Arterial thrombosis after vehicular trauma and humeral fracture in a dog

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Case Description—A 3-year-old 19-kg (42-lb) spayed female mixed-breed dog was referred after being hit by a car. Injuries included pneumothorax, hemothorax, pulmonary contusions, a full-thickness axillary skin wound, and a grade I transverse fracture of the midshaft of the right humerus. Following patient stabilization, open reduction and internal fixation of the fracture were performed. The dog had weight-bearing lameness at the time of discharge. Eight days after fracture repair, the dog was reevaluated for acute onset of signs of pain and non–weight-bearing lameness in the right forelimb.

Clinical Findings—Physical examination findings in the right forelimb (knuckling and coolness, with absent digital pulses) were suggestive of a thrombus. Ultrasonography confirmed a right brachial artery thrombus with minimal blood flow to the affected limb.

Treatment and Outcome—Unfractionated heparin was administered via continuous IV infusion for the first 36 hours of hospitalization. Clopidogrel administration was also started at this time. During hospitalization, rapid clinical improvement occurred, and the dog was discharged 48 hours after admission. The transition to outpatient therapy was achieved by discontinuation of the unfractionated heparin infusion at 36 hours and beginning SC administration of dalteparin. Outpatient treatment with dalteparin and clopidogrel was continued. Repeated physical examination and ultrasonography 5 weeks later revealed resolution of the thrombus and normal blood flow to the limb. Anticoagulant administration was discontinued at that time.

Clinical Relevance—Thrombosis should be suspected in any dog with signs of acute pain after severe trauma or fracture repair, with or without concurrent lameness, that do not resolve with appropriate treatment. Restoration of blood flow to the affected limb after initiation of unfractionated heparin and clopidogrel administration followed by outpatient treatment with dalteparin and clopidogrel was achieved in this case. (*J Am Vet Med Assoc* 2013;243:394–398)

A 3-year-old 19-kg (42-lb) spayed female mixed-breed dog was referred to the emergency service of the Foster Hospital for Small Animals at Cummings School of Veterinary Medicine, Tufts University, after being hit by a car. The dog was initially evaluated at a nearby veterinary clinic, where thoracic radiographs were obtained and the right forelimb was splinted before the dog was referred for further care. Physical examination identified profound tachypnea with a marked abdominal component. Mucous membranes were grayish white with a capillary refill time of 4 seconds. Lung sounds were absent dorsally bilaterally, and femoral pulses were weak but palpable. Evaluation of the radiographs provided by the referring veterinarian revealed a diffuse severe interstitial pattern suspected to be secondary to pulmonary contusions, moderate-volume pneumothorax, a mild amount of pleural effusion, and a transverse fracture of the midshaft of the right humerus (with a longitudinal fissure in the distal fragment). Moderate fracture overriding was seen. Initial evaluation revealed mild anemia (PCV, 34%) and hypoproteinemia (3.4 g/dL) secondary to hemorrhage. The dog had mild metabolic acidosis (pH, 7.308; reference range, 7.337 to 7.467), low HCO_{3^-} (12.9 mEq/L; reference range, 18 to 24 mEq/L), low P_{CO_2} (25 mm Hg), high lactate concentration (6.7 mmol/L; reference range, 0.0 to 2.0 mmol/L), and a base excess (–13.7 mmol/L).

Initial stabilization and supportive care consisted of a bolus administration of lactated Ringer's solution (20 mL/kg [9.1 mL/lb] IV, followed by 60 mL/kg/d [27.3 mL/lb/d]), an antimicrobial (cefazolin; 22 mg/kg [10 mg/lb], IV, q 8 h), and analgesic medications (hydromorphone; 0.1 mg/kg [0.05 mg/lb], IV, once, followed by a fentanyl infusion at 3 µg/kg/h [1.4 µg/lb/h]). Right-sided thoracocentesis yielded approximately 100 mL of air and a moderate amount of hemorrhagic nonclotting fluid. The dog's dyspnea improved initially following thoracocentesis but then worsened after 30 minutes. Right-sided thoracocentesis was repeated, yielding approximately 300 mL of air, and a thoracostomy tube[a] was placed in the right hemithorax, which was evacuated every 4 hours as needed. The splint was removed to better evaluate the humeral fracture. An approximately 4 × 12-cm full-thickness wound in the right axilla was noted. The tissue in this area appeared healthy and did not appear to be contiguous with the fracture. The dog was sedated with fentanyl (5 µg/kg [2.3 µg/lb], IV), and the wound area was clipped, cleaned, debrided, and copiously flushed with sterile saline (0.9% NaCl) solution. A wet-to-dry bandage was placed and

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changed daily, and supportive care in the form of IV administration of fluids, cephazolin, and pain management was continued. Fracture repair was performed 48 hours after admission.

Fracture repair consisted of open reduction and internal fixation by means of anatomic reduction with neutralization plate fixation. Primary closure of the axillary wound was performed at this time. Anesthesia was performed without complications, and mechanical ventilation was not needed. Oxygen saturation as measured by use of pulse oximetry remained between 93% and 98% throughout surgery, with intermittent thoracic tube evacuation, and no other abnormalities were detected. The dog was discharged from the hospital 4 days after surgery with instructions for physical therapy (passive range of motion of the elbow and shoulder joints for 10 to 15 minutes 3 times daily), strict exercise restriction, and administration of cephalexin (500 mg, PO, q 8 h), carprofen (37.5 mg, PO, q 12 h), and tramadol (75 mg, PO, q 8 h). The dog had a mild weight-bearing lameness at the time of discharge.

Eight days after fracture repair, the dog was re-evaluated by the referring veterinarian for acute onset of signs of severe pain and non–weight-bearing lameness in the right forelimb. The referring veterinarian administered buprenorphine (0.01 mg/kg [0.005 mg/lb], SC) and again referred the dog to the Cummings School of Veterinary Medicine. The owner reported that the dog had been using the limb almost normally with minimal lameness until the dog was found panting and acutely non–weight bearing earlier that day. On physical examination, knuckling of the affected limb was observed. The right forelimb was cool on palpation, compared with the left forelimb, and digital pulses were absent. Both incisions (the fracture and wound repair sites) were healing well and were clean, dry, and intact. Radiographs of the right humerus were unchanged, compared with postoperative views, and revealed appropriate fracture alignment and apposition. A CBC was unremarkable (PCV, 38%; total solids concentration, 6.0 g/dL; platelet count, 287,000 platelets/µL). A serum biochemical profile was unremarkable other than an aspartate aminotransferase activity of 274 U/L (reference range, 9 to 54 U/L) and creatine kinase activity of 5,493 U/L (reference range, 22 to 422 U/L). The triglyceride concentration was within reference range. Given that a serum biochemical profile was not performed during the original visit, it could not be determined whether these changes were related to the acute lameness or secondary to the original traumatic event. The prothrombin time was unremarkable at 13 seconds (reference range, 12 to 17 seconds), and the partial thromboplastin time was unremarkable at 78 seconds (reference range, 71 to 102 seconds). A thromboelastogram was obtained, which revealed mild hypercoagulability (R, 3.7 minutes [reference range, 2.0 to 7.0 minutes]; K, 1.2 minutes [reference range, 1.0 to 4.0 minutes]; angle, 72.1° [reference range, 48° to 77°]; MA, 66.5 mm [reference range, 45 to 64 mm]; G, 9.9 Kd/s [reference range, 3.9 to 8.4 Kd/s]). On the basis of the physical examination findings and initial testing, an arterial thrombus affecting the right forelimb was strongly suspected. Unfractionated heparin was administered IV as a 50 U/kg (22.7 U/lb) bolus followed by constant rate infusion (25 U/kg/h [11.4 U/lb/h], IV) and was adjusted to achieve a target partial thromboplastin time of 1.5 to 2.5 times that of baseline. Initially, the partial thromboplastin time was monitored every 4 to 6 hours until stable, and then it was monitored every 24 hours until administration of the medication was discontinued.

Ultrasonography of the limb and axillary region performed the next morning confirmed a thrombus in the right brachial artery with minimal flow to the affected limb (**Figure 1**). Additional small vessels with blood flow were identified that were compatible with collateral circulation. The heparin infusion was continued, and clopidogrel administration (37.5 mg, PO, q 24 h) was added. At this time, the dog had signs of clinical improvement; the limb was slightly weight bearing, and although still cool when compared with the left forelimb, was noticeably warmer to the touch. Within 48 hours, signs of pain had subsided and the dog was again using the limb with a moderate weight-bearing lameness. Because of the rapid clinical improvement and in preparation for discharge from the hospital, the unfractionated heparin constant rate infusion was discontinued and replaced with intermittent SC administration

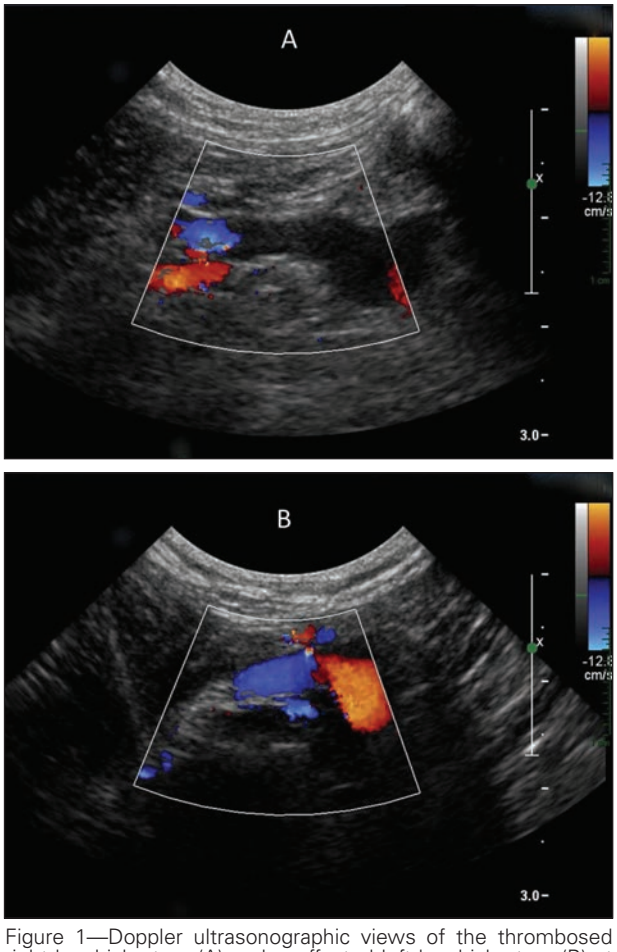

Figure 1—Doppler ultrasonographic views of the thrombosed right brachial artery (A) and unaffected left brachial artery (B) at the level of the axilla in a dog with a midshaft fracture of the right humerus. The marker is distal in both images. Notice the lack of color flow signal in the affected limb and normal color flow signal in the unaffected limb.

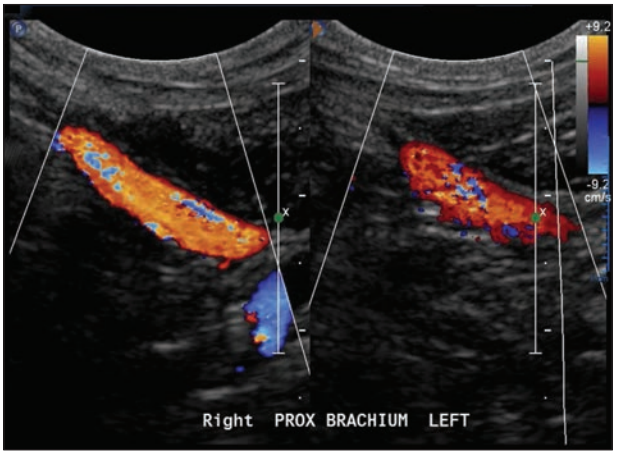

Figure 2—Bilateral color flow Doppler ultrasonographic views of the right and left brachial arteries at the level of the axilla of the same dog as in Figure 1, 5 weeks after treatment with dalteparin and clopidogrel. The marker is distal. Notice normal color flow bilaterally. Prox = Proximal.

of dalteparin. The dog was discharged, and the owner was given instructions to administer dalteparin (2,500 U, SC, q 12 h) and clopidogrel (37.5 mg, PO, q 24 h) and to continue the cephalexin, carprofen, and tramadol administration as prescribed.

Five weeks later, 6 weeks after fracture repair, the dog was reevaluated. Ultrasonography revealed complete resolution of the thrombus with normal blood flow to the affected limb (**Figure 2**). The dog's gait had improved, and only a minimal lameness was observed. Radiography of the right humerus revealed that the orthopedic implants were unchanged in position. Early bone healing bridging the fracture was observed. Anticoagulant administration was discontinued. Seven months after cessation of anticoagulant administration, the dog had full mobility of the limb and was clinically normal.

Discussion

Arterial thrombosis has been reported in dogs with a variety of diseases, including cardiac disease, neoplasia, bacterial endocarditis, protein-losing nephropathy, fungal disease, ehrlichiosis, hyperadrenocorticism, and hypothyroidism.[1–5] The development of a femoral artery thrombus following crush injury resulting from limb entrapment in a crate has been described in 1 dog.[6] To the authors' knowledge, arterial thrombosis after vehicular trauma and long bone fracture repair has not been previously described. Ideally, further testing including urinalysis, measurement of thyroxine concentration, and blood pressure measurement would have taken place once the dog was stable to more completely screen for underlying diseases that could contribute to arterial thrombus formation. However, given the lack of clinical signs that could be attributed to other disease processes both before the traumatic event as well as at the 7-month follow-up examination, the presence of an underlying disease contributing to arterial thrombus formation was considered unlikely.

Hemostatic complications of trauma are commonly encountered in humans and are thought to be caused by dysfunction of components of Virchow's triad. Virchow's triad describes the 3 broad categories of factors that are thought to contribute to thrombosis and include hypercoagulability, blood stasis, and endothelial injury. Human trauma patients are considered to be at high risk for venous thromboembolism, and increased thrombin generation has been detected in this patient population.[7] Venous thromboembolism occurs in up to 50% of human trauma patients in the absence of thromboprophylaxis and is associated with increased mortality rates, morbidity rates, duration of hospitalization, and economic burden.[8] In contrast, arterial thrombosis after trauma is less common in this population but is particularly noted to occur after humeral trauma and fracture repair.[9] In humans, fractures of the proximal portion of the humerus account for 4% to 5% of all fractures. The low incidence of trauma to the humerus and surrounding vasculature may be explained by the fact that these structures are surrounded and well protected by the bones and muscles of the shoulder. However, the anatomic proximity of the axillary and brachial vasculature to the humeral head renders these structures more vulnerable to blunt trauma during shoulder injury and fractures of the proximal portion of the humerus.[10,11] Approximately 85% of these fractures are minimally displaced, whereas the remaining 15% have substantial displacement.[12] Arterial thromboembolism is more commonly seen when these fractures are displaced.[13,14]

Arterial thrombi can form under conditions of high flow and are composed mainly of platelet aggregates bound together by thin fibrin strands.[15] In humans, potential mechanisms of arterial thromboembolism following humeral trauma and fracture repair include direct injury to the artery from sharp bony fragments (partial or complete laceration), the development of an arteriovenous fistula, or endothelial disruption secondary to arterial stretching or spasm resulting in tearing of the endothelial intima. Given the anatomic proximity of the axillary and brachial vasculature to the humeral head, direct injury to the vasculature in this area is most often associated with proximal humeral fractures.[10] The local vessel and tissue injury predisposes to thrombus formation.[13,14,16–19]

The dog described in this report had a displaced humeral fracture; however, the fracture location was not proximal, and it was therefore deemed unlikely that the thrombus was secondary to direct arterial injury from the fracture itself. There was only a mild hypercoagulable state, as documented by the thromboelastogram. Therefore, it is unlikely that a hypercoagulable state was an important factor in the development of the arterial thrombus. A large degree of blunt trauma was evidenced by the severity of thoracic trauma and pulmonary contusions in addition to the axillary wound and fracture. The humeral fracture and blunt trauma may have both contributed to shear injury of the axillary vessels. Given the extent of blunt trauma, it is possible that factors such as changes in blood flow and endothelial injury played a more important role in thrombus formation than did a hypercoagulable state. The axillary wound was superficial, and we believe it was unlikely to have directly contributed to thrombus formation.

Anticoagulants are recommended for all human patients after major trauma or long bone fracture.[20] In

general, guidelines recommend the use of low–molecular-weight heparin or unfractionated heparin as soon as it is considered safe to do so after trauma.[20] Similar recommendations have not been made for dogs.

In humans, the existence of collateral circulation in the shoulder region may initially mask the presence of an arterial thrombus, and a delay in treatment may have disastrous consequences, including permanent weakness in the affected limb or prolonged ischemia that ultimately requires amputation.[12,16,17,21] For evaluation and treatment of vascular insufficiency in affected individuals, recommendations include immediate imaging and surgical exploration of the area if bone alignment fails to restore normal circulation.[16] In some cases, minimally displaced fractures associated with mild vascular compromise may be managed conservatively without the need for surgical intervention.[14] The prevalence of arterial thrombosis in dogs is unknown, yet presumed not to be a concern.

Systemic thrombolytics are sometimes administered in humans with acute thrombosis for rapid reduction of thrombus size and restoration of perfusion. Alternative interventional and anticoagulant methods are also described, including CT and angiography for better visualization of the thrombus, followed by catheter placement for local administration of fibrinolytics such as a tissue plasminogen activator for clot dissolution.[22] However, the use of thrombolytics for acute thrombosis is a controversial subject in human medicine. Systematic reviews of randomized trials[23,24] have documented inherent risks of bleeding associated with these medications without providing enough evidence to prove a clear survival benefit. In the dog described in the present report, unfractionated heparin administration was initiated as a continuous infusion once a thrombus was suspected because therapeutic anticoagulation could be achieved rapidly to prevent additional thrombus formation. Fibrinolytics were not administered at the time of initial evaluation because of the risk of bleeding and because the presence of a thrombus could not be confirmed until the following day. Given the dog's rapid clinical improvement by the time the thrombus was definitively diagnosed the following morning, anticoagulation was continued and thrombolytics were not used. Clopidogrel administration was added after the initial response to broaden the anticoagulant effect through platelet inhibition because arterial thrombi are known to be platelet rich. The administration of dalteparin (low–molecular-weight heparin) in place of unfractionated heparin allowed for outpatient management. There is presently no consensus in veterinary medicine regarding which anticoagulant medications to use to prevent further thrombus formation after thrombosis has been confirmed. In this patient, both unfractionated heparin and clopidogrel were used as combination therapy; however, a variety of anticoagulant strategies would also have been appropriate. The decision to administer multiple anticoagulants in this case was based on clinician preference and a clinical impression that this type of combination therapy is generally well tolerated; however, single-agent therapy might have yielded similar results.

In the dog reported here, anticoagulant administration was discontinued after 5 weeks. There is presently no consensus on the duration of time required for an artery to heal and to restore endothelial integrity. Given the dog's marked clinical improvement, the complete resolution of the brachial thrombus as determined via ultrasonography, and our low suspicion for additional ongoing disease processes that could predispose the dog to further thrombus formation, we decided to stop administration of anticoagulants. There are no presently accepted protocols for cessation of anticoagulant treatment. Although rebound hypercoagulability may be a concern, this has not been reported in dogs, and therefore no weaning protocol was followed.

Although not previously reported in dogs, arterial thrombosis should be considered a potential complication after severe trauma or humeral fracture. Thrombosis should be suspected in any dog with signs of acute pain after fracture repair, with or without concurrent lameness. Screening for hypercoagulability and thrombosis in dogs after trauma or long bone fractures is not routinely performed. Further studies are indicated to determine whether these diagnostic tests and subsequent interventions are warranted.

a. Thoracostomy tube, MILA International Inc, Erlanger, Ky.

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