MESOTHELIOMA OF THE PERICARDIUM IN A BERNESE MOUNTAIN DOG - A CASE REPORT

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On the basis of a clinical case we describe the symptoms, development and surgical method used for a six-year-old Bernese mountain dog affected by mesothelioma growing OUI of the pericardium. We provide an overview of the incidence of the tumor, risk factors, pathogenesis and possibilities of therapy in this canine breed. In our clinical case we did not confirm any contact of the dog with asbestos or larger amount of pesticides, which are described as etiological factors of mesothelioma in the literature. The dog's owner did not visit our clinic due to suspicion of a tumor, but because of the general weakness of the dog accompanied by hematuria. The owner later added that the dog had already been suffering from general weakness and depression for a longer lime. The radiological examination showed a non-specific effusion in the thoracic cavity, and the ultrasound examination located the mass in the area of the heart with production of exudate into the thoracic cavity. As a result of cytological and histological examinations, a mesothelioma was detected. During thoracotomy a tumorous mass was diagnosed between the pericardium and the left thoracic wall, located on the right accessory pulmonary lobe. The tumor mass was connected with the diaphragm. Because of the bad prognosis and after consultation with the owner, the dog was euthanized. The incidence of mesothelioma in Bernese mountain dogs is described for the first time.

Key words dog, tumor, mesothelioma, pericardiectomy, thoracic cavity.

Introduction

According to statistics from various countries, the incidence of tumors has been increasing continuously. In our country, it can also be connected with the fact that dogs live longer. An increased risk of tumors in geriatric patients has been associated with longer life spans, but the occurrence of tumors in dogs of a medium or younger age is not rare. Nevertheless, the incidence of tumors in dog remains connected mainly with age (WITHROW and VAIL, 2007).

Mesothelioma is a very rare tumor in dogs and cats that grows in an uncoordinated way from mesothelial cells of the epithelium of body cavities. The prevalence of mesothelioma has been reported as one case in every 1000 dogs (GARRETT, 2007). Primary mesothelial tumors in dogs occur in the pleura, pericardium, peritoneum and in the tunica vaginalis of the scrotum. Malignant biphasic peritoneous mesothelioma has already been described in a dog (SEVCIKOVA *et al.,* 2000).

A risky etiologic factor of mesothelioma is long-term contact with asbestos. It has been reported that owners of dogs with mesothelioma have jobs during which they come into contact with this agent, and a higher concentration of asbestos has also been detected in the lungs of these dogs (GLICKMANN *et al.,* 1983). OGILVIE and MOORE (2006) also consider pesticides an ethiologic factor that increases the risk of mesothelioma. Mesothelial tumors occur in older dogs, mainly at the age of approximately eight years. GLICKMANN *et al.* (1983), KIM et al. (2002) published a case of juvenile mesothelioma in a crossbreed dog, and VURAL et al. (2007) described epitheloid mesothelioma in a nine month-old crossbreed. The tumor is more characteristic of male dogs than bitches, and no breed predisposition for this oncological disease has been found so far. In terms of breed predisposition, we describe herein the first case of mesothelioma in a Bernese mountain dog.

Classical mesotheliomas are diffuse nodular multi focal masses that cover body cavities. Extensive effusions in cavities arise due to infiltration and exudation of tumorous surfaces or lymphatic vessels that have been compressed by tumorous tissue. Therefore, the most significant and trustworthy sign of mesothelioma is dyspnoea caused by pleural exudation or an enlarged abdominal cavity in which peritoneal fluid has accumulated. Affected dogs manifest decreased tolerance to load, and cough (HARBISON and GODLESKI, 1983; OGILVIE

and MOORE, 2006). Dogs with mesothelioma in the pericardium may show signs of acute tamponade of the right side of the heart (COBB and BROWNLIE, 1992). Ultrasonographic examination of the abdominal cavity need not have any diagnostic significance, since tumorous cells may grow on the epithelial surface and therefore are, for this type of diagnostic imaging, invisible. Computer tomography (CT) of the thoracic cavity will specifically demonstrate nodular changes of the pulmonary parenchyma as well as freely within thoracic cavity itself (STEPIEN *et al.,* 2000).

Differentiation of mesothelioma from adenocarcinoma or sarcoma is often very difficult on the basis of cytological examination. Diagnosing mesothelioma requires taking an adequate quantity of tissue from an open biopsy. It is possible to carry out sampling with the assistance of thoracoscopy or laparoscopy, which is associated with a lower risk of iatrogenic damage (PETERS *et al.,* 2003). Histological mesotheliomas should be differentiated from carcinomas, adenocarcinomas, or sarcomas depending on the type of mesothelioma. There are no established cell markers which would define mesothelial cells (CORSON, 2004).

According to many authors, no successful therapy of mesotheliomas exists. Pericardiectomy in dogs may be regarded as a palliative method of therapy only after finding signs of cardiac tamponade. The median survival of patients after pericardiectomy with mesothelioma was found to be 13.6 months, during which three of them also received adjuvant intravenous chemotherapy (DUNNING *et al.,* 1998). MOORE *et al.* (1991) applied intracavitarily cisplatina as a form of palliative therapy with good tolerance, while the production of exudate stopped. Since the penetration of chemotherapy into tissues is only on the surface (2-3 cm), local forms of chemotherapy have been unsuccessful in cases of large mesothelioma (GARRETT. 2007). Palliation of clinical symptoms caused by effusion can be achieved by thoracocentesis or pericardiectomy, which may be tolerated by the patient for some months (BIRCHARD and GALLAGHER, 1988).

Materials and methods

History- A six-year-old male Bernese mountain dog was admitted to the Small Animal Clinic in the Department of Surgery, Orthopaedics and Radiology for an X-ray examination of the caudal abdominal cavity for suspected enlargement of the prostate. Its history indicated general weakness and blood in urine.

Diagnostics and evaluation. We performed radiological and ultrasound examinations with a thoracocentesis. Whilst being positioned for the radiological examination, the dog started to collapse. The visible mucosal membranes were blue-violet, which suggested cardiopulmonary insufficiency. After successful resuscitation, a radiograph of the dog's chest in the latero-Iateral right position was completed. On the radiograph, a large quantity of exudation in the thoracic cavity was visible (Fig. 1), and the caudal pulmonary lobes were being pressed caudally and proximally with reduced radiolucency. The silhouette of the heart was invisible. Simultaneous auscultation confirmed the presence of fluid in the pericardium as well as its surroundings. We performed an ultrasonographic examination with the dog in a sitting position with the left thoracic extremity raised by a five MHz probe in the 4th and 8th intercostal areas. During the ultrasound examination, we observed a heteroechogenic mass between the thoracic wall and the heart, in the ventral part of the chest. Anechogennic fluid was located dorsally and cranially from this mass.

Fig. 1. Radiogram: latero-Iateral right position of thorax. Trachea is pressed towards proximal cranial rnediastine. We can observe effusion of thoracic cavity. Pulmonary parenchyma of caudial lobes is pressed and collapsed by fluid and mass.

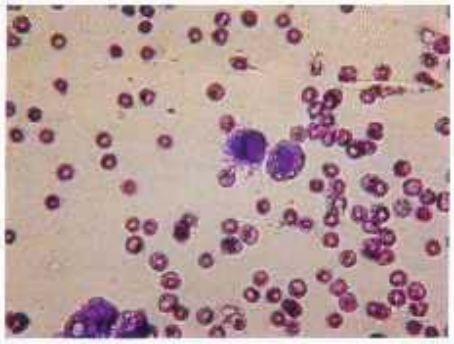

Fig. 2a. Presence of normal resp. reactive mesothelial cell of oval shape with peripherally located core. On the outer side of cytoplasrnatic membrane it is possible to observe the presence of slightly pink to colorless lining, the finding of which is characteristical for this type of cells. In immediate closeness is located the tumorous cell in phase of mitotic activity. Pleural effusion, Diff-Quik, 40 x 2.

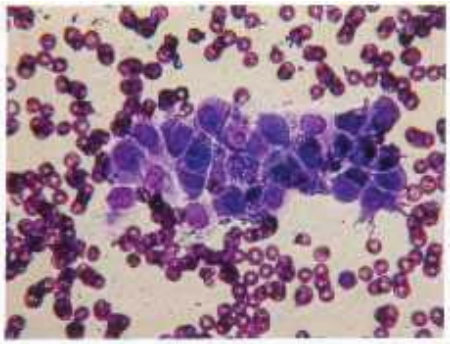

Fig. 2b. Presence of a cluster of tumorous mesothelial cells, on which it is possible to observe a significant variability regarding the shape and size of cells (cell heterotypia), hyperchromatosis, mitotic activity and vacuolisation of cytoplazrna Pleural effusion, Diff-Quik, 40 x 2

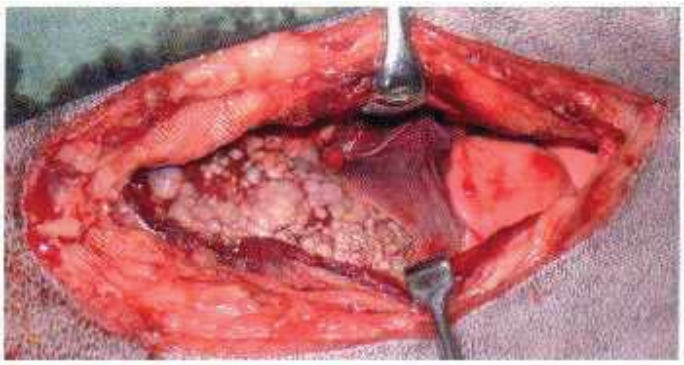

Fig. 3. Thoracotomy. Airy pulmonary tissue (pink color). Under it is seen the atelectatic lobe (red color). Cystic and granulomatous formation on pericardium - mezotheliornous mass.

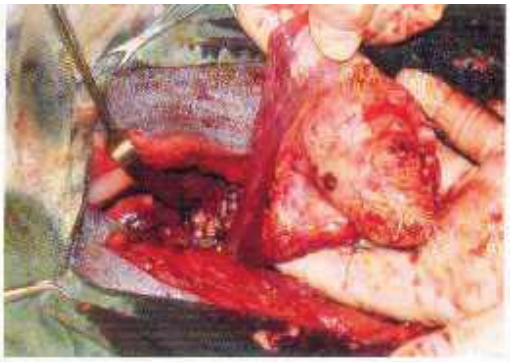

Fig. 4. Accessory pulmonary lobe from the right side of the thorax - atelectasis of lobe with mezotheliornous mass on its point.

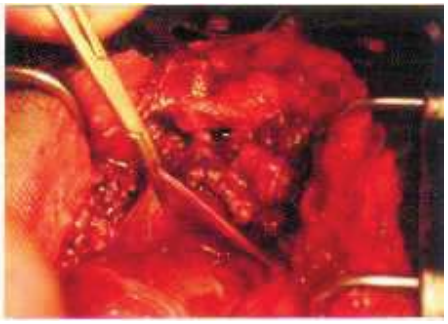

Fig. 5 . Partial pericardiectomy. Behind the pericardium is seen the mesoteliornous granular mass.

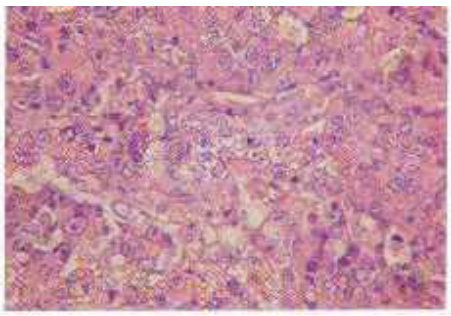

Fig. 6. Presence of epitheloid cells and high mitotic activity. Tumorous tissue taken from accessory pulmonary lobe. H&E; 40 x 2.

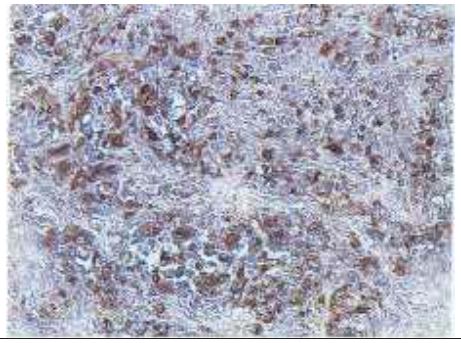

Fig. 7. Positive immunohistochemical staining for cytokeratine in tumorous epithelial cells. Biotin streptavidin peroxidase detection system; 20 x 2.

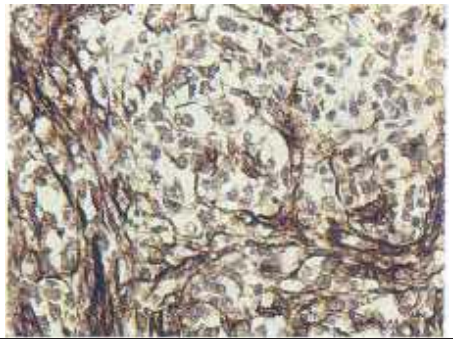

Fig. 8. Positive immunohistochemical staining fo vimentin intermediate protein in stromal cells of the tumour. Biotin streptavidin peroxidase detection system; 40 x 2.

Simultaneously, we carried out thoracocentesis from the left side in the area of the 4th intercostal area under the control of a probe. We aspirated about 40 mL of hemorrhagic viscosal fluid, from which we prepared a cytological sample. After fixation, it was stained by Diff-Quik, and we carried out the cytological examination having suspected the presence of a mesothelioma (Fig. 2a, 2b).

Surgical intervention. .On the basis of examinations proceeding from the suspected diagnosis - pericardial mesothelioma - we carried out a thoracotomy from the left side after resection in the 4th intercostal area with an osteotomy of the 5th rib in the distal part of its arch, in order to take samples for histological examination before conducting a partial pericardiectomy. After the thoracotomy, hemorrhagic fluid (simultaneously with expirium) started to flow from the surgical wound, and we observed a mass with a number of cysts growing out of the pericardium, in the area of the right atrium and ventricle (Fig. 3). After using openers on the thoracic cavity and lifting the left side of the thoracic wall, we found that the newly grown mass located in the caudal direction was connected with the left diaphragmatic arch and, on the ventral side, was adhering to the inner wall of the sternum. As a result of an investigation of the right part of the caudal pulmonary lobes, we retracted the rigid elastic mass into the surgical wound and identified it as a mass coming out of the accessory pulmonary lobe (Fig. 4). The pulmonary parenchyma was collapsed and atelectatic, of a dark red color. The tumorous mass was very frail to the touch, and hemorrhagic fluid was flowing out of the opened cysts. At first we decided on a partial pericardiectomy (Fig. 5). However, because of very extensive adhesions in the sternum, the left membrane pillar and the pulmonary lobe, with the consent of the owner we stopped the operation, while we took part of the mesothelial mass, as well as the mass growing out from the accessory pulmonary lobe, for histological

examination. After sampling for the histological examination, we ended the operation and the dog was euthanized. Samples were fixed in a 10% neutral phosphate-buffered formalin, sectioned at 5 urn, and stained with hematoxylin and eosin. This histological finding was based on the sampled pericardial mass as well as the mass on the accessory pulmonary lobe (Fig. 6.). In all samples we observed cells of round to oval shape which, by their arrangement and shape, reminded us of the epithelium. The cells showed significant heterotypia and mitotic activity.

To confirm the diagnosis, immunohistochemistry was carried out. The expression of cytokeratine and vimentin intermediate filaments was analysed on formalin-fixed, paraffin-embedded tissue sections. The reactivity to immunohistochemical markers was done by means of the Biotin-Streptavidin amplified peroxidase detection (B-SA) system (Biogenex, Sam Ramon, CA, USA). The antibodies used are summarized in Table 1.

Table 1. Details of primary antibodies used

Specific antibody	Pretreatment	Type	Dilution	Sources
HMW	Digested	Monoclonal anti mouse	1:50	Biogenex
Vimentine	Undigested	Polyclonal antirabbit	1:50	Biogenex

Tumour epithelial cells strongly demonstrated an expression of cytokeratine (Fig.7), and the positivity for vimentine was proved in the fibrous stromal cells of the tumor (Fig. 8). Negative controls were obtained omitting the primary antibodies.

On the basis of histological and immunohistochemical pictures, the diagnosis of malignant epithelial mesothelioma was established.

Discussion

The clinical case of a dog with confirmed mesothelioma in the pericardium described above had all the clinical signs and development described by other authors. ECHANDI *et al.* (2007) reported the occurrence of pleural mesothelioma in a Welsh Corgi dog with a two-month history of progressive coughing, pleural effusion and the collapse of the right central pulmonary lobe. The granular form of cardial mesothelioma in a ten-year-old golden retriever was diagnosed by BROWER et al. (2006). In our case, it was a Bemese mountain dog. From the point of view of etiology, the owner of the dog cannot confirm that the dog had contact with asbestos either directly or indirectly. Asbestos can have an effect directly and also indirectly in connection with phenotypical and genetic changes in the affected cells. The loss of genes for tumor suppression is regarded as the reason for the transformation of mesothelial cells (JAURAND and FLUERY-FEITH, 2005). The owner also thinks that the patient did not have excessive contact with pesticides, which could have been the cause of the origin of mesothelioma (OGILVIE and MOORE, 2006). The owner retrospectively reports that for about half a year she had observed reluctance in the dog for long-term walking and training. The dog had dyspnoea and became exhausted easily, which the owner connected to the untypically hot summer in the location where the dog had lived. She came with the dog for treatment of another probably concomitant disease, and only a targeted radiological examination with respect to the positioning of the dog on the table caused stress and dyspnoea. Indirect symptoms of the presence and development of mesothelioma have also been described by other authors (GARRETT, 20070 HARBISON and GODLESKI, 1983). MACHIDA *et al.* (2004) published their work on the development of pericardial mesothelioma after 30 to 40 months following the occurrence of idiopatic hemorrhagic pericardial effusion and support the concept of chronic inflammation, which can cause the neoplastic transformation of mesothelial cells in dogs. Radiological examination of the thoracic cavity confirmed the presence of exudation, and ultrasonographic examination determined the presence of a mass situated between the pericardium and the thoracic wall on the left side, without more detailed specification. DiPINTO *et al.* (1995) regarded ultrasonography as a very useful and successful method of diagnosing diseases of the thoracic and abdominal cavities, although they add that mesotheliomas very rarely penetrate through the surfaces of organs in these cavities. We can also confirm this finding in our clinical

case, since, after pericardiectomy only hemorrhagic fluid was flowing out of the pericardium, causing a cardiac tamponade, while the inner lining of the pericardium was rather smooth without the invasion of cells or a tumorous mass.

The cytological examination directing our approach indicated that it might be a mesothelioma, though the majority of authors require two-nucleic or multi-nucleic cells for this diagnosis. The definitive diagnosis was determined histologically after an excision was opened from the newly grown mass in the thoracic cavity. According to KIM *et al.* (2002), visceral metastases from mesotheliomas are rare, but in our case we found atissue mass on the accessory pulmonary lobe on the right side, histologically confirming mesothelioma.

We conducted a thoracotomy for the purpose of diagnostic sampling for a histological examination and removal of the diagnosed mass growing out of the pericardium into the thoracic cavity and, according to sonographical examination, touching the thoracic wall. Pericardiectomy confirmed the presence of fluid and provided the possibility for a histological diagnosis. Due to the extent and the involvement of the pulmonary tissue of the later detected mesothelioma, and without thepossibility of using chemotherapy, we recommended euthanasia of the dog and the owner gave us consent.

We have given an overview of the etiology, symptomatology, pathogenesis, diagnostics and possibilities for therapy in connection with the occurrence of pericardial mesothelioma in a dog at the age of six years. We did not confirm either the contact of the dog with asbestos or a large amount of pesticides as etiological factors, which are described in literature. The clinical case had an identical course with cases that have been published before. The visit of the dog's owner to our clinic resulted from a reason other than suspicion of respiration-circulation failure. Radiological and ultrasonographical examination indicated non-specific effusion of the thoracic cavity. Cytological and histological examination confirmed mesothelioma. Intraoperationally, a mass of tumorous tissue was also diagnosed on the right accessory pulmonary lobe. After consultation with the owner, the dog was euthanized.

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