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Complete atrioventricular block due to primary cardiac lymphoma in a dog

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Abstract
A histological investigation of the atrioventricular (AV) conduction system was performed in an 11-year-old golden retriever with complete AV block. Necropsy revealed a large grayish-white mass with an irregular shape located in the AV junctional area of the lateral aspect of the left heart. Histological and immunohistochemical examinations provided a diagnosis of primary cardiac lymphoma of T-cell origin. Histological findings in the AV conduction system included severe infiltration of neoplastic lymphoid cells into the AV nodal region, causing total destruction of the AV node. Similarly, neoplastic cell infiltration had entrapped the AV bundle, causing various degrees of degeneration, atrophy, and loss of conduction fibers. Such neoplastic lesions of the AV conduction system were associated with complete AV block.

Key Words: complete atrioventricular block, dog, primary cardiac lymphoma

In dogs and cats, complete atrioventricular (AV) block is a common arrhythmia that occurs when conduction of the cardiac impulse is completely and permanently interrupted in the region of the AV node, the AV bundle, or all bundle branches. Clinical signs associated with this arrhythmia are exercise intolerance, weakness, syncope, sudden death, or congestive heart failure. Complete AV block is usually associated with heart diseases, especially myocardial disorders including congenital heart defects, hypertrophic cardiomyopathy (HCM), infiltrative cardiomyopathy (amyloidosis or neoplasia), idiopathic fibrosis, myocardial infarction, bacterial endocarditis, and myocarditis. However, there have been few histopathological studies on the AV conduction system in such cases of complete AV block, and the anatomical basis of this arrhythmia remains unsolved. The present report describes the histopathological lesions observed in the AV conduction system in a canine case of complete AV block secondary to primary cardiac lymphoma (PCL). To our knowledge, few reports have documented complete AV block caused by PCL in dogs.

An 11-year-old, neutered male golden retriever was referred to the Animal Medical Center of
Tokyo University of Agriculture and Technology for evaluation and treatment of recurrent pericardial effusion and bradycardia. According to the referring veterinarian, the pericardial effusion had been drained on four occasions over a period of 2 months. An initial pericardiocentesis had yielded no tumor cells; thereafter, further cytological examinations of the pericardial fluid had not been performed.

On physical examination, the dog was in relatively good body condition. Cardiac auscultation identified marked bradycardia and grade II/VI left basilar systolic murmur, and the heart sounds were somewhat muffled. Six-lead electrocardiography revealed complete AV block with an atrial rate of 176/min and a ventricular rate of 32/min (Fig. 1). No abnormalities were found in the duration and configuration of the QRS complexes. Chest radiography disclosed a moderate generalized increase in the size of the cardiac silhouette. Two-dimensional echocardiography demonstrated mild pericardial effusion and a markedly thickened pericardial sac that contained a large amount of echogenic material within its cavity. A large, multi-lobulated, echogenic mass with an irregular shape was observed in the AV junctional area of the lateral aspect of the left heart, involving the left atrial and ventricular walls and the atrial septum (AS). Color flow Doppler interrogation of the mitral valve identified mild regurgitation. Pericardiocentesis was performed for diagnostic purposes and 5 ml of thick serosanguinous fluid was withdrawn; however, cytological examination of the fluid revealed only clusters of reactive mesothelial cells, macrophages, and red blood cells. The complete blood count and serum biochemistry results were unremarkable.

On the same day, the dog underwent median sternotomy for exploration of the heart and, if possible, implantation of an epicardial permanent pacemaker. Surgical inspection demonstrated diffuse fibrinous or fibrous adhesions between the pericardium and the epicardium. The mass visualized by echocardiography invaded both the left atrium (LA) and left ventricle (LV), extending to the surrounding region to various extents. The infiltration of the mass into the myocardium was too extensive to allow pacemaker implantation; therefore, a specimen measuring approximately $0.5 \times 0.5 \times 0.5 \text{ cm}$ was obtained for pathological diagnosis. Histological examination revealed proliferation of neoplastic lymphoid cells that were arranged in sheets, confirming malignant lymphoma involving the heart. Despite treatment with antibiotics, cardiotonics, and diuretics, the dog’s condition gradually worsened and it died due to severe congestive heart failure 8 days later.

**Fig. 1.** Electrocardiogram recording, showing complete atrioventricular (AV) block with an atrial rate of 176 beats/min and a ventricular rate of 32 beats/min. Bipolar standard limb leads I, II and III, 50 mm/s, 1 cm/mV.
At necropsy, both lungs were congested and edematous with cranioventral segmental and subsegmental areas of collapse. The pericardial cavity was totally obliterated by shaggy and tangled fibrin strands or bands, and dense coagulum adhered to the pericardial and epicardial surfaces. The excised heart was encased by gray-white to red-tan fibrin aggregates. The largest mass located in the AV junctional area of the left heart was composed of multiple, firm, raised, irregular, frequently coalescing nodules measuring 0.5–2 cm, and extended to the ascending aorta and pulmonary trunk, surrounding them. The liver and spleen were slightly congested and enlarged. No other gross abnormalities were detected in the thoracic and abdominal cavities.

After gross examination, the whole heart was fixed in 10% phosphate-buffered formalin. Evaluation of a longitudinal section of the fixed heart identified extensive infiltration of grayish-white neoplastic tissue into the myocardium, especially the LA and AS and the upper-half portion of the left ventricular free wall (Fig. 2). Multiple myocardial tissue blocks were sampled from both atrial and ventricular walls. For a histological study of the AV conduction system, the regions of the AV node and the AV bundle and bundle branches were sectioned at 3-mm intervals in the same manner as described previously\(^3,4\). Samples were processed by routine methods and embedded in paraffin wax, and sections 5 \(\mu\)m thick were stained with hematoxylin and eosin (HE) for light microscopy. Furthermore, neoplastic lymphoid infiltrates were evaluated immunohistochemically with monoclonal antibodies (Dako, Glostrup, Denmark) against T lymphocytes (CD3) and B lymphocytes (CD79a) using the avidin-biotin-peroxidase method (Vectastain; Vector Laboratories, Burlingame, CA, USA), with hematoxylin as a counterstain. Tissue samples were also obtained from the lungs, thyroid glands, parathyroid glands, esophagus, stomach, small and large intestines, mesenteric lymph nodes, pancreas, liver, spleen, adrenal glands, kidneys, urinary bladder, brain, spinal cord, skeletal muscles, and skin.

Microscopically, the myocardium of the LA, LV and AS was markedly disrupted and effaced by non-demarcated areas of densely packed neoplastic lymphoid cells arranged in sheets (Fig. 3A). Immunohistochemical labelling revealed large numbers of CD3-positive neoplastic lymphoid cells in the myocardium (Fig. 3B), whereas only occasional cells were positive for CD79a, providing a diagnosis of T-cell origin lymphoma. No neoplastic involvement was found in any other tissue examined; therefore, the diagnosis of PCL of T-cell origin was established.

Histological findings in the AV conduction system included marked infiltration and proliferation of neoplastic lymphoid cells into the AV node region, causing total disappearance of the AV node (Figs. 4A and 4B). Moderate to severe neoplastic cell infiltration had also entrapped both penetrating (Figs. 4C and 4D) and branching (Figs. 4E and 4F) portions of the AV bundle, causing various degrees of degeneration, atrophy, and loss of conduction.
Fig. 3. (A) Microscopic section taken from the left ventricular wall, showing extensive infiltration of neoplastic lymphoid cells into the myocardium. Sheets of neoplastic cells separate individual muscle fibers. Hematoxylin and eosin (HE). (B) Immunohistochemical labelling of the neoplastic lymphoid cells, showing a positive reaction to CD3, a T cell marker. Hematoxylin counterstain. Bar, 100 μm.

Fig. 4. (A) The AV nodal region, showing total disruption of the AV node (arrow) and its approaches as a result of severe infiltration and proliferation of neoplastic lymphoid cells. HE. Bar, 1 mm. (B) The outlined square area in A is shown at higher magnification. HE. Bar, 100 μm. (C) The penetrating portion of the AV bundle (arrow), showing degeneration, atrophy, and loss of conduction fibers due to infiltration of neoplastic lymphoid cells. HE. Bar, 1 mm. (D) The outlined square area in C is shown at higher magnification. HE. Bar, 100 μm. (E) The branching portion of the AV bundle (arrow), showing degeneration, atrophy, and loss of conduction fibers due to infiltration of neoplastic lymphoid cells. HE. Bar, 1 mm. (F) The outlined square area in E is shown at higher magnification. HE. Bar, 100 μm. AS, atrial septum; TV, tricuspid valve; VS, ventricular septum.
fibers. When traced distally, the conduction fibers of the left and right bundle branches were found not to be involved in the disease process.

Other significant histopathological changes were confined to the lungs, liver and spleen. The lungs showed alveolar edema with various numbers of macrophages containing erythrocytes or hemosiderin. The liver had centrilobular congestion with dilatation of the lymphatics. In the spleen, vascular congestion and expansion of the red pulp were present. The remaining organs were normal.

The present report has described a case of complete AV block secondary to PCL in a dog. In dogs, complete AV block is a common arrhythmia that occurs when conduction of the cardiac impulse is completely and permanently interrupted in the region of the AV node, the AV bundle, or all bundle branches\(^8\). This type of block is usually associated with heart disease, especially myocardial disorders\(^1\). We previously reported a detailed histological study of the cardiac conduction system in dogs presenting with complete AV block, i.e. elderly dogs with mitral regurgitation\(^3\) and young dogs with lymphocytic myocarditis\(^3\). The pathological findings observed in such cases suggested that the blocks were induced by marked loss and disappearance of the conduction fibers at the AV node and/or the AV bundle\(^3,4\).

PCL is a very rare malignancy in both humans and dogs; fewer than 200 human cases were reported during the period 1949–2009\(^7\) and, to our knowledge, only three canine case reports with pathological findings have been confirmed to date\(^9\)–\(^11\). This type of lymphoma is extremely aggressive and can damage all of the endocardium, myocardium and epicardium, and/or the pericardium. Symptoms vary depending on the heart site involved. According to Petrich et al.\(^7\), who reviewed clinical data for 197 human cases of PCL, the most frequent cardiac manifestations associated with PCL were pericardial effusion, heart failure, and arrhythmia. Among cases where the heart rhythm was described, 56% (83 of 149) had an arrhythmia other than sinus tachycardia/bradycardia; one of the most common arrhythmias observed was AV block at 22% (33 of 149). Interestingly, 20 of 33 (61%) reported cases of AV block were complete.

In the case reported here, this type of block was one of the main cardiac manifestations. The histological examination of the heart demonstrated marked and extensive infiltration of neoplastic lymphoid cells into the AV junctional region, causing total or subtotal destruction of the AV node and AV bundle. These neoplastic lesions of the AV conduction system were thought to have set the stage for blocking the AV conduction of cardiac impulses. In this connection, complete AV block has been reported in a canine case of malignant lymphoma involving the heart, and the conduction disturbance was attributed to total disappearance of the AV nodal tissue as a result of neoplastic infiltration\(^10\).

References


