Case Report

A case of spontaneous purulent granulomatous pericarditis in a beagle

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Abstract: The present report describes a case of spontaneous purulent granulomatous pericarditis in a 16-month-old beagle. A gross necropsy revealed pericardial effusion and multiple nodules on the surface of the heart and around the aorta adjacent to the heart. The cut surface of these nodules was solid and white in color, containing partially yellowish white regions. Microscopically, granulomatous inflammation characterized by central necrotic cellular debris surrounded by neutrophils, macrophages, lymphocytes, plasma cells, fibroblasts and collagen fibers was observed in the epicardium. In addition, degeneration or necrosis of the arterial wall with inflammation was observed in the nodules. No gross and histological findings were observed in any organs other than the heart. Bacteria and fungi were not detected by Periodic acid-Schiff staining, Gram-Hucker staining and Ziehl-Neelsen staining. Based on these findings, the dog was diagnosed as having purulent granulomatous pericarditis. Purulent pericarditis is usually caused by pyogenic bacterial or fungus infections; however, no changes indicating a possible infection were observed in this case. In cases with spontaneous vascular changes, such as idiopathic canine polyarteritis or beagle pain syndrome, epicarditis could be secondarily caused by vascular lesions. Since this case showed different pathological features from those of spontaneous vascular changes, the pathogenesis may be different and remains unclear. To the best of our knowledge, this is the first report describing purulent pericarditis in beagles. Our case report is expected to be useful information that can be used as cardiac background findings for evaluating heart lesions in preclinical toxicology studies performed in beagles. (DOI: 10.1293/tox.2017-0010; J Toxicol Pathol 2017; 30: 251–254)

Key words: purulent granulomatous pericarditis, beagle dog, heart lesion, infection, idiopathic canine polyarteritis

Spontaneous purulent pericarditis is an uncommon disease in dogs1–3. Purulent pericarditis is generally caused by pyogenic bacterial or fungus infections3–6. These infections are usually the result of hematogenous infection or extension of local infections, such as endocarditis, pleuritis or pulmonary infection, to the myocardial tissue3, 5, 7. Occasionally, trauma such as bites or intrapericardial foreign bodies are also associated with the occurrence of purulent pericarditis3, 5, 6, 8. Furthermore, spontaneous vascular changes, such as idiopathic canine polyarteritis or beagle pain syndrome, could be associated with the occurrence of purulent pericarditis9. Such vascular changes sometimes occur in dogs9–11, especially beagles10. With this disease, arteritis characterized by various degrees of inflammatory cell infiltration and medial fibrinoid necrosis is observed histopathologically9–11. This vascular lesion can be observed in multiple organs, and the arteries of the heart are frequently affected10, 11. Occasionally, epicarditis and myocarditis are secondarily caused by such vascular lesions9.

Spontaneous heart lesions of the beagle dog are rare, but understanding the variety of possible spontaneous lesions is important for distinguishing drug-related changes from spontaneous ones in preclinical toxicity studies. Here, we report a case of spontaneous purulent granulomatous pericarditis in a beagle.

A 16-month-old male beagle was housed and maintained for the collection of clinical pathological background data. The dog was sacrificed at the age corresponding to the age of study termination in a chronic toxicity study for the collection of histological background data. The dog was not used in any toxicity studies and did not undergo any kind of invasive procedure. The dog was purchased from Covance Research Products Inc. (Cumberland, VA, USA) at the age of 6 months. It was housed in an individual pen-type cage for dogs, fed approximately 250 g/day of DS-A laboratory diet (Oriental Yeast Co., Ltd., Tokyo, Japan), and given access to an automatic water supply. The animal room was maintained at a temperature of 18°C to 28°C and a humidity of 30% to 70%. Animal care and use conformed with the guidelines of the Institutional Animal Care and Use Committee of Taisho Pharmaceutical Co., Ltd. The animal showed no clinical signs at the age of 6 months, 10 months, or 16 months (before necropsy). During the quarantine pe-
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The dog was anesthetized with an intravenous injection of pentobarbital sodium (Somnopentyl, Kyoritsu Seiyaku Corporation, Tokyo, Japan) and euthanized by exsanguination from the femoral artery and vein prior to necropsy. At necropsy, pericardial effusion and multiple nodules on the surface of the heart (left and right atrium, right ventricle) (10 × 8 × 4 to 15 × 10 × 10 mm) and around the aorta (20 to 35 mm in width) adjacent to the heart were observed. The surfaces of the nodules were mostly smooth and accompanied by a focal area of granular appearance. The cut surface of these nodules was solid and white in color, containing partially yellowish white regions. No gross lesions were observed in any other organs. The heart was removed and fixed in 10% neutral buffered formalin with other organs: the aorta, liver, spleen, kidney, lung, trachea, esophagus, stomach, small intestine, large intestine, pancreas, and mesenteric lymph node. All the tissues were embedded in paraffin and then sectioned and stained with hematoxylin and eosin (H&E). Additionally, Periodic acid-Schiff staining, Gram-Hucker staining and Ziehl-Neelsen staining were performed to differentiate bacterial species, and immunohistochemical staining for Iba1 (Wako Pure Chemical Industries, Ltd., Osaka, Japan) was performed for sections of the nodules.

The nodules in the heart were histopathologically characterized by suppurative granulomatous inflammation that was composed of central necrotic cellular debris surrounded by neutrophils, mononuclear cells, lymphocytes, plasma cells, fibroblasts and collagen fiber. H&E stain. Bar = 100 μm. D: Higher magnification of B. Immunohistochemically, most of the mononuclear cells were positive for Iba1. Immunohistochemical staining of Iba1. Bar = 100 μm.

Purulent pericarditis is a relatively rare form of heart disease in dogs. It is most commonly caused by a foreign body such as food like bone by esophageal perforation, penetrating wounds, systemic infections, or extension from local infections like endocarditis, pleu-

Fig. 1. Histopathological features of a nodule in the right atrium. A: H&E stain. Bar = 2,000 μm. B: Immunohistochemical staining for Iba1. Bar = 2,000 μm. C: Higher magnification of A. The nodule was characterized by central necrotic cellular debris surrounded by scattered neutrophils, numerous mononuclear cells with features of epithelioid cells, a small number of lymphocytes and plasma cells, fibroblasts and collagen fiber. H&E stain. Bar = 100 μm. D: Higher magnification of B. Immunohistochemically, most of the mononuclear cells were positive for Iba1. Immunohistochemical staining of Iba1. Bar = 100 μm.
ritis, or pulmonary disease\textsuperscript{3–8}. In cases of purulent pericarditis, the purulent exudate, which is often mixed with fibrin, fills the pericardial space, and the entire epicardium becomes covered with coagulum\textsuperscript{4, 5}. *Streptococcus*, *Klebsiella*, *Pasteurella*, *Staphylococcus*, *Mycoplasma*, and *Nocardia spp* are often detected in the lesions\textsuperscript{4}. In the present case, the pericarditis was initially suspected to have been caused by a bacterial or fungal infection, since suppurative granulomatous inflammation was observed in the epicardium and subepicardium. However, bacteria and fungi were not detected using Periodic acid-Schiff staining, Gram-Hucker staining or Ziehl-Neelsen staining of the lesion. In addition, no changes indicating a possible infection were observed in any of the other organs.

Spontaneous vascular changes, such as idiopathic canine polyarteritis or beagle pain syndrome, can be associated with the occurrence of pericarditis\textsuperscript{9}. In this disease, clinical signs such as fever, body weight loss and cervical pain manifested by a stiff gait and neck with a hunched position are often observed\textsuperscript{10}. Histopathologically, acute to chronic arterial lesions can be observed in multiple organs, and the arteries of the heart are frequently affected\textsuperscript{9–11}. The acute changes range from histiocytic-lymphocytic periartrial inflammation to transmural neutrophilic inflammation with medial fibrinoid necrosis\textsuperscript{11}. In our case, degeneration or necrosis of the vascular wall was observed with inflammatory cell infiltration in the nodules. However, this vascular lesion was only observed focally in the nodules, and no histological vascular findings were observed in any other organs. In addition, no clinical signs were observed in the animal. Since our case showed different pathological features from cases with spontaneous vascular changes, the pathogenesis might have been different.

Spontaneous purulent pericarditis is an uncommon disease in dogs\textsuperscript{1–3}. To the best of our knowledge, this is the first report of purulent pericarditis in beagles, although the pathogenesis of this case remains unclear. Since beagles are commonly used in preclinical toxicity studies, it is important to be familiar with spontaneous lesions so as to differentiate them from drug-related changes. We believe that this case report will provide useful information that can be used as cardiac background findings for evaluating heart lesions in preclinical toxicology studies performed using beagles.

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