

# ECG of the Month

A 15-year-old 18.3-kg (40.3-lb) spayed female mixed-breed dog was referred for treatment of stage V multicentric B-cell lymphosarcoma. Lymphoma of the spleen was diagnosed by means of microscopic examination of a fine-needle aspirate sample; detection of circulating malignant lymphocytes in peripheral blood was suggestive of bone marrow involvement. Chemotherapy with the University of Wisconsin-Madison protocol<sup>1</sup> was initiated in February 2012. The dog responded well to chemotherapy and had been in remission since commencement of chemotherapy.

On physical examination at the time that chemotherapy was initiated, the dog's body condition was considered normal (body condition score, 5/9). Mild tachypnea was evident (70 breaths/min), but the dog was panting intermittently. The heart rate was apparently normal (120 beats/min) with strong and synchronous femoral pulses. Thoracic auscultation revealed no cardiac murmurs or arrhythmias and no detectable abnormalities in the lungs. A CBC was performed weekly

(7 days after treatment with chemotherapeutic agents) as a part of the chemotherapy protocol; results did not indicate any important abnormalities that would prompt cessation of treatment. These physical examination findings remained unchanged throughout the chemotherapy treatment period. An ECG recording was obtained prior to each administration of doxorubicin (administered at weeks 4, 9, 17, and 25) to screen for any arrhythmias.

## ECG Interpretation

Initial ECG recordings obtained from the dog revealed no abnormalities (data not shown). However, prior to administration of doxorubicin during the 17th week of chemotherapy, a survey 6-lead ECG recording was obtained from the dog for evaluation (Figure 1). The heart rate was 111 beats/min. The duration of each qRs complex was 120 milliseconds (reference range, < 70 milliseconds) with an amplitude of 1.9 mV (upper reference limit, 3.0 mV).<sup>2</sup> The QRS complexes were wide with a positive R wave in tracings from leads I, II, III, and aVF. These findings were consistent with complete left bundle branch block.

At week 25 of chemotherapy, a 6-lead ECG recording was obtained from the dog prior to doxorubicin administration (Figure 2). At this time, the heart rate

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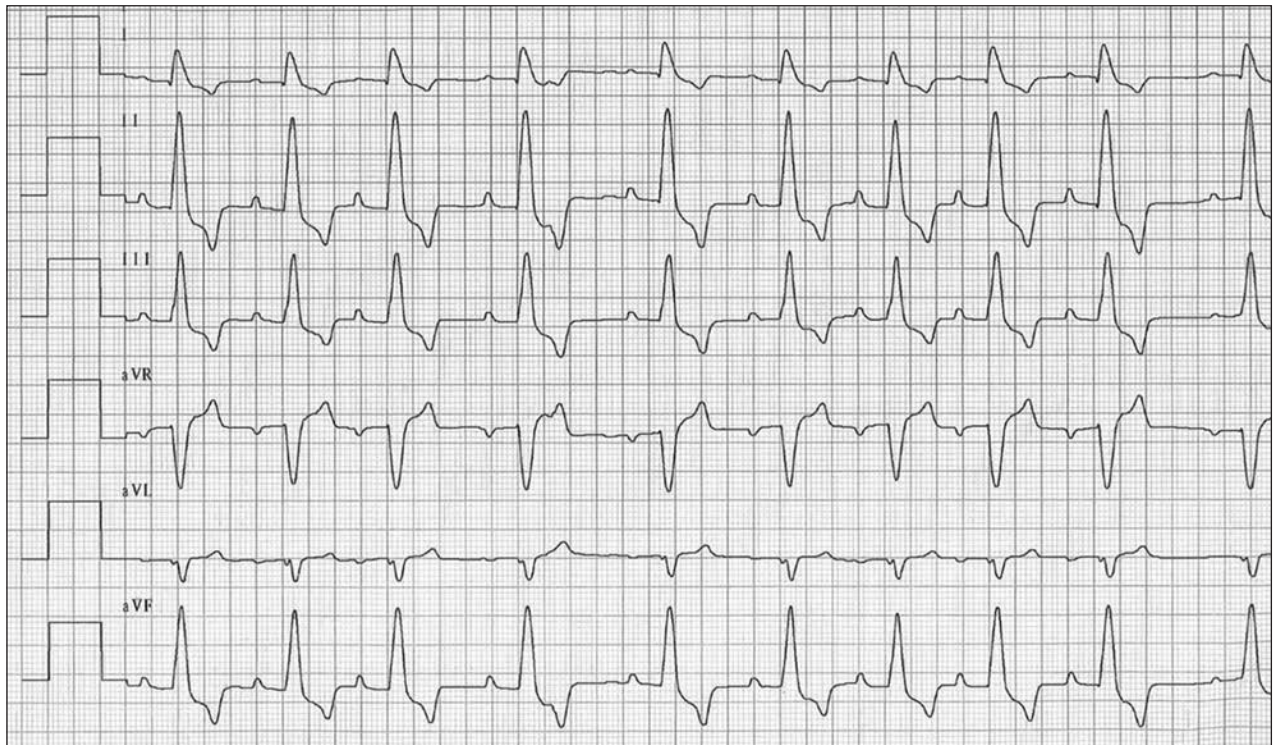


Figure 1—Six-lead ECG tracings obtained from a 15-year-old mixed-breed dog that was receiving chemotherapy for treatment of stage V multicentric B-cell lymphosarcoma. The tracings were recorded during the 17th week of chemotherapy (prior to the third administration of doxorubicin as directed by the chemotherapy protocol). Notice that the duration of the qRs complexes is 120 milliseconds (reference range, < 70 milliseconds) and the amplitude is 1.9 mV (upper reference limit, 3.0 mV). The QRS complexes are wide with positive R waves in leads I, II, III, and aVF. All of these findings are consistent with a complete left bundle branch block. Paper speed = 50 mm/s; 1 cm = 1 mV.

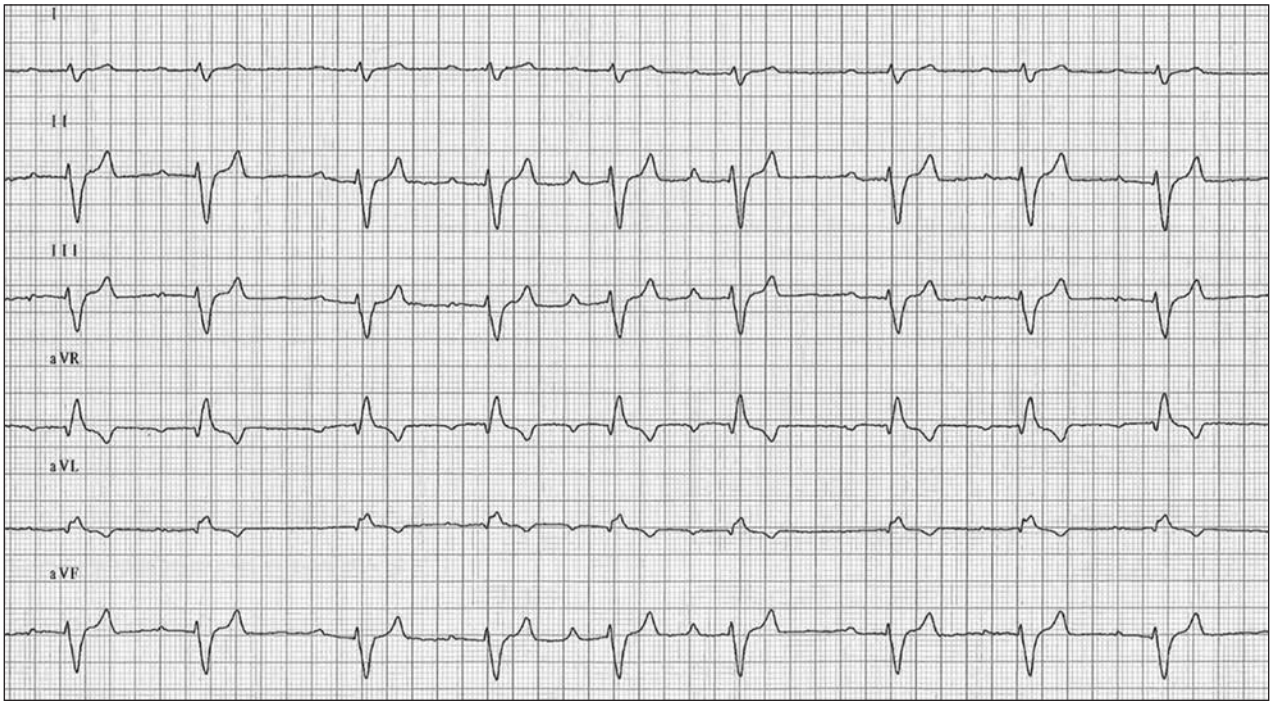


Figure 2—Six-lead ECG tracings obtained from the dog in Figure 1 during the 25th week of chemotherapy (after third administration of doxorubicin and prior to mitoxantrone administration). The QRS complexes are wide and bizarre; duration is 140 milliseconds and amplitude is 1.2 mV. The qrS complexes have large S waves in leads I, II, III, and aVF. The P-R interval is prolonged (140 milliseconds; reference range, 60 to 130 milliseconds). These findings are consistent with first-degree atrioventricular block and right bundle branch block. Paper speed = 50 mm/s; 1 cm = 1 mV.

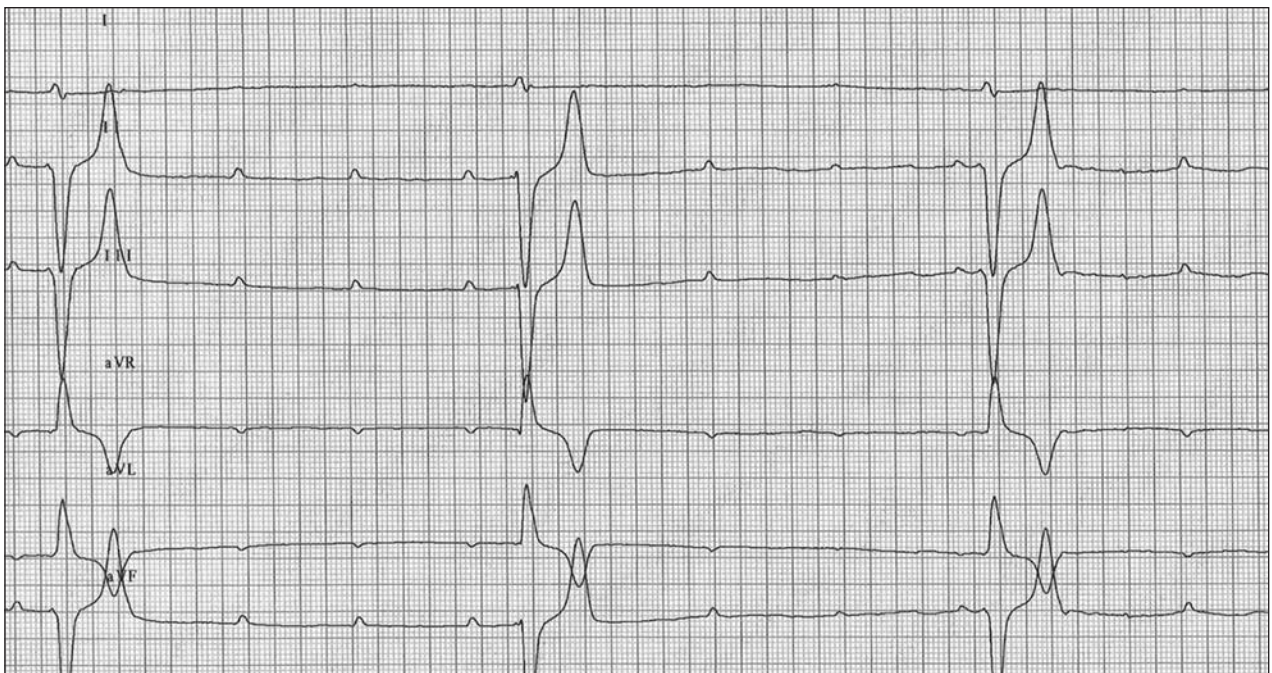


Figure 3—Six-lead ECG tracings obtained from the dog in Figure 1 during the 26th week of chemotherapy. The P-P interval is constant (440 milliseconds), whereas the P-R interval is variable. The ventricular escape rhythm is 40 beats/min. These findings are consistent with complete atrioventricular block. Paper speed = 25 mm/s; 1 cm = 1 mV.

was 110 beats/min. The QRS complexes were wide and bizarre; complex duration was 140 milliseconds, and amplitude was 1.2 mV. The qrS complexes had large S waves in tracings from leads I, II, III, and aVF. The P-R interval was prolonged at 140 milliseconds (reference range, 60 to 130 milliseconds).<sup>2</sup> These findings were

consistent with first-degree atrioventricular (AV) block and right bundle branch block. Echocardiography was performed and revealed mild mitral and tricuspid valve regurgitation. The left ventricle was slightly dilated in both systole and diastole and had decreased systolic function.<sup>3</sup>

During the echocardiographic evaluation, ECG monitoring revealed that the dog had 2 episodes of advanced (high-grade) second-degree AV block with occasional monomorphic ventricular premature complexes and intermittent atrial tachycardia (heart rate, 150 beats/min). The P-R interval remained constant (90 milliseconds) throughout the ECG assessment, suggesting that this was an advanced second-degree AV block, rather than a third-degree AV block. There was T-P summation during some QRS complexes. This was not considered third-degree (complete) AV block because that condition, by definition, has no P-R wave association.<sup>2</sup>

Given the rapid progression of the cardiac abnormalities including development of right bundle branch block and advanced second-degree AV block, it was recommended to discontinue doxorubicin administration because of possible cardiotoxicosis. Mitoxantrone hydrochloride (5 mg/m<sup>2</sup>) was administered instead of doxorubicin. Because neoplastic infiltration of the myocardium and conduction system was also considered a possibility, treatment with a high dose of prednisone (2 mg/kg [0.9 mg/lb], PO, q 24 h) was started. Because of the dog's decreased systolic function, treatment with enalapril (0.5 mg/kg [0.23 mg/lb], PO, q 12 h), pimobendan (0.25 mg/kg [0.11 mg/lb], PO, q 12 h), and fish oil capsules (1,000 mg, PO, q 24 h) was initiated.

One week later, the dog was reevaluated because of syncope episodes and weakness at home. Electrocardiography revealed complete (third-degree) AV block with no P-R wave association (Figure 3). The P-P interval was constant (440 milliseconds), but the P-R intervals were variable, confirming the dissociation. There was a ventricular escape rhythm of 40 beats/min. Pacemaker implantation was recommended for the dog, but the owner declined.

## Discussion

Administration of doxorubicin is known to have cardiotoxic effects that can result in arrhythmias and cardiomyopathies.<sup>4,5</sup> The current recommended cumulative lifetime dose of doxorubicin in dogs is 150 to 180 mg/m<sup>2</sup> of body surface area/dog, which is typically approximately 5 doses for most dogs.<sup>4</sup> Doxorubicin-induced cardiotoxicosis leads most commonly to decreased systolic function, which resembles dilated cardiomyopathy, and subsequent heart failure.<sup>5</sup> Doxorubicin-associated ECG abnormalities in dogs have been reported, the most common of which are monomorphic ventricular premature complexes, supraventricular arrhythmias, and R-wave amplitude changes.<sup>5</sup> In humans, arrhythmias (most commonly atrial premature complexes) related to doxorubicin treatment have been identified during initial administration of the chemotherapeutic agent or a few years after treatment was completed.<sup>6</sup>

To our knowledge, there are no reports in the veterinary medical literature of doxorubicin chemotherapy causing progression of left bundle branch block to right bundle branch block to complete AV block in a dog. In the human medical literature, a doxorubicin-induced arrhythmia characterized by a Mobitz type II second-degree AV block that progressed to complete AV block during a doxorubicin infusion has been reported.<sup>7</sup> Although the dog of this report was in clinical remission

at the time of the described ECG examinations, the possibility of infiltrative neoplastic disease as opposed to doxorubicin cardiotoxicosis as a cause of the conduction disturbances cannot be ruled out.

In a study of companion animals by Appurelle et al.,<sup>8</sup> primary cardiac lymphoma was not as common as other primary cardiac tumors, such as hemangiosarcoma. Cardiac metastasis of lymphoma was more common than development of primary cardiac lymphoma. Most metastases of lymphoma involving the heart were detected by postmortem histologic evaluation of samples of the myocardium.<sup>8</sup> The most common site of metastatic neoplastic cells was the inner third of the left free ventricular wall or throughout the interventricular septum (18/24 [75%] dogs).<sup>8</sup>

Cases of primary cardiac lymphoma causing complete AV block in humans have been described.<sup>9</sup> In the dog of this report, cardiac lymphoma that was unresponsive to chemotherapy might have also caused the conduction disturbance. However, because aggressive treatment with corticosteroids and mitoxantrone failed to prevent progression of the conduction disturbances, infiltration of the myocardium by the lymphoma was considered less likely. The dog was euthanized, but a necropsy was not performed; thus, the cause of the conduction disturbances remained unknown.

The use of an ECG as a screening tool for cardiac abnormalities before administration of doxorubicin is a low-yield test.<sup>10</sup> In a recent publication,<sup>8</sup> ECG recordings and echocardiograms revealed preexisting cardiac abnormalities in < 10% of dogs, which subsequently precluded them from receiving doxorubicin. Further research is needed to evaluate serial diagnostic testing as a means of early detection of cardiac abnormalities that will terminate the use of doxorubicin to prevent the risk of doxorubicin-induced cardiomyopathy in dogs.

## References

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