Hemothorax in Three Dogs with Intrathoracic Extracardiac Hemangiosarcoma

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ABSTRACT

Intrathoracic extracardiac hemangiosarcoma (HSA) is rare in dogs. This report describes three dogs with acute onset dyspnea due to hemorrhagic pleural effusion resulting from intrathoracic extracardiac masses, which were confirmed as HSA by histopathology. The dogs were stabilized with thoracocentesis and intravascular fluid resuscitation. Computed tomography identified intrathoracic masses, which were not originating from the heart or pulmonary parenchyma. Surgical exploration was performed in all cases. Case 1 was euthanized intraoperatively as the tumor could not be dissected from the aorta. In cases 2 and 3, hemostasis and resection of the tumors was successful. Case 2 was euthanized 1 mo after surgery and case 3 was alive at the time of writing, 5 mo postoperatively. Intrathoracic extracardiac HSA should be considered as a differential for nontraumatic hemothorax and surgical treatment can be palliative. (J Am Anim Hosp Assoc 2016; 52:325–329. DOI 10.5326/JAAHA-MS-6362)

Introduction

Hemangiosarcoma (HSA) is a malignant endothelial tumor and is common in dogs.1,2 Canine HSA predilection sites are the spleen, right atrium, liver, and skin, although they can originate from any vascular tissue.2–6 The initial treatment of choice is surgical excision of the mass.2 However, treatment is palliative with most dogs succumbing to metastatic disease and 80% of cases having overt metastasis on presentation.2,7 Median survival time for splenic HSA is short, ranging from 19 to 240 days.8,9 In dogs with splenic HSA, administration of chemotherapy has been shown to increase survival times compared to dogs treated with splenectomy only.1 Doxorubicin has the greatest efficacy against canine HSA.2

The clinical presentation is dependent on HSA location, but patients often present collapsed due to hemorrhage and hypovolemia with a history of episodic collapse and lethargy.2 A case of intrathoracic extracardiac HSA has been reported in one dog, where stabilization was not successful and the dog died.10 This case series reports three HSA cases that presented with collapse and dyspnea due to intrathoracic haemorrhage. The hemothorax in these cases was due to intrathoracic HSA that did not originate from the heart or pulmonary parenchyma. Two of these cases survived surgical mass excision.

Case Study

Case 1

A 10 yr old male neutered golden retriever presented to the referring veterinarian with a 12 hr history of dyspnea and exercise intolerance. There was no history of trauma. Pleural effusion was diagnosed by thoracic ultrasound and 400 mL of bloody fluid was removed by needle thoracocentesis.

At presentation to Queen Mother Hospital for Animals, Royal Veterinary College, London, the dog was tachypneic with a respiratory rate of 40 breaths per min with tachycardic, hypodynamic pulses with a rate of 160 beats per min (bpm). Respiratory sounds were bilaterally dull ventrally. Venous blood gas and biochemical analysis revealed marked hyperlactatemia (40 mg/
Iohexol, an iodine based contrast medium, at a dose of 2 mL/kg was used to opacify the esophagus ventrally and compress the vena cava (ventral to thoracic vertebra 8 to 10, displacing the aorta and pleura). A large volume of pleural effusion with collapsed lung lobe was present in the caudal aspect of the spleen. It was not aspirated. A single focal hypoattenuating 7 mm nodule was present in the caudal aspect of the spleen. It was not aspirated.

Histopathology of biopsy samples was consistent with HSA and revealed populations of proliferative partially vasoformative spindle cells forming channels containing erythrocytes. There were several large areas of extravasated erythrocytes consistent with recent hemorrhage.

Case 2
A 6 yr old male neutered Rottweiler presented to the Emergency service at Queen Mother Hospital for Animals with a 2 day history of progressive dyspnea, lethargy, polydipsia, and anorexia. The respiratory rate was 60 breaths per min and lung sounds were dull bilaterally over the ventral lung fields. The pulse rate was 200 bpm with poor peripheral pulse quality. The PCV on presentation was 25% with TS of 5.2 g/dL. After IV crystalloid resuscitation, with compound sodium lactate at a rate of 10 mL/kg as two boluses, the PCV fell to 16% and the TS to 4.0 g/dL. There was marked hyperlactatemia (102 mg/dL RI 5–22 mg/dL) on serum biochemical analysis. Ultrasound analysis was used to confirm pleural effusion and 1760 mL of hemorrhagic fluid was drained; PCV of the fluid was 25% and TS was 3.6 g/dL. The dog had a blood type Pd and was DEA 1.1 positive. The dog was stabilized with lactated Ringer’s solution fluid resuscitation (10 mL/kg bolus) and one unit of PRBCs. The dog was not coagulopathic with a PT of 14 sec (RI 11–17 sec) and aPTT of 87 sec (RI 72–102 sec).

Two days after initial presentation, thoracic and abdominal CT under general anesthesia was performed to determine the etiology of the hemothorax. Methadone was administered (0.1 mg/kg) and anesthesia was induced by propofol 1.2 mg/kg and midazolam 0.4 mg/kg coinduction. The CT showed bilateral moderate pleural effusion with collapse of the left cranial and left caudal lung lobes. There was an 8 cm multilobulated peripherally hyperattenuating mass lesion ventral to the right middle lung lobe. The mass lesion was adjacent to the right atrium but was separated from the cardiac silhouette by a thin layer of pericardial fat (Figure 1B). The origin of the mass lesion could not be determined based on the CT. There was a 5 mm pulmonary nodule in the right caudal lung lobe. The sternal lymph node was enlarged as it measured 8 mm in diameter. A single focal hypoattenuating 7 mm nodule was present in the caudal aspect of the spleen. It was not aspirated.

Surgical exploration via a right sixth intercostal thoracotomy was performed under general anesthesia. On entry to the thorax, 1.5 L of hemorrhagic effusion were removed with suction. The pulmonary nodule identified on CT was not visible or palpable. There was an 8 cm spherical, multiple lobulated, firm, dark purple mass in the caudoventral mediastinum attached to the ventral sternum. Dorsally the mass surrounded the vena cava but was not adherent to it. The mass was circumferentially dissected from its pleural attachments using a bipolar tissue sealing device and blunt dissection. The entire mass was removed; however, there were multiple small 1 to 2 mm dark coloured nodules throughout the pleura, adjacent and distant to the mass.

A right-sided thoracic drain was placed exiting in the eighth intercostal space. The dog recovered well and the thoracic drain was removed 2 days postoperatively. Radiographs taken 5 days postoperatively revealed minimal pleural effusion and the dog was discharged. Histopathology was consistent with HSA with neoplastic spindlyloid cells forming blood-filled channels. Neoplastic cells forming channels containing erythrocytes. There were several large areas of extravasated erythrocytes consistent with recent hemorrhage.

The dog received a transfusion of 2 units of packed red blood cell (PRBC) and two intravenous crystalloid fluid boluses of lactated Ringer’s solution at a rate of 20 mL/kg over 20 min. When cardiovascularly stable as determined by a sustained reduction in heart rate to 100 bpm, the dog was anesthetised for a computed tomographic (CT) scan of the thorax and abdomen. Methadone (0.1 mg/kg) was administered and anesthesia was induced by alfaxalone 0.005 mg/kg and midazolam 0.4 mg/kg coinduction. A second unit of PRBC were administered after induction. On CT, there was a large volume of pleural effusion with collapsed lung lobes. No pulmonary lesions were identified. A 9 cm heterogeneous soft tissue attenuating mass was visible in the dorsal mediastinum, ventral to thoracic vertebrae 8 to 10, displacing the aorta and esophagus ventrally and compressing the vena cava (Figure 1A). Iohexol, an iodine based contrast medium, at a dose of 4.6 g/dL was administered IV. The mass had heterogenous uptake of IV contrast. The origin of the mass could not be determined. Abdominal CT was unremarkable.

The primary differential diagnosis was a malignant vascular neoplasm, such as HSA. Exploratory thoracotomy was performed via median sternotomy. The mass was adherent to the aorta; therefore, dissection of the mass was not possible and the dog was euthanized intraoperatively. Postmortem was declined; however, histopathology of biopsy samples was consistent with HSA and revealed populations of proliferative partially vasoformative spindle cells forming channels containing erythrocytes. There were several large areas of extravasated erythrocytes consistent with recent hemorrhage.
cells were present at the surgical margins and as were hemosiderin-containing macrophages indicating historical hemorrhage.

While an appointment 2 wk after surgical discharge was recommended with the oncology service, the owners returned 4 wk postoperatively for re-evaluation. The incision had healed well and no further dyspneic episodes had been noted. A chemotherapy protocol was initiated; doxorubicin (30mg/m²) was administered IV. Cyclophosphamide (200mg/m²) was dispensed and was to be given in a divided dose per os for 2 days, 10 days after each doxorubicin administration.11

The dog represented 2 days after doxorubicin administration. Physical examination findings were consistent with hypovolemic shock. The dog was moderately dyspneic with bilateral pleural effusion confirmed with thoracic ultrasound. Thoracocentesis revealed hemorrhagic fluid with a PCV of 24%. The owners elected for euthanasia. No further diagnostic tests were performed. Postmortem examination was declined.

**Case 3**

A 9 yr old male neutered Labrador retriever presented for management of hemothorax diagnosed by the referring veterinarian and a 24 hr history of dyspnea and lethargy. On presentation, respiratory rate was 72 breaths per min with muffled respiratory and cardiac sounds ventrally. The heart rate was 180 bpm with hyperdynamic pulses. The PCV was 22% and TS 4.8 g/dL. Emergency blood gas and serum biochemical analysis was unremarkable. Hemothorax was diagnosed on the basis of hemorrhagic pleural fluid on thoracocentesis with PCV of 24%. The owners elected for euthanasia. No further diagnostic tests were performed. Postmortem examination was declined.

**FIGURE 1** (A) Postcontrast CT sagittal reconstruction of the thorax of case 1. There was a dorsal mediastinal mass (arrow) displacing the aorta and esophagus ventrally and flattening the caudal vena cava with pooling of contrast in irregular dilated vascular structures in the centre of the mass. Pleural effusion was also present. (B) Postcontrast transverse CT images of the caudal thorax of case 2. There was a multilobulated, peripherally hyperattenuating structure displacing the heart to the left (arrow). There was a moderate volume of pleural effusion.

Crystallloid boluses of lactated Ringer’s solution at 10 mL/kg for 2 boluses. A blood type was performed and was DEA 1.1 positive. One unit of PRBC (DEA 1.1 positive) was administered. The dog was not coagulopathic with a PT of 15 sec (RI 11–17 sec) and aPTT of 85 sec (RI 72–102 sec).

Methadone was administered (0.1 mg/kg) and anesthesia was induced by propofol titrated to effect and midazolam 0.4 mg/kg coinduction. A CT scan revealed a discrete, smoothly marginated, multilobular, 6 cm diameter mass lesion in the caudo-ventral thorax, which was heterogeneously enhancing following intravenous contrast administration (Figure 2). The mass was adjacent to the xiphoid process at the level of the sixth and seventh ribs. It was not possible to determine the origin of the mass from the CT scan.

As a result of ongoing hemorrhage, exploratory surgery was performed. Due to the location of the mass on the dorsal aspect of the sternum, a cranial midline laparotomy and transdiaphragmatic approach was performed. A discrete mass was present in the caudoventral thorax arising from a broad base on the right dorsal aspect of the xiphisternum. The mass was purple in colour with a highly vascular surface. No other adhesions or areas of invasion to the pulmonary parenchyma or pleura were present making surgical excision of the mass feasible, although a midline sternotomy from the xiphoid to the level of the fifth sternebrae was necessary to improve exposure. The mass was not cut into using this approach, but an ostectomy of the xiphisternum and sixth sternebrae was necessary as they were firmly attached to the broad base of the mass. An oscillating saw was used for removal of the sternebrae. The intercostal vessels and any aberrant vasculature to the mass were ligated. A right-sided silicone thoracic drain was placed in the
eighth intercostal space. Tension-free reconstruction of the thoracic wall deficit was achieved by diaphragmatic advancement and apposing the rectus abdominus muscle.

The dog received a further unit of PRBC, but made an uneventful recovery from general anesthetic and the surgery. The thoracic drain was removed 12 hr postoperatively and the dog was discharged 4 days postoperatively. Histopathology of the mass was consistent with an intramuscular HSA with spindloid neoplastic cells forming sheets and irregular vascular channels containing erythrocytes. The neoplastic cells extended to the surgical margins and there were large areas of necrosis present.

The dog presented to the Oncology service for a scheduled re-examination 2 wk postsurgery. Physical examination and in-house hematology were unremarkable. The surgical incision had healed well. The same chemotherapy protocol as case 2 was employed.11

The dog presented 3 wk after the initial doxorubicin1 dose. The owners reported mild polyuria and polydipsia. The surgical site had healed well and no abnormalities were detected on clinical examination. Hematology revealed a leukopenia with a white blood count of 2.82 × 10^9/l (RI 5.5–16.9 × 10^9/l) and neutrophil count of 1.23 × 10^9/l (RI 2–12 × 10^9/l). The doxorubicin1 was postponed for two days and prophylactic oral amoxicillin-clavulanate16 mg/kg was initiated twice daily.

Five mo postoperatively, at the time of writing, the dog had no reoccurrence of dyspnea or lethargic episodes. No further imaging studies were performed. The dog received four cycles of doxorubicin1 and cyclophosphamide1 protocol. Following the second cycle of Doxorubicin/ Adriamycin and cyclophosphamide chemotherapy the dog experienced grade III neutropenia (Veterinary cooperative oncology group – common terminology criteria for adverse events v1.1), so the doxorubicin dosage was reduced to 27 mg/m2 and the cyclophosphamide dosage was reduced to 150 mg/m2. This was successful and no further postchemotherapy episodes of neutropenia were noted.

**Discussion**

This case series reports three dogs that presented acutely with dyspnea caused by hemothorax. All of the cases had advanced imaging using CT and had attempted surgical resection of the intrathoracic masses.

CT scans were used to fully stage all dogs and revealed intrathoracic masses with similar contrast-enhancing heterogeneous appearances. Thoracic radiographs or thoracic ultrasonography were performed by the referring vets, which had demonstrated pleural effusion. We elected to preform advanced imaging by CT in all cases rather than repeating radiography.13 The differential diagnoses for soft tissue attenuating cavitatary mass lesions are neoplasia, granuloma, cyst, hematoma, and abscess. The origin of the masses and possible organ invasion could not be determined on CT scan. This was highlighted in case 2 where the mass appeared to envelop the caudal vena cava on CT but was not adherent to it at surgery. This is in agreement with a retrospective study that found that CT had a low sensitivity for predcating vascular invasion of mediastinal masses and highlighted the shortcomings in using CT for decision making preoperatively.12,13 It is important to emphasize that surgical exploration was required to determine if the intrathoracic masses were indeed resectable and even this small case series has shown that CT, although helpful for intraoperative planning, cannot definitively be used to determine if a mass is resectable.

The cases reported in this series are novel in the veterinary literature, as they were intrathoracic but not cardiac in origin. HSA commonly affects visceral organs, namely the spleen, liver, and right auricular appendage.7,13,14 Patients with cardiac HSA

**FIGURE 2** Early-phase postcontrast transverse plane CT image of the thorax of case 3. A broad-based poor-contrast enhancing, rounded mass is visible in the right ventral pleural space (*). The arrowheads outline the margin of the lesion, which is poorly differentiated from the adjacent pleural effusion. The heart is displaced to the left.
often present with cardiac tamponade due to hemorrhagic pericardial effusion. Surgical resection of the mass, if possible, is the initial treatment of choice.7,13,14 A case of periaortic HSA has been reported; the dog in this report died before surgical exploration was attempted.10 We felt that our case series is an important addition to the veterinary literature as it documents that surgical resection with survival to discharge is possible for intrathoracic, extracardiac HSA.

Due to the high suspicion of HSA based on the CT scans, all owners were advised of the guarded long-term prognosis, but they all opted to pursue palliative surgery followed by chemotherapy. Although obtaining a cytologic sample or tissue biopsy would have been useful in the decision making process, it would not have changed the decision to perform surgery because of the high risk of ongoing hemorrhage in these cases. Based on these cases and the current literature on HSA, surgical exploration and resection of the bleeding mass is required.1–6,17 This case series has reported that it is possible for intrathoracic HSA cases to survive until discharge and that as with other locations of HSA surgical treatment is palliative. It is important to counsel the owners of the palliative nature of the surgery and that, as in case 1, surgical resection may not be possible.

Conclusion
Intrathoracic extra-cardiac HSA can be treated in a similar fashion to HSA in other locations with surgical hemostasis and resection of the tumor followed by adjuvant chemotherapy. We have reported three dogs that presented with acute onset dyspnea due to hemorrhagic pleural effusion from intrathoracic HSA. CT was used to demonstrate the mass but was not able to determine if the mass was surgically removable. Intrathoracic extra-cardiac HSA should be considered as a differential diagnosis for nontraumatic hemothorax and surgical treatment can be palliative.

FOOTNOTES
a Vetivex 11; Dechra Veterinary Products, Shrewsbury, United Kingdom
b Computed tomography 16-slice scanner Mx8000 IDT; Philips, Best, The Netherlands
c Physeptone; GlaxoSmithKline, Middlesex, United Kingdom
d Alfaxan; Jurox, Malvern, United Kingdom
e Hypnovel; Roche Products Ltd, Welwyn Garden City, United Kingdom
f Omnipaque; GE Healthcare, Cork, Ireland
g Vetofol; Norbrook, Corby, United Kingdom
h Enseal bipolar tissue sealer; Ethicon, Livingstone, United Kingdom
i Thoracic drain 18 Fr; Vygon, Swindon, United Kingdom
j Doxorubicin; Pfizer Ltd., Kent, United Kingdom
k Cyclophosphamide; Baxter Healthcare Ltd., Norfolk, United Kingdom

REFERENCES
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