What Is Your Diagnosis?

In collaboration with the American College of Veterinary Radiology

An 8-year-old 3.0-kg spayed female Papillon was referred to the Veterinary Teaching Animal Hospital at the Okayama University of Science because of erythrocytosis and decreased exercise tolerance. On referral examination, the dog was quiet and alert and had differential cyanosis affecting its vulva but not its tongue. Thoracic auscultation revealed a grade 5/6 diastolic murmur over the pulmonic valve area with no respiratory abnormalities. Hematologic evaluations revealed a high RBC count (1,288 X 10^{12} RBCs/L; reference interval [RI], 5.7 X 10^{12} to 8.8 X 10^{12} RBCs/L), PCV (88%; RI, 37% to 57%), and hemoglobin concentration (268 g/L; RI, 129 to 184 g/L). Oxygen saturation of hemoglobin measured by pulse oximetry (SpO_2) was 94% at the pinnae and 82% at the vulva (RI, > 95%). Thoracic radiographic images were obtained (Figure 1).

Formulate differential diagnoses, then continue reading.

Diagnostic Imaging
Findings and Interpretation

The right lateral radiographic image showed rounding of the cranial heart margin, but no increase in sternal contact (Figure 2). The ventrodorsal radiographic image showed rounding of the right ventricle, which resulted in an inverted D-shaped heart; bulging at the 1 o'clock position of the cardiac silhouette; and enlargement of the caudal pulmonary arteries. These findings indicated right ventricular enlargement and bulging of the aorta, pulmonary artery, or both.

Echocardiography revealed severe dilatation and concentric hypertrophy of the right ventricle, ventricular septal flattening, and enlargement of the right atrium and main pulmonary artery (Figure 3). Moreover, an enlarged ductus arteriosus was observed; however, there was no blood flow detected through the ductus arteriosus. Additionally, the dog had a mildly thickened mitral valve, mild mitral valve regurgitation, small left ventricular internal dimensions, and echocardiographically normal left atrial size. The pulmonary valve appeared structurally normal but had severe insufficiency, which when evaluated with continuous-wave Doppler ultrasonography (not shown) had a high end-diastolic pressure of 88.9 mm Hg. Saline (0.9% NaCl solution) contrast echocardiography (not shown) revealed no evidence of intracardiac shunt; however, within seconds of the peripheral venous injection of agitated saline, microbubbles were seen in the abdominal portion of the aorta.

On the basis of findings, primary or secondary erythrocytosis was considered as a differential diagnosis for the high RBC count, whereas chronic pulmonary disease, congenital cardiac disease, and...
left atrial hypertension were considered differential diagnoses for pulmonary hypertension. Measurement of the dog’s serum erythropoietin concentration revealed a high concentration (96.5 mU/mL; RI, 1.3 to 13.4 mU/mL).

Considering that the dog had differential cyanosis, an enlarged ductus arteriosus, severe pulmonary hypertension, no evidence of intracardiac shunt but microbubbles detected in the abdominal portion of the aorta on contrast echocardiography, and high serum erythropoietin concentration, we diagnosed severe secondary erythrocytosis from Eisenmenger syndrome (ES) associated with patent ductus arteriosus (PDA).

**Treatment and Outcome**

Phlebotomy to remove 40 mL of the dog’s blood was performed to help prevent hyperviscosity of blood, and treatment was initiated with sildenafil (0.51 mg/kg, PO, q 12 h). Five days later, the dog’s PCV was 62.9%. Forty days after treatment was started, the dog’s SpO₂ (98% at the pinnae and 94% at the vulva) and exercise tolerance were improved but PCV was slightly increased (67.0%). Thus, we increased the sildenafil dosage (1.02 mg/kg, PO, q 12 h) to prevent further increase in PCV. Fifty-five days after treatment was started, the dog’s PCV was 65.0% and SpO₂ was 100% at the pinnae and 95% at the vulva. Eighteen months after the initiation of treatment, the
dog showed no abnormal clinical signs. Further, no adverse effects of treatment were noticed, and at last follow-up 36 months after the initiation of treatment, the dog’s PCV and SpO₂ were successfully maintained with continued treatment with sildenafil (1.53 mg/kg, PO, q 12 h).

Comments

Erythrocytosis is a relative or an absolute increase in the number of peripheral erythrocytes. Primary erythrocytosis is caused by a disorder of cells in the bone marrow, and erythropoietin concentrations are low or within reference limits. Secondary erythrocytosis is induced by either hypoxemia associated with pulmonary disorders or cardiac disorders with arteriovenous shunts or by renal diseases or neoplasia without hypoxia; erythropoietin concentrations are high. Thoracic radiography is the first choice modality for evaluating differential diagnoses of erythrocytosis.

Eisenmenger syndrome is a clinical condition that is characterized by advanced pulmonary hypertension (PH) in conjunction with congenital cardiac shunt (eg, PDA or ventricular septal defect) and shunt reversal and that can cause secondary erythrocytosis. Standard evaluation of a dog with PH includes assessment for underlying disease or contributing causes of PH, including evaluation for pulmonary venous and left atrial hypertension, pulmonary thromboembolic disease, and chronic pulmonary disease.

The most characteristic radiographic finding of PDA is an aneurysmal bulge in the aorta, at the level of the ductus, often called a ductus bump. The dog of the present report had a bulge at the 1 o’clock position of the cardiac silhouette in the ventrodorsal image, and we prioritized consideration for a ductus bump, main pulmonary artery enlargement, or both. Thus, we performed routine and saline contrast echocardiography, and diagnosis of ES is generally confirmed with contrast echocardiography. Because we agitated the saline before administering it IV, resulting microbubbles in the saline generated echocardiographic contrast. Following a peripheral venous injection, such microbubbles circulate through the right chambers of the heart and are effectively removed by the pulmonary capillaries. Thus, the appearance of microbubbles in the left atrium or left ventricle is indicative of a right-to-left intracardiac shunt. However, in ES caused by PDA, intracardiac shunting does not occur because shunting occurs through the PDA, and the presence of microbubbles in the abdominal portion of the aorta on ultrasonography is diagnostic of ES associated with PDA.

In patients with ES associated with PDA, shunting is bidirectional or causes reversal of normal flow, and shunting can be observed occasionally with color-flow Doppler ultrasonography. However, the shunt velocity is very low, which often makes the shunt difficult to delineate. Furthermore, the dog of the present report had severe polycythemia, which may have increased blood viscosity and decreased blood flow velocity. There was no blood flow detected through the ductus arteriosus in the dog of the present report; however, enlargement of its ductus arteriosus was ultrasonographically observed along with microbubbles in the abdominal portion of the aorta. Consequently, the dog was diagnosed with ES associated with PDA and secondary erythrocytosis.

Severe erythrocytosis may lead to hyperviscosity syndrome and thromboembolic disease. In ES, surgical correction should not be attempted because it can lead to severe right heart failure, progressive PH, and death. Medical management of dogs with ES is aimed to prevent hyperviscosity of blood. Thus, to prevent hyperviscosity syndrome in this dog, a single phlebotomy was performed, treatment with sildenafil was initiated, and the dog's PCV and SpO₂ were successfully maintained.

The dog in the present report had clinical, radiographic, and echocardiographic signs that mirrored ES associated with PDA. Although cardiac catheterization with angiography is used for a definitive diagnosis of ES, the procedure requires sedation or anesthesia and specialized equipment and is a moderately invasive procedure. Therefore, we recommend to first perform contrast and conventional echocardiography to help diagnose ES. Additionally, nonsubtraction angiography from a peripheral vessel may help in diagnosing ES in dogs with no shunt detected on conventional echocardiography.

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References