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Case report

MALIGNANT MESENCHYMOMA OF THE AORTIC VALVE IN A DOG

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Summary: A malignant mesenchymoma of the aortic valve with an infiltrative growth into the myocardium in an 8-year-old intact male German shepherd is presented. Macroscopically, the aortic valve leaflets were markedly thickened, yellowish-grey and rough, with rounded edges, a rubbery consistency and greyish and smooth cut surface. Approximately 90% of the valve tissue was altered. Microscopically, alteration consisted predominantly of liposarcomatous, fibrosarcomatous and leiomyosarcomatous components and a focus of chondrosarcomatous cells. Focally, liposarcomatous cells infiltrated the myocardial muscle fibres. Mitoses were rare. Histopathologically, malignant mesenchymoma of the aortic valve was diagnosed. The diagnosis was confirmed by immunohistochemistry. A strong diffuse positive reaction for vimentin and a negative reaction for desmin were observed in all neoplastic components. In leiomyosarcomatous component a strong positive reaction for smooth muscle actin (SMA) was detected multifocally. Severe dilatation of all heart chambers, mild endocardiosis of the mitral and tricuspidal valves, severe congestion of the liver, spleen, kidneys and lungs with severe pulmonary oedema, moderate ascites and mild hydrothorax were also observed. We conclude that the dog died of chronic heart failure induced by malignant mesenchymoma of the aortic valve and endocardiosis of the mitral and tricuspidal valves.
Malignant mesenchymomas are uncommon tumours in animals and humans, rarely reported in dogs. To the best of our knowledge, this is the first report of a malignant mesenchymoma of the aortic valve with an infiltrative growth into the myocardium in animals.

Key words: malignant mesenchymoma; aortic valve; German shepherd; histopathology; immunohistochemistry

Introduction

Cardiac tumours are uncommon in dogs, with the prevalence of 0.19%. To date, haemangiosarcoma, rhabdomyo(sarco)ma, chondro(sarco)ma, leiomyo(sarco)ma, fibro(sarco)ma, myxoma, myxo-, lipo- and neurofibroma, haemangioma, lymphangioendothelioma, squamous cell carcinoma, mixed spindle cell and round cell sarcoma, pericardial mesothelioma and malignant myocardial mesenchymoma have been reported (1).

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Malignant mesenchymomas are soft tissue tumours of mesenchymal origin characterized by the presence of two or more unrelated, malignant cell lines, e.g. fibrosarcoma, liposarcoma, chondrosarcoma, leiomyosarcoma or rhabdomyosarcoma, in the same tumour. These tumours, rare in animals as well as in humans, have an unpredictable biological behaviour and can develop in different anatomic sites. Malignant mesenchymomas usually have a longer course than most malignant neoplasms and any one or all of the individual components may metastasize (2, 3). In animals, malignant mesenchymomas have to date been described in the liver (4), long

bones (5), spleen (6), heart (1, 7), soft tissue of the rear limb (8), intermandibular area (9) and dorsal area of the abdomen (10) in dogs, in the nasal cavity in a bull (11) and in the intra-abdominal soft tissue in a ferret (2).

Pathomorphological and immunohistochemical features of a malignant mesenchymoma of the aortic valve in a German shepherd, accidentally encountered during necropsy, are reported. To the best of our knowledge, this is the first report of a malignant mesenchymoma of the aortic valve in animals.

Material and methods

Case history

Eight-year-old intact male German shepherd with no anamnestic and clinical data was necropsied at the Institute for Pathology, Forensic and Administrative Veterinary Medicine, Veterinary Faculty, University of Ljubljana for education purposes.

Necropsy, histopathological and immunohistochemical examination

Heavily altered aortic valve leaflets, myocardium, lungs, liver, kidneys and spleen were collected during the necropsy for histopathological and immunohistochemical examination. All samples were fixed in 10% buffered formalin, routinely embedded in paraffin, sectioned at 4 µm, stained with hematoxylin and eosin (HE) and Toluidine and examined under a light microscope.

Immunohistochemical assays were performed on 4 µm sections of formalin-fixed, paraffin-embedded tissue samples. The mouse monoclonal antibody anti-human smooth muscle actin (clone 1A4, DAKO), mouse monoclonal antibody anti-human desmin (clone D33, DAKO) and mouse monoclonal antibody anti-human vimentin (clone V9, DAKO), at 1:50 dilution were used for the immunolabelling. Antigen retrieval was performed by microwave treatment at medium power (550 W) for 15 minutes in 0.1M citrate buffer (pH 6.0) for desmin and vimentin, and in EDTA buffer (pH 9.0) for desmin. The sections were incubated with primary antibodies for one hour at room temperature in a humid chamber. Endogenous peroxidase activity was quenched in Peroxidase-Blocking Solution, Dako REAL™ (DAKO) for 30 minutes at room temperature. Subsequently, visualization kit DAKO REAL™ EnVision™ Detection System Peroxidase/DAB+, Rabbit/Mouse (DAKO) was applied according to the manufacturer's instructions. Sections were counterstained with Mayer's haematoxylin and mounted.

Sections of normal canine small intestine were used for positive control. Negative control included incubation with DAKO Cytomation Antibody Diluent (DAKO) without the primary antibody.

Results

The thoracic cavity contained 200 ml of red-tinged serous fluid and the abdominal cavity 500 ml. The liver, spleen and kidneys were severely congested, the other abdominal viscera were grossly normal. The lungs were severely congested and oedematous and partially displaced by the severely enlarged heart. The pericardial sac was without effusions. Atria and ventricles of the heart were markedly dilated. A mild endocardiosis of the mitral and tricuspidal valves was noticed. When the aorta was opened, yellowish-gray, rough, 0.5 cm thick aortic leaflets with rounded edges and rubbery consistency were observed. Approximately 90% of the valve tissue was altered. On the cut surface, the leaflets were pink-greyish and smooth.

Histologically, a large mass composed of neoplastic mesenchymal cells was observed within the aortic valves. The tumour consisted predominantly of liposarcomatous, fibrosarcomatous and leiomyosarcomatous components. An islet of chondrosarcomatous cells was incorporated in the fibrosarcomatous component. A liposarcomatous component, with dense infiltrates of eosinophils, was multifocally penetrated by wide, irregularly oriented fascicles of fibrosarcomatous cells. Between those fascicles narrow bundles of leiomyosarcoma were found. The islet of chondrosarcomatous tissue was surrounded by a thick strand of collagenous stroma. Vascular stroma was abundant. The mitotic rate ranged from 0 to 2 per high power field. Focally, the tumour infiltrated the myocardial muscle fibres. The tumour was diagnosed as a malignant mesenchymoma of the aortic valve. Immunohistochemical examination demonstrated

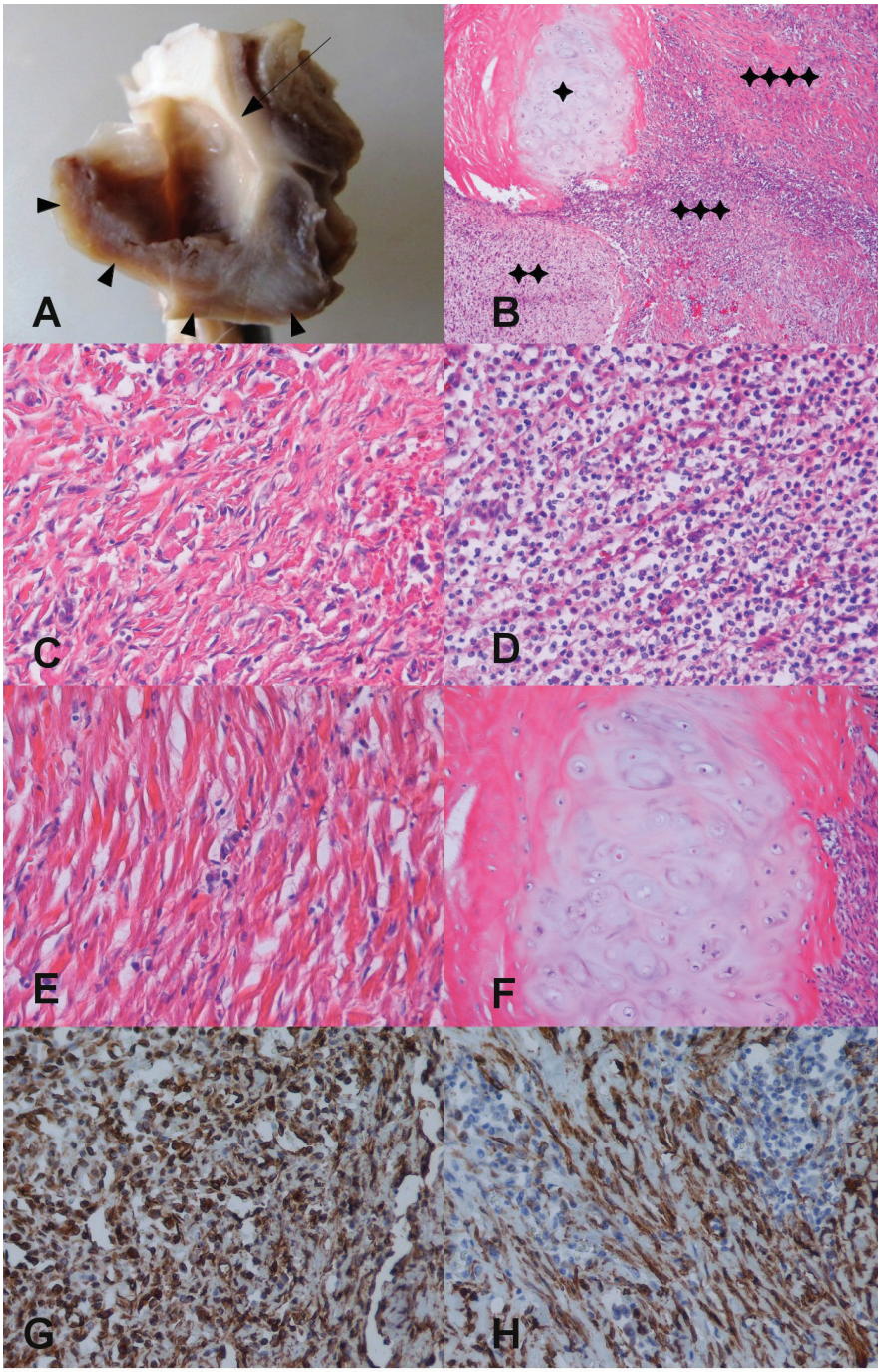

Figure 1: Macroscopic, histopathologic and immunohistochemical features of the malignant mesenchymoma of the aortic valve from a dog. **A**, cut surface of the aortic valve after formalin fixation. Note heavily altered, rough, pink-greyish valve leaflet (arrowheads) of the aorta (arrow). **B**, histological section from malignant mesenchymoma (MM) of the aortic valve showing chondrosarcomatous (**+**), liposarcomatous (**++**), leiomyosarcomatous (**+++**), and fibrosarcomatous (**++++**) components. Hematoxylin and eosin (HE), 40x. **C,** histological section of MM of the aortic valve showing fibrosarcomatous component. HE, 200x. **D**, histological section of MM of the aortic valve showing liposarcomatous component. HE, 200x. **E**, histological section of MM of the aortic valve showing leiomyosarcomatous component. HE, 200x. **F**, histological section of MM of the aortic valve showing an islet of chondrosarcomatous cells. HE, 100x. **G**, immunohistochemistry (IHC) of MM of the aortic valve showing strong diffuse positive labelling for vimentin. IHC, 200x. **H**, immunohistochemistry of MM of the aortic valve showing labelling for SMA. IHC, 200x

a strong diffuse positive reaction for vimentin. Furthermore, a strong SMA reactivity was noticed in areas with the leiomyosarcomatous component. The staining for desmin was negative. The results of immunohistochemical examination confirmed the previous histopathological diagnosis of malignant mesenchymoma.

The only pathological lesion diagnosed in other examined organs was a severe congestion.

Discussion

The described malignant mesenchymoma was diagnosed in the aortic valve. The tumour showed locally invasive growth into the myocardium, but no distant metastases were noted. Malignant mesenchymomas very rarely affect dogs. To date, they have been described in the liver (4), radius (5), spleen (6), soft tissue of the rear limb (8),

intermandibular area (9) and dorsal area of the abdomen (10) and in the heart (1, 7). The primary tumour may be locally invasive, but metastases to distant sites can occur (2). Metastases to the lung (7, 8, 9, 10), kidney, abdominal wall, mediastinum and parietal pleura (9), axillary lymph nodes, adrenal glands and liver (10), and mesentery (4) were observed in other cases of malignant mesenchymoma in animals.

Malignant mesenchymoma of the aortic valve had four malignant cell lines: liposarcomatous, fibrosarcomatous, leiomyosarcomatous, and chondrosarcomatous. This is in accordance with the diagnosis of malignant mesenchymoma. Malignant mesenchymoma is characterised by a combination of at least two unrelated neoplastic cell lines of mesenchymal origin within a single tumour (10). In dogs, other authors reported rhabdomyosarcomatous, myxosarcomatous and hemangiosarcomatous differentiation in the hepatic malignant mesenchymoma (4); fibrosarcomatous, rhabdomyosarcomatous, liposarcomatous and chondrosarcomatous elements in the malignant mixed mesenchymal tumour of the heart (1); leiomyosarcomatous, rhabdomyosarcomatous, chondrosarcomatous and liposarcomatous components in the malignant mesenchymoma of the heart base (7); liposarcomatous and osteosarcomatous (10), as well as osteosarcomatous and fibrosarcomatous cell lines (2) in soft tissue of the abdomen; areas of chondrosarcoma, leiomyosarcoma and osteoid in the soft tissue of the rear limb (8); and myxosarcomatous and osteosarcomatous tissue in soft tissue of the intermandibular area (9).

In the malignant mesenchymoma of the aortic valve, the reaction for vimentin was strongly positive and the reaction for desmin was negative. A strong multifocal reaction for SMA was detected only in the leiomyosarcomatous components. Results of immunohistochemical examination are in accordance with the previously described cases of malignant mesenchymoma in animals. In literature, immunohistochemistry has only been described in three cases of malignant mesenchymoma in animals: in a ferret a positive reaction for vimentin was found (2), in a dog a positive reaction for desmin and SMA was reported (1) and in another dog a positive reaction for vimentin and actin occurred (9). We believe that the German shepherd died of chronic heart failure caused predominantly by the malignant mesenchymoma of the aortic valve. Unfortunately, no data on the clinical signs and the course of the disease were available.

The described case is the first report of a malignant mesenchymoma of the aortic valve in animals. In humans to date, the only case of mesenchymoma involving heart valves was a chondrosarcomatous mesenchymoma, which was diagnosed in the mitral valve (12).

References

1. Machida N, Kobayashi M, Tanaka R, Katsuda S, Mitsumori K. Primary malignant mixed mesenchymal tumour of the heart in a dog. J Comp Pathol 2003; 128: 71–4.

2. Petterino C, Bedin M, Vascellari M, Mutinelli F, Ratto A. An intra-abdominal malignant mesenchymoma associated with nonabsorbable sutures in a ferret (*Mustela putorius furo*). J Vet Diagn Invest 2010; 22: 327–31.

3. Pull RR, Thompson KG. Tumors of joints. In: Meuten DJ, ed. Tumors in domestic animals. 4th ed. Ames: Iowa State Press, 2002: 241–3.

4. McDonald R, Helman RG. Hepatic malignant mesenchymoma in a dog. J Am Vet Med Assoc 1986; 188: 1052–3.

5. Misdorp W, van der Heul RO. An osteo-(chondro-)liposarcoma ("Malignant Mesenchymoma") of the radius in a dog, with two types of metastases. Zentralbl Veterinärmed A 1975; 22: 187–92.

6. Spangler WL, Culbertson MR, Kass PH. Primary mesenchymal (Nonangiomatous/ Nonlymphomatous) neoplasms occurring in the canine spleen: anatomic classification, immunohistochemistry, and mitotic activity correlated with patient survival. Vet Pathol 1994; 31: 37–47.

7. Gómez-Laguna J, Barranco I, Rodríguez-Gómez IM et al. Malignant mesenchymoma of the heart base in a dog with infiltration of the pericardium and metastasis to the lung. J Comp Pathol 2012; 147: 195–8.

8. Moore RW, Snyder SP, Houchens JW, Fox JJ. Malignant mesenchymoma in a dog. J Am Anim Hosp Assoc 1983; 19: 187–90.

9. Murphy S, Blunden AS, Dennis R, Neath P, Smith KC. Intermandibular malignant mesenchymoma in a crossbreed dog. J Small Anim Pract 2006; 47: 550–3.

10. Robinson TM, Dubielzig RR, McAnulty JF. Malignant mesenchymoma associated with an unusual vasoinvasive metastasis in a dog. J Am Anim Hosp Assoc 1998; 34: 295–9.

11. Puff C, Kehler W, Baumgärtner W, Herden C. Malignant mesenchymoma in the nasal cavity of a bull. J Comp Pathol 2011; 145: 148–51.

12. Muir CS, Seah CS. Primary chondrosarcomatous mesenchymoma of the mitral valve. Thorax 1966; 21: 254–62.

MALIGNI MEZENHIMOM AORTNE ZAKLOPKE PRI PSU

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Povzetek: V prispevku predstavljamo primer malignega mezenhimoma v aortni zaklopki z infiltrativnim vraščanjem v srčno mišico pri osemletnem nemškem ovčarju. Na Inštitutu za patologijo, sodno in upravno veterinarstvo Veterinarske fakultete smo med raztelesbo psa, o katerem nismo imeli nobenih kliničnih podatkov, opazili zelo spremenjeno aortno zaklopko. Ta je bila zelo zadebeljena, rumenosiva, hrapava, gumaste konsistence, z močno zaobljenimi robovi, na prerezu gladka in sivkasta. Spremenjeno je bilo približno 90 % aortne zaklopke. S patohistološko preiskavo smo ugotovili, da je sprememba tumor, zgrajen iz štirih različnih komponent mezenhimskega izvora: iz prevladujočih liposarkomatozne, fibrosarkomatozne in leiomiosarkomatozne komponente ter majhnega otočka hondrosarkomatoznih celic. Liposarkomatozne celice so se na enem mestu infiltrativno vraščale med mišične celice srca. Mitoze so bile redke, in sicer od 0 do 2 mitozi na polje velike povečave. Žilna stroma je bila dobro razvita. Tumor smo diagnosticirali kot maligni mezenhimom aortne zaklopke ter diagnozo potrdili z imunohistokemično preiskavo, ki je pokazala močno difuzno pozitivno reakcijo na vimentin in negativno na desmin. Močno pozitivno reakcijo na aktin gladkih mišičnih celic (SMA) smo zgolj multifokalno ugotovili v leiomiosarkomatozni komponenti tumorja. Med raztelesbo psa smo ugotovili še: blago endokardiozo mitralne in trikuspidalne zaklopke, močno razširitev vseh srčnih votlin, močno polnokrvnost jeter, vranice, ledvic in pljuč, močen pljučen edem, zmeren ascites in blag hidrotoraks. Na osnovi vseh ugotovljenih sprememb menimo, da je pes poginil zaradi kronične odpovedi srca, ki je bila v največji meri posledica malignega mezenhimoma v aortni zaklopki in endokardioze mitralne in trikuspidalne zaklopke.
Maligni mezenhimom je redek tumor pri živalih in ljudeh, zelo redko je bil opisan pri psih. Po nam dostopnih podatkih iz literature je to prvi opis malignega mezenhimoma aortne zaklopke z infiltrativnim vraščanjem v srčno mišico pri živalih.

Ključne besede: maligni mezenhimom; aortna zaklopka; nemški ovčar; patohistologija; imunohistokemija