Aortic valvular endocarditis in a dog

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Abstract — A 4-year-old German Shepherd was evaluated for progressive depression, lethargy, anorexia, and dyspnea. Despite treatment with diuretics and antibiotics, the dog died. Based on clinical, radiographic, and pathologic findings, the diagnosis was heart failure resulting from aortic valvular endocarditis.

Résumé — Endocardite de la valvule aortique chez un chien. Un Berger allemand âgé de 4 ans a été évalué pour dépression progressive, léthargie, anorexie et dyspnée. En dépit d'un traitement aux diurétiques et aux antibiotiques, le chien est décédé. En se basant sur les trouvailles cliniques, radiologiques et pathologiques, un diagnostic de défaillance cardiaque résultant d'une endocardite de la valvule aortique a été posé.

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A 4-year-old, 32.5-kg, neutered male German Shepherd was presented with a 7-day history of progressive depression, inappetence, and lethargy. In the 24 h prior to presentation, the dog had become dyspneic and restless, and seemed unable to rest comfortably in any position other than sternal recumbency. The dog had no prior history of clinical disease and had visited the veterinarian only for annual vaccinations.

On clinical examination, the dog was very lean. Rectal temperature was 39.8°C, and respiratory rate and effort were both moderately increased. Cardiac auscultation revealed intense, markedly irregular heart sounds. Heart rate was 84 bpm and the pulse had a bounding quality. A cardiac murmur was audible, loudest over the left heart base, but difficult to characterize due to the dysrhythmia. Upon abdominal palpation, the dog was mildly pained in the ventral mid-abdominal area. Differential diagnoses after clinical examination included pneumonia and heart failure.

Initial diagnostic plans included in-clinic hematologic and serum biochemical profiles, urinalysis, thoracic radiographs, electrocardiographs, and heartworm testing.

The complete blood (cell) count (CBC) revealed leukocytosis (23.5×10^9 cells/L; reference range, 4.9 to 15.4×10^9 cells/L), with a mature neutrophilia (16.2×10^9 cells/L; reference range, 2.9 to 10.6×10^9 cells/L); a left shift (2.5×10^9 cells/L; reference range, 0.0 to 0.3×10^9 cells/L); and monocytosis (2.2×10^9 cells/L; reference range, 0.0 to 1.1×10^9 cells/L). The serum biochemical profile showed hypoalbuminemia (21 g/L; reference range, 29 to 43 g/L). Analysis of a free-flow urine sample showed mild hematuria, trace proteinuria, mild bacteriuria, and a specific gravity of 1.022.

A blood test for *Dirofilaria immitis* antigen (Snap Heartworm Antigen Test; Idexx Laboratories, Toronto, Ontario) was performed because the dog had not been receiving heartworm preventative medication. The test result was negative.

Lateral and dorsoventral thoracic radiographs revealed a diffuse alveolar pattern, characterized by irregularly marginated, coalescing radiopacities of soft tissue density, and air bronchograms. On the left lateral projection, the cardiac silhouette was enlarged in both the horizontal and vertical planes, and the left atrium was moderately dilated. The electrocardiogram showed a sinus rhythm. The P wave in lead II was prolonged (0.06 s; reference range, < 0.04 s), which suggested left atrial enlargement. The QRS complexes were also prolonged (0.08 s in lead II; reference range, < 0.065 s), which suggested a cardiac conduction abnormality or left ventricular enlargement.

The dog was diagnosed with left-sided heart failure and treated with furosemide (Lasix; Hoechst Roussel Vet, Regina, Saskatchewan), 2.0 mg/kg bodyweight (BW), IM; it was hospitalized to allow close observation (day 1). Two hours after admission, the respiratory rate and effort had decreased only mildly, and 9 h later, theophylline (Theo-Dur; Key Pharmaceuticals, Kenilworth, New Jersey, USA), 18.5 mg/kg BW, PO, and enrofloxacin (Baytril; Bayer, Shawnee Mission, Kansas, USA), 9.2 mg/kg BW, PO, were administered.

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Physical examination on the morning of day 2 revealed little change in clinical status. Rectal temperature was 39.8°C, respiratory rate was 88 bpm with increased effort, and heart rate was 120 bpm. The dysrhythmia, intense heart sounds, heart murmur, and bounding femoral pulses were still readily apparent. The theophylline and enrofloxacin treatments were repeated. Less than 2 h later, the dog died in his kennel; a necropsy was performed.

The heart appeared mildly enlarged. The leaflets of the mitral valves were irregularly thickened and lined along their free margins with coalescing, smooth, opaque, grey-white nodules, 0.4 cm in diameter. The chordae tendineae were thickened at the valve attachments. The aortic valve leaflets were distorted by tan and brown irregular granular masses measuring 0.3 to 0.5 cm in diameter. Additional findings included renal infarcts, splenic infarcts, and pulmonary congestion and edema. Samples of the atrial and ventricular myocardium, aortic valve, mitral valve, lung, kidney, spleen, and liver were collected into 10% buffered formalin and submitted for histopathologic evaluation (Animal Health Laboratory, University of Guelph, Guelph, Ontario).

Histologically, the spongiosa of the aortic valve leaflet was markedly thickened due to increased extracellular matrix, while the fibrosa was decreased in thickness. The aortic valvular stroma was markedly thickened due to areas of hemorrhage, fibroplasia, and mineralization. Although the aortic valvular lesions were not submitted for bacterial culture, histological sections showed multiple colonies of gram-positive cocci within the fibronecrotic masses. Histopathologic examination confirmed acute renal infarction and demonstrated evidence of mild glomerulonephritis. Pulmonary histopathologic sections revealed hemosiderin-laden alveolar macrophages. Necropsy and histopathologic findings were consistent with acute left-sided heart failure caused by bacterial endocarditis (BE) involving the aortic valve, with concurrent myxomatous degeneration of the mitral valve.

Bacterial endocarditis is an infection of the valvular or mural endocardium that may have both cardiac and extracardiac sequelae. The most common isolates include *Staphylococcus aureus, Escherichia coli,* β-hemolytic streptococci, *Corynebacterium* spp., *Pseudomonas aeruginosa,* and *Erysipelothrix rhusiopathiae* (1,2). These organisms may originate from disrupted oral, gastrointestinal, or urogenital mucosal surfaces, or from any other localized source of infection (1,3).

Many factors are involved in the development of BE. Proliferative lesions are most often located at the free margins of the valvular endocardium of the left heart (1–4). Lesions tend to be located in areas where high pressure and velocity gradients exist, such as occur at the mitral and aortic valves. Due to the Venturi effect, colonization tends to occur on the lower pressure surfaces; those are, the atrial surface of the mitral valve and the ventricular surface of the aortic valve (5). However, valvular lesions are uncommon: reported prevalence of BE at necropsy in dogs varies from 0.06% to 6.6% (2,6). Host defence mechanisms adequately protect the endocardium from infection, unless host defences are compromised due to concurrent illness or immunosuppression (6). Prior valvular endocardial damage is one of the most significant factors increasing the likelihood of endocardial infection (3,7). High velocity regurgitant vortices and jets from turbulent blood flow may mechanically damage the endocardium (5,7). The resultant exposure of subendothelial collagen activates platelet aggregation and the coagulation cascade, and bacteria are able to adhere to the platelet-fibrin matrix. Bacteria capable of producing extracellular polysaccharides, such as dextrans, have a greater ability to adhere. Animals with congenital heart abnormalities are at a higher risk of developing valvular BE, because altered blood flow favors endocardial trauma (7). Approximately 25% of dogs with BE have some form of congenital heart disease (1,7). Still, many dogs with valvular BE have no prior history of valvular disease or congenital heart defect (1). In these cases, BE may be caused by bacteria, such as *S. aureus* or β-hemolytic streptococci, that produce proteases that damage endothelial surfaces, subsequently exposing the subendothelial matrix (6).

Resolution of established BE is difficult, because the bacterial colonies become tightly enmeshed in an avascular network of platelets and fibrin that host humoral factors and blood phagocytes cannot easily traverse. The rate of propagation of the vegetative lesion varies with the virulence of the infecting organism. Highly virulent organisms cause rapid necrosis of the valvular stroma and may even perforate the valve (5). Conversely, organisms of lower virulence damage the valvular stroma to a lesser degree and produce a slowly enlarging vegetative lesion that evolves over weeks to months (4). Hyalinization or calcification of the vegetative lesion may be observed in older lesions (5,7). Perforation, tearing, or valvular leaflet distortion due to vegetative lesions alter leaflet coaptation and cause valvular insufficiency. If the regurgitant blood flow is small and develops slowly, the heart can adapt through compensatory measures. However, if severe regurgitation is present, the heart cannot compensate, and congestive heart failure ensues.

Bacterial endocarditis is often suspected when cardiac dysfunction develops acutely. Detection of a new heart murmur or cardiac arrhythmia raises the suspicion of BE. However, clinical signs are not limited to cardiac manifestations and may result from sepsis, septic embolization, and immune-mediated complications. Commonly, as in this case, dogs present with nonspecific signs of pyrexia, anorexia, depression, and lethargy. Clinical signs associated with septic embolization vary, depending on the location of the embolization, the degree of vascular obstruction, and the degree of collateral circulation remaining (2). The kidney and spleen are the most common sites of embolization in the dog (2,3). Splenic inflammation, secondary to septic embolization and infarction, may result in abdominal pain, which may have been the cause of the mild abdominal pain in this case (9). Although histopathologic examination did not confirm splenic inflammation, gross evidence of acute splenic infarction was present. When the clinical course of BE is prolonged, a strong immune response to circulating antigen may be induced, resulting in the formation of immune complexes with deposition in the glomeruli of the kidney or synoviae of the joints. Histopathologic evidence of mild glomerulonephritis was present in this

case, suggesting possible immune-complex disease. Alternatively, glomerulonephritis may have been a consequence of nephric thromboembolism.

Laboratory and diagnostic test findings may yield nonspecific results suggesting multi-organ dysfunction, including normocytic, normochromic, nonregenerative anemia and leukocytosis with a mature neutrophilia and monocytosis (5). Serum chemical abnormalities result from changes in organ systems secondary to metastatic infection, embolization, immune-mediated damage, or congestive heart failure (6). The dog in this case showed little evidence of extracardiac organ dysfunction. Thoracic radiographic findings may be useful in identifying heart disease or heart failure, as suggested by chamber enlargement, venous congestion, or pulmonary edema (10). Electrocardiographs may demonstrate chamber enlargement, conduction disturbances, or supraventricular or ventricular arrhythmias (6,9), commonly AV blocks, premature ventricular contractions, atrial fibrillation, and ventricular tachycardia (6)

Echocardiographic evidence of vegetative lesions with compatible clinical signs is highly suggestive of BE (10). However, the absence of echocardiographic evidence does not rule out the presence of a vegetative lesion, as the lesion may be small, may vary in echogenic character, or may not be present in the imaging planes examined (10). A positive blood culture is expected in 75% of affected dogs (6). The absence of a positive blood culture, however, does not rule out BE, because many factors, such as previous antimicrobial treatment, chronicity of the endocarditis, right-sided endocarditis, uremia, and failure to perform anaerobic culture, may result in negative blood cultures (2,7).

An interesting finding in this case was the concurrent myxomatous degeneration of the mitral valve. No evidence exists to support a relationship between BE and myxomatous degeneration of the valves (2,4,6). Myxomatous degeneration occurs only occasionally in large breed dogs (4). Affected dogs are afebrile, do not show clinical signs of multi-organ dysfunction, and commonly have a prior history of a heart murmur. The etiology is unknown. The disease most commonly affects the mitral valve and tends to follow a slowly progressive course. Nodular thickenings first appear at the leaflet free margins, then slowly coalesce and extend towards the base of the valve leaflet (4). The valve leaflets become distorted and fail to coapt properly, resulting in blood regurgitation through the valve. Jet lesions are common findings in the left atrium and are recognized as fibrinous plaques on the endocardium, caused by the impact of the high velocity mitral regurgitant blood flow (4). In this case, myxomatous degeneration of the mitral valve may have contributed to the hemodynamic burden imposed on the heart, but the absence of major gross structural changes suggested that the contribution was minor.

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