ml of cloudy and bloody exudate were found in the thoracic cavity. The parietal pericardium was covered with greyish-yellow coloured multilobular nodular masses ranging from about 1 to 5 cm in diameter. The lungs were collapsed and atelectatic due to exudation and the pleura was covered by rough irregular velvet-like proliferations, greyish-yellow in colour, and approximately 1 to 5 mm length (Figure 1). The presence of abscess foci with liquefied-centrum was observed when a section surface of the lung was examined. The appearances of the oesophageal serosa, thoracic aorta and the thoracic surface of the diaphragm were similar to pleural and pericardial surfaces. There were no changes on the visceral pericardium, tracheobronchial lymph nodes and the peritoneum along with internal organs.

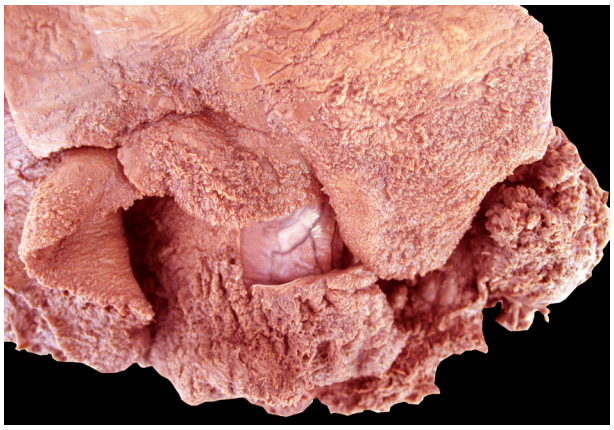

Figure 1. Macroscopic appearance of the pericardial and pleural surfaces

Histologically, papillary proliferations composed of mesothelial cells similar to cubic or cylindrical epithelium covering a connective tissue rich in capillary proliferations were observed in the pericardium (Figure 2A). It was observed that some tumour cells contributed to giant cell formation through integration (Figure 2B). There were extensive neutrophil infiltrations in the connective tissue. The pleura were also of similar histological appearance and there were marked lymphocyte and plasmocyte infiltrations adjacent to the lungs (Figure 2C). The integrity of the pleural basal membrane was preserved in the examination performed with PAS-H (Figure 2D). Neoplastic cells had nuclei with large eosinophilic granular cytoplasms and with large vesicular and single nucleoli. Some neoplastic cells were determined to include intracytoplasmic vacuoles. The neoplastic cells contained a few mitotic figures. In the lungs and the bronchial lymph nodes, macrophages with extensive cytoplasmic hemosiderin pigment were detected. The alveoli in some regions of the lungs were atelectatic and some were emphysematous. Immunohistochemically, these gave weak positive reactions with anti-pancytokeratin staining (Figure 2E, F) while giving intense reactions with anti-vimentin staining (Figure 2G, H).

DISCUSSION AND CONCLUSIONS

Pericardial mesothelioma accompanying pleural effusion results in cardiac insufficiency (Cobb and Brownlie 1992). While the tumour shows its effect where it is first located, it is recognised as a malignant tumour as it invades the lymph vessels or rapidly spreads by implantation (Ikede et al. 1980). In the present case, nodular or velvet-like proliferative lesions were observed on the visceral pleura, diaphragm and the esophageal serosa, as well as the pericardial surface. When the development of lesions was considered, the present case was diagnosed as pericardial mesothelioma spreading to the pleura and serosal surfaces by implantation.

Although clinical and pathological characteristics have been defined in natural mesothelioma

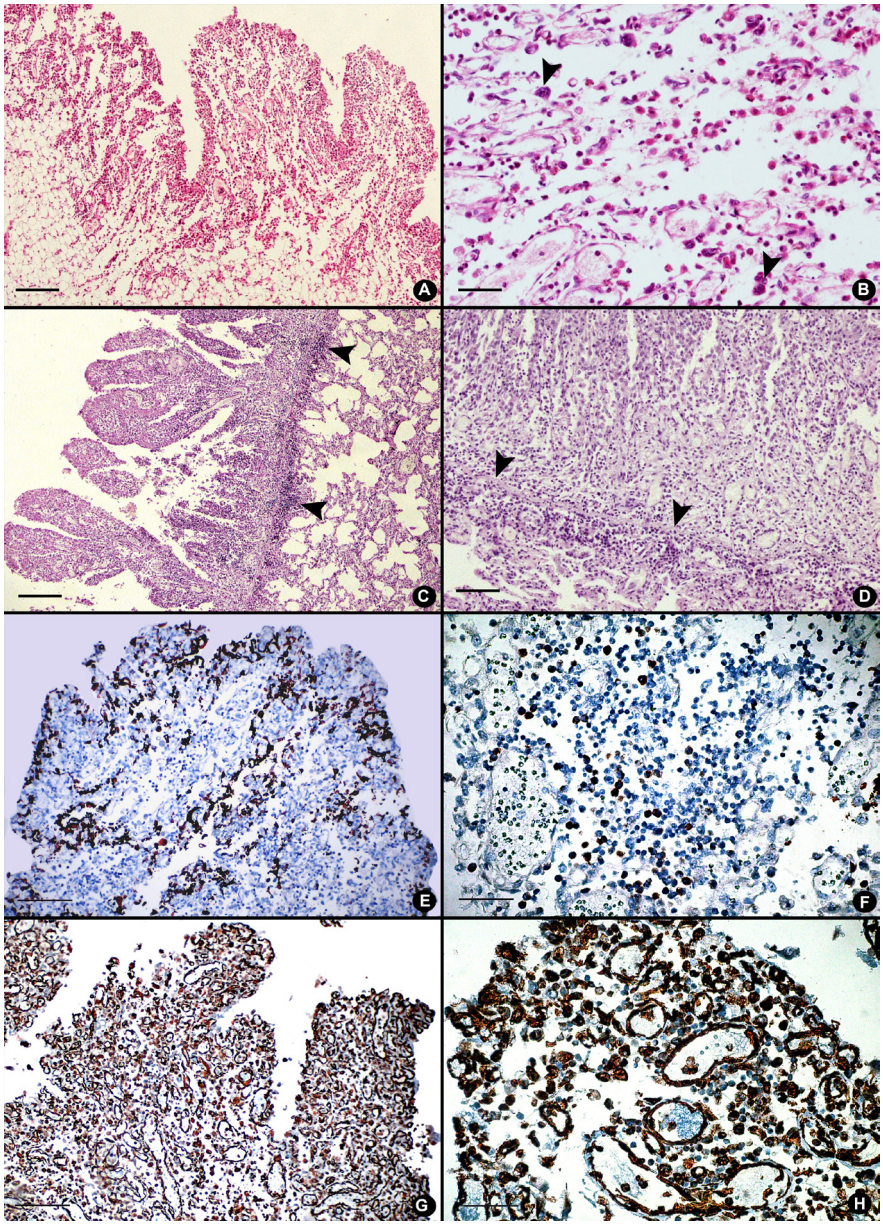

Figure 2. **A**. Histological appearance of the pericardium, HE, bar = 200 µm. **B**. Giant cell formations in the tumour cells (arrow heads), HE, bar = 50 µm. **C**. Mononuclear cell infiltrations in the border of the pleura (arrow heads), PAS-H, bar = 200 µm. **D**. Appearance of pleural basement membrane (arrow heads), PAS-H, bar = 50 µm. **E**. Weak immunohistochemical reaction with anti-pancytokeratin antibody in the neoplastic cells, MH, bar = 200 µm. **F**. Higher magnification anti-pancytokeratin staining in the neoplastic mesothelial cells, MH, bar = 50 µm. **G**. Intense immunohistochemical reaction with anti-vimentin antibody in the tumour cells, MH, bar = 200 µm. **H**. Higher magnification anti-vimentin staining in the neoplastic cells, MH, bar = 50 µm

cases in dogs, the etiological and epidemiological factors that cause these tumours are not yet understood. One of the etiological factors of mesothelioma is contact with chemical substances such as asbestos (primarily), iron, and silicate (Harbison and Godleski 1983; Head et al. 2002; Caswell and Wiliams 2007). According to the reports of dog owners, high rates of asbestos were detected in the lungs of dogs belonging to people in contact with asbestos in their professional life (Glickmann et al. 1983). It has been stated that pesticides are important etiological factors in the development of mesothelioma (Ogilvie and Moore 2006). However, genetic factors and some viruses have also been reported to lead to tumour development (Cacciotti et al. 2001). Asbestos particles taken in through the

respiratory tract in humans spread to the pleura through the lymphatic system and cause chromosomal defects in mitotic mesothelial cells. Genetic mutations in mesothelial cells have been reported to occur by inactivation or loss of tumour suppressor genes (Jaurand and Fleury-Feith 2005). In this case, the animal was a tracking dog; the tumour may have developed as a result of lung exposure to asbestos and other chemical substances through the respiratory tract.

Mainly three types of mesotheliomas have been histologically defined in domestic animals: epitheloid, sarcomatoid and biphasic or mixed. The most common form is the epitheloid type, because of the similarity of the tumour cells to epithelial cells and papillary formations (Caswell and Wiliams 2007). The sarcomatoid type, which is similar in appearance to a fibrosarcoma has been described less frequently (Head et al. 2002; Kapakin et al. 2012). Biphasic or mixed type denotes mesotheliomas that carry both characteristics of the epitheloid and sarcomatoid types (Sevcikova et al. 2000). Mesotheliomas show malignant characteristics at low rates, invade the tissues at minimal degrees, and rarely metastasise to lymph nodes and remote tissues (Head et al. 2002; Caswell and Wiliams 2007). The visceral metastasis of mesothelioma has been reported to be rare (Kim et al. 2002), but metastasis to the accessory lobe of the right lung was detected in a dog with pericardial mesothelioma (Ledecka et al. 2010). The differential diagnosis of mesotheliomas generally depends on its basic histological characteristics. In the differentiation of epitheloid mesotheliomas, carcinomas and other epithelium-originated tumours, and in the differentiation of sarcomatoid mesothelioma, sarcoma and other spindle cell tumours, and in the differentiation of mixed type, other mixed tumours such as synovial-originating tumours should be considered (Head et al. 2002; Caswell and Wiliams 2007). Immunohistochemistry is useful in differentiating mesothelioma. Vimentin-positivity is used to differentiate mesothelioma from pulmonary carcinoma by vimentin negativity; pancytokeratin-positivity in sarcomatoid type mesotheliomas is generally used to differentiate it from cytokeratin-negative sarcomas (Kapakin et al. 2012). Both positive pancytokeratin and vimentin staining are constant features of mesotheliomas which may differentiate as mesothelial cells distinct from epithelial and mesenchymal cells (Attanoos et al. 2000). In the present case, the tumour cells were positive for the epithelial marker pancytokeratin and the mesenchymal marker vimentin.

In conclusion, in this case, a diagnosis of pericardial epitheloid mesothelioma was made based on the macroscopic appearance and distribution of the tumour and the histopathological and immunohistochemical characteristics.

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