

# 犬の三尖弁に発生した心臓粘液肉腫

誌名	動物の循環器 = Advances in animal cardiology
ISSN	09106537
著者名	町田,登 星,克一郎 田中,綾 山根,義久 勝田,新一郎 三森,国敏
発行元	獣医循環器研究会
巻/号	36巻2号
掲載ページ	p. 110-116
発行年月	2003年

農林水産省 農林水産技術会議事務局筑波産学連携支援センター  
Tsukuba Business-Academia Cooperation Support Center, Agriculture, Forestry and Fisheries Research Council  
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## CASE REPORT

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### Cardiac Myxosarcoma of the Tricuspid Valve in a Dog

Noboru MACHIDA<sup>1)</sup>, Katsuichiro HOSHI<sup>2)</sup>, Ryou TANAKA<sup>2)</sup>, Yoshihisa YAMANE<sup>2)</sup>,  
Shin-ichiro KATSUDA<sup>3)</sup> and Kunitoshi MITSUMORI<sup>1)</sup>

1) *Department of Veterinary Pathology, Tokyo University of Agriculture and Technology, 3-5-8 Saiwai-cho, Fuchu, Tokyo 183-8509, Japan*

2) *Department of Veterinary Surgery, Tokyo University of Agriculture and Technology, 3-5-8 Saiwai-cho, Fuchu, Tokyo 183-8509, Japan*

3) *Department of Physiology, Fukushima Medical University School of Medicine, 1 Hikari-ga-oka, Fukushima 960-1295, Japan*

(Received 14 November 2003; Accepted 22 December 2003)

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**Abstract.** A case of cardiac myxosarcoma arising from the tricuspid valve is described in a 9-year-old dog that died of right-sided congestive heart failure. At necropsy, an oval-shaped, space-occupying mass of the right heart, measuring 5.5×3×2.5 cm, was found attached to the septal leaflet of the tricuspid valve. The cut surface of the mass was variegated gray, yellow, and red with extensive areas of necrosis and hemorrhage. Histologically, the mass had an amorphous to finely fibrillar myxoid background rich in acid mucopolysaccharides, and was composed of pleomorphic and hyperchromatic cells containing a large number of mitotic figures. Immunohistochemically, the tumor cells showed a tendency toward smooth muscle differentiation.

**Key words:** canine, cardiac myxosarcoma, tricuspid valve.

*Adv. Anim. Cardiol. 36(2): 110-116, 2003*

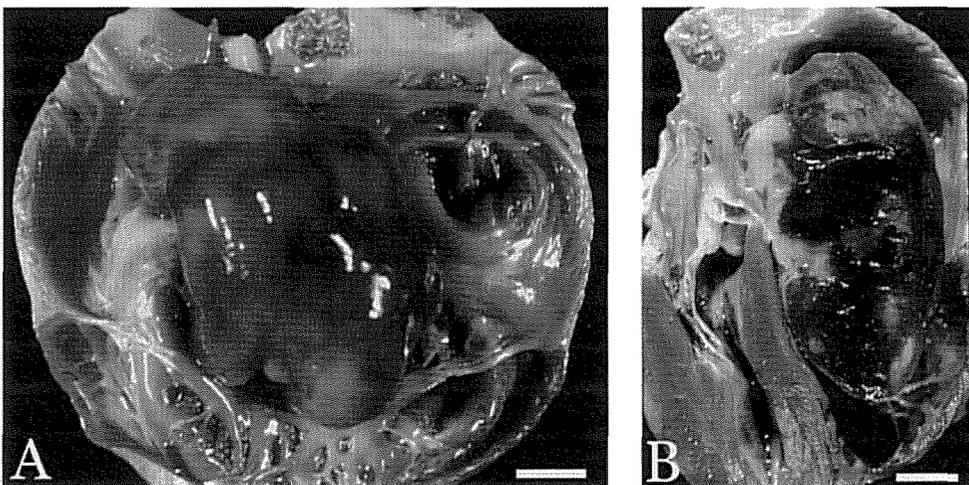
Primary cardiac tumors are uncommon in dogs; hemangiosarcomas form the vast majority.<sup>1,2)</sup> Other types of primary cardiac tumor that have been reported in dogs include rhabdomyo(sarco)ma, chondro(sarco)ma, leiomyo(sarco)ma, fibro(sarco)ma, myxo(sarco)ma, malignant mesenchymoma, myxofibroma, lipofibroma, neurofibroma, heman-gioma, lymphangioendothelioma, squamous cell carcinoma, mixed spindle cell and round cell carcinoma, aortic body tumor and ec-

topic thyroid or parathyroid tumor at the heart base, and pericardial mesothelioma.<sup>1-8)</sup> Among these tumors myxosarcoma is one of the most rare, and to the author's knowledge, there are only two other published canine case reports, involving a right atrial intracavitary myxosarcoma and a left ventricular myocardial myxosarcoma.<sup>1,8)</sup> This paper describes a case of myxosarcoma arising from the septal leaflet of the tricuspid valve in a dog.

A 9-year-old, 12.7-kg, male mixed-breed dog was presented with the complaint of exercise intolerance and labored breathing. On physical examination, the dog was dyspneic with open-mouthed breathing, pale mucous membranes, jugular vein distension and weak but regular femoral pulses. The abdomen was noticeably distended, and an abdominal fluid wave could be balloted. The lung sounds were harsh, and heart sounds were muffled on thoracic auscultation. The results of a complete blood count were within reference ranges. Serum biochemical analysis disclosed a marked increase in alanine aminotransferase of 394 IU/L. Thoracic radiographs revealed a large amount of pleural effusion that obscured the cardiac shadow. Two-dimensional echocardiography demonstrated an enormous intracavitary mass attached to the septal leaflet of the tricuspid valve, filling most of the right

atrial and right ventricular cavities. The clinical diagnosis was right-sided congestive heart failure as a result of neoplasia arising from the tricuspid valve. The dog was treated with furosemide, digitalis, and angiotensin converting enzyme (ACE) inhibitor, but his condition progressively became worse and death followed in one week.

At necropsy, 1660 ml of serosanguineous fluid was in the abdominal cavity, and 1090 ml was in the thoracic cavity. The liver was enlarged and firm with a 'nutmeg' appearance on the cut surface. The spleen was engorged with blood. The lungs were moderately congested and edematous. The heart was slightly enlarged, weighing 140 g. In a longitudinal section of the right heart, a 5.5 × 3 × 2.5 cm oval-shaped mass was found attached to the septal leaflet of the tricuspid valve and almost completely obliterating the right atrial and right ventricular cavities



**Fig. 1** Oval-shaped, smooth-surfaced cardiac myxosarcoma of the tricuspid valve obliterating the right atrial and right ventricular cavities (A). The cut surface of the mass is variegated gray, yellow, and red with extensive areas of necrosis and hemorrhage (B). Bar, 1 cm.

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(Fig. 1A). The mass had a rounded, smooth external surface, and its cut surface was variegated gray, yellow, and red, containing extensive areas of necrosis and hemorrhage. The septal leaflet was totally enclosed within the basal portion of the mass (Fig. 1B). The remainder of the heart and all other organs were grossly normal.

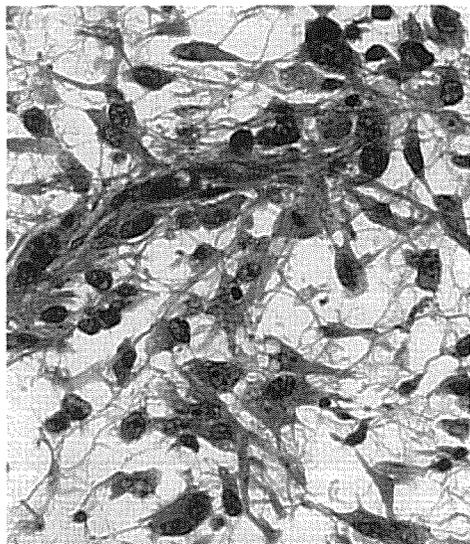
For light microscopy, representative portions of all major organs were fixed in 10% neutral buffered formalin, embedded in paraffin wax, sectioned at  $5\mu\text{m}$ , and stained with hematoxylin and eosin (HE). Selected sections of the intracardiac mass were stained by periodic acid-Schiff (PAS), alcian blue (pH 2.5), toluidine blue for metachromatic substances, Masson's trichrome, elastica van Gieson, Weilder's reticulum, and Perl's Prussian blue techniques. Immunohistochemical labeling was performed on paraffin-wax embedded tissue by the avidin-biotin-peroxidase method (Vectastain, Vector Laboratories, Burlingame, CA, USA) for identification of cytokeratin (MNF116; Dako Corp., Santa Barbara, CA, USA), vimentin (V9; Dako), desmin (D33; Dako),  $\alpha$ -sarcomeric muscle actin (Alpha-Sr-1; Dako),  $\alpha$ -smooth muscle actin (1A4; Dako), an endothelial marker CD34 (QBEnd10; Dako), macrophage (KP1; Dako), and S-100 protein (Dako). Diaminobenzidine tetrahydrochloride (Sigma Chemical Co., St Louis, MO, USA) served as the chromogen for the procedures, and the slides were counterstained with Mayer's hematoxylin.

Histologically, the intracardiac mass con-



Fig. 2 Histological section of the mass. The constituent cells of the mass occur singly or in small clusters surrounding vascular-like channels lined by a layer of endothelial-like cells. HE $\times$ 200.

tained extensive areas of necrosis and hemorrhage, and the remaining areas had a diffuse myxoid background that stained weakly to moderately positive with the PAS and alcian blue techniques, and metachromatically with toluidine blue, the staining differing in various portions of the mass. In addition to acid mucopolysaccharides the stroma contained a small amount of collagenous, elastic and reticular fibers. The constituent cells of the mass usually occurred singly or in small clusters, the latter often surrounding vascular-like channels lined by a layer of endothelial-like cells (Fig. 2). These channels contained eosinophilic substances or a few blood cells. The cells embedded within the myxoid matrix were pleomorphic, had moderately to markedly



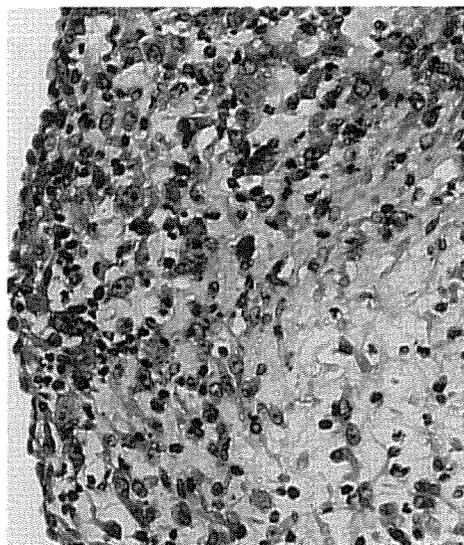
**Fig. 3** High-power view of the pleomorphic and hyperchromatic tumor cells embedded within a myxoid matrix. They have irregular nuclear membranes and medium to large-sized nucleoli, and show extreme atypia and high mitotic activities. HE×502.

clumped chromatin, irregular nuclear membranes, medium to large-sized nucleoli, and multinucleation, and showed extreme atypia and high mitotic activities (2 to 7 per high power field), assuming malignancy (Fig. 3). The surface of the mass was covered by a single or multiple layers of polygonal cells that were often seen to be in continuity with the underlying pleomorphic cells (Fig. 4). Other cells observed were lymphocytes, plasma cells, neutrophils, and frequent hemosiderin-laden macrophages, which showed a positive reaction with Perl's Prussian blue for ferric iron. The cardiac tumor did not invade the adjacent myocardium.

By immunohistochemistry, the tumor cells were uniformly positive for vimentin

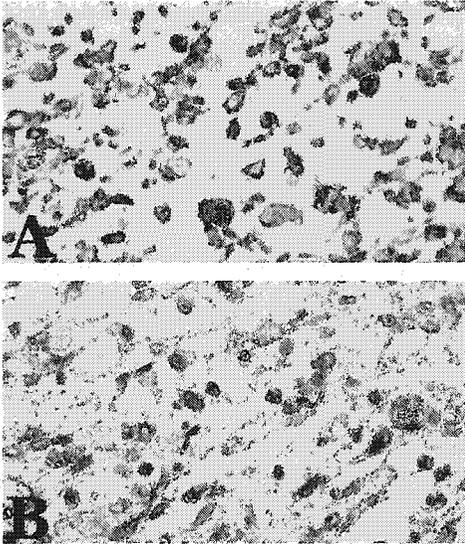
throughout the lesion (Fig. 5A) and negative for cytokeratin,  $\alpha$ -sarcomeric muscle actin, KP1, and S-100 protein. Labeling of  $\alpha$ -smooth muscle actin and desmin in the cytoplasm of the tumor cells were frequent but weak (Fig. 5 B). The endothelial marker CD34 was found only in a small proportion of the vascular-like lumen-lining cells and surface cells.

Other important histological findings were limited to the liver, spleen, and lungs. The liver was characterized by diffuse sinus congestion and centrilobular and sinusoidal fibrosis, compatible with chronic, passive congestion. The spleen showed vascular congestion and expansion of the red pulp, and the capsule was lined with a single layer of hypertrophic mesothelial cells. The lungs



**Fig. 4** Histological section through the surface of the mass. A single or multiple layers of polygonal lining cells often communicate with the underlying pleomorphic cells. HE×386.

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**Fig. 5** Immunolabeling of the tumor cells within a cellular area of the mass, showing vimentin (A) and  $\alpha$ -smooth muscle actin (B) in the cytoplasm. Hematoxylin counterstain  $\times 413$ .

showed congestive edema. The cardiac tumor produced no obvious metastases.

A diagnosis of cardiac myxoid tumor, that is, malignant or benign myxoma, was considered for the cardiac mass composed of pleomorphic and hyperchromatic cells containing a large number of mitotic figures, because it was characterized by a diffuse myxoid background rich in acid mucopolysaccharides. Cardiac myxomas consist of a hypocellular mass of amorphous acid mucopolysaccharide matrix covered by a single layer of endothelial cells with a supporting structure of spindle-like, stellate or polygonal cells in varying formations.<sup>6, 9-14</sup> They should never show pleomorphism, atypia or mitotic figures of the constituent cells and these are indicators of a malignant tu-

mor.<sup>15, 16</sup> The cardiac myxoid tumor in the present case, therefore, was characterized as myxosarcoma rather than its benign counterpart. The immunohistochemical analysis of the present case indicated a tendency toward smooth muscle differentiation of the tumor cells. The immunohistochemical profile was similar to that of cardiac myxoma of the tricuspid valve that has been described previously in a dog,<sup>6</sup> suggesting that distinction between canine cardiac myxosarcoma and myxoma may be difficult on immunohistochemical grounds.

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## 犬の三尖弁に発生した心臓粘液肉腫

町田 登<sup>1)</sup>, 星 克一郎<sup>2)</sup>, 田中 綾<sup>2)</sup>, 山根義久<sup>2)</sup>,  
勝田新一郎<sup>3)</sup>, 三森国敏<sup>1)</sup>

- 1) 東京農工大学農学部獣医学科家畜病理学教室  
〒183-8509 東京都府中市幸町 3-5-8
- 2) 東京農工大学農学部獣医学科家畜外科学教室  
〒183-8509 東京都府中市幸町 3-5-8
- 3) 福島県立医科大学医学部生理学第一講座  
〒960-8157 福島県福島市光が丘 1

### 要 約

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右心不全により死亡した9歳の犬の三尖弁に心臓粘液肉腫の発生がみられた。剖検では、三尖弁中隔尖に付着した卵円形の腫瘍は5.5×3×2.5 cmの大きさで、右心房と右心室を占拠していた。腫瘍の断面は灰白色、黄色、赤色などさまざまで、広範な壊死・出血領域を伴っていた。組織学的には、酸性粘液多糖類に富んだ無定形ないし細線維状の粘液様基質と、核内に豊富なクロマチンを有し旺盛な増殖活性を示す多形性の細胞からなっていた。これらの腫瘍細胞は免疫組織化学的に平滑筋分化の傾向を示した。

キーワード: 犬, 心臓粘液肉腫, 三尖弁