Non-coagulopathic spontaneous hemothorax in dogs

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Abstract

Objective: To determine the history, clinicopathologic findings, underlying causes, and outcomes for dogs with non-coagulopathic spontaneous hemothorax.

Design: Retrospective case series.

Setting: University referral hospital.

Animals: Sixteen client-owned dogs.

Interventions: The medical records database was searched for dogs with hemothorax. Dogs with trauma, secondary coagulopathy, recent thoracic surgery, or pericardial intervention were excluded. For the remaining dogs, signalment, clinical signs, clinicopathologic findings, radiographic findings, histopathologic findings, interventions, and outcome were recorded.

Measurements and main results: The most common presenting signs were tachypnea (n = 9) and lethargy (n = 5), typically of <1-week duration. The most common cause of non-coagulopathic spontaneous hemothorax in dogs was neoplasia, which was diagnosed in 14 patients (88%). Identified malignancies included hemangiosarcoma (n = 1), malignant mesothelioma (n = 1), metastatic ovarian carcinoma (n = 1), osteosarcoma (n = 2), and pulmonary carcinoma (n = 2). An intrathoracic mass was visualized in 7 other dogs; however, histopathology was not obtained. Pancreatitis and lung lobe torsion were each diagnosed in 1 dog, and survival was prolonged with both surviving at least 1 year post discharge. Only 6 of 14 dogs that were diagnosed with neoplasia were discharged from the hospital. For the 4 dogs with cancer with available outcome data, median survival time was 16 days (range 1–70 days). Two dogs were lost to follow-up and had unknown survival times.

Conclusions: The development of non-coagulopathic spontaneous hemothorax warrants a high-index suspicion for neoplasia, in particular thoracic wall neoplasia.


Keywords: hemorrhage, pleural effusion, pulmonary neoplasia

Introduction

Hemothorax is defined as an effusion in the pleural cavity with a packed cell volume (PCV) that is at least 25% of peripheral blood.1 Spontaneous hemothorax is a hemothorax unrelated to trauma, while non-coagulopathic hemothorax refers to hemothorax unrelated to systemic coagulopathy. Clinically, traumatic injuries and coagulopathies appear to be the most common causes of hemothorax in the dog. While defects in secondary hemostasis are frequently associated with hemothorax, defects in primary hemostasis may also result in hemothorax.2 However, the most common causes of spontaneous hemothorax in dogs with no evidence of trauma and normal coagulation studies have not been determined. The syndrome of non-coagulopathic spontaneous hemothorax is rare in human medicine and typically involves rupture of intrathoracic masses or underlying vascular pathology such as an aneurysm.3 There have been case reports in veterinary literature documenting Dirofilaria immitis,4 hemangiosarcoma,5 mesothelioma,6 and Spirocerca lupi7 as causes of hemothorax in dogs. To the authors’ knowledge, a clinical case series of non-coagulopathic spontaneous hemothorax has not been reported in dogs. Therefore, the purpose of this study is to characterize the signalment, clinical signs, clinicopathologic abnormalities, radiographic findings, histopathologic findings,
treatments, and survival times in dogs with non-coagulopathic spontaneous hemothorax.

Materials and Methods

The cytology log of the Foster Small Animal Hospital at the Tufts Cummings School of Veterinary Medicine was evaluated for pleural effusion samples from dogs using the keywords ‘hemorrhage’ or ‘hemorrhagic effusion’ between January 1, 1994 and March 1, 2006. The medical records of affected dogs were reviewed. Dogs with a history of trauma within the preceding week or evidence of a systemic coagulopathy were excluded from this study. Coagulopathy was defined as prolongation of the activated clotting time (ACT) or either prothrombin time (PT) or activated partial thromboplastin time (aPTT) >25% of the upper limit of the reference range.8–10 Dogs with a history of recent thoracic surgery or any previous pericardial intervention were also excluded. Assessment of primary hemostasis was not required unless the dog’s platelet count was low enough to cause spontaneous bleeding (e.g., <40,000 platelets/μL)11 or there were clinical signs of a primary hemostatic disorder such as petechiation, ecchymoses, or epistaxis.12 The PCV of the pleural effusion was compared with the PCV of the dog’s peripheral blood. Hemothorax was identified if the pleural effusion PCV was at least 25% of the peripheral blood PCV.1

Data recorded included breed, age, sex, duration of clinical signs before presentation, clinical findings, and results of the complete blood count (CBC) and serum biochemical analysis. In addition, pleural fluid analysis, radiographic findings, treatment modalities, final diagnosis (when available), and overall outcome were recorded.

Statistical Methods

Descriptive statistics with results are listed as median and range as appropriate.

Results

Sixteen dogs met the criteria for inclusion in this study. Breeds represented included Golden Retrievers (n = 5), Labrador Retrievers (n = 2), Basset Hound (n = 1), Cairn Terrier (n = 1), German Shepherd Dog (n = 1), Irish Setter (n = 1), Portuguese Water Dog (n = 1), and Rottweiler (n = 1). The median weight was 34.5 kg (range 9.1–55 kg). Only 1 of the dogs, the Cairn Terrier, weighed <15 kg. Eight dogs were spayed females, 4 were castrated males, 3 were intact males, and 1 was an intact female. Median age was 7.4 years (range 1.75–14 years).

The median duration of clinical signs was 4.5 days (range 1–280 days). The most common presenting signs were tachypnea (n = 9), lethargy (n = 5), and cough (n = 4). Vomiting (n = 3), anorexia (n = 3), diarrhea (n = 2), and collapse (n = 2) were documented less frequently. Physical examination abnormalities most commonly reported included tachypnea (n = 9), tachycardia (heart rate >160/min) (n = 5), and muffled heart or lung sounds (n = 5). Pulse quality was noted in 12 patients and characterized as weak in 5 dogs, normal in 5 dogs, and bounding in 2 dogs.

Ten of 16 dogs were anemic (reference interval, 37–55%; median, 31%; range, 24–35%). Only 1 of the anemic dogs had a reticulocyte percentage performed and the corrected reticulocyte percentage was consistent with a mild regenerative response (1.8%, reference interval >1.5%). One dog was leukopenic (3200 cells/μL; reference interval, 4900–16,900 cells/μL) and 3 dogs had a leukocytosis (median, 33,200 cells/μL; range, 19,700–49,000 cells/μL). Thrombocytopenia (<200,000 cells/μL) was identified in 13 of 16 dogs, although exact platelet counts were only available in 11 of 14 dogs (reference interval, 200–500,000 cells/μL; median, 114,000 cells/μL; range, 72–181,000 cells/μL). Two dogs with platelet estimates based on blood smear evaluation suggested actual platelet counts between 90 and 120,000 cells/μL. One dog had thrombocytosis with 551,000 cells/μL.

The most common biochemical abnormalities were elevated aspartate transferase (AST) (n = 6), alkaline phosphatase (ALKP) (n = 6), and amylase (n = 5). Hyperglycemia, hyperphosphatemia, and elevation in alanine transferase (ALT) were each documented in 3 dogs. Hypoproteinemia (<55 g/L [<5.5 g/dL]) was documented in 2 dogs with neither <50 g/L [5.0 g/dL]. Hypoalbuminemia was found in 1 dog (27 g/L [2.7 g/dL], reference interval, 28–40 g/L [2.8–4.0 g/dL]). The remaining dogs had albumin measurements within the normal reference range.

Thoracic radiography identified pleural effusion in all 16 dogs. In 2 dogs, lytic sternebrae were identified. This radiographic finding was determined as the cause of the hemothorax and no further imaging of the thorax was performed. An abdominal ultrasound identified pancreatitis in 1 dog on presentation. Further thoracic imaging was not performed until re-check thoracic radiographs 2 weeks post discharge confirmed almost complete resolution of the hemothorax. There was clinical suspicion of a mass from either the thoracic wall or pulmonary parenchyma in 6 other dogs. However, the radiographic images were not considered conclusive enough to make a definitive diagnosis.

Additional diagnostic imaging of the thorax was performed in 13 dogs. Thoracic ultrasonography was performed in 8 dogs, echocardiography was performed
in 5 dogs, and thoracic computed tomography (CT) in 1 dog. In 10 dogs, further imaging definitively diagnosed the cause of the hemothorax. Thoracic wall masses were found in 6 dogs, pulmonary parenchymal masses in 2 dogs, and a right atrial mass and a lung lobe torsion were each noted in 1 dog. In 3 dogs, no definitive cause of hemothorax was identified. However, 2 dogs had consolidated lung lobes and the remaining had no visible abnormalities. These 3 dogs were subsequently diagnosed with pulmonary carcinoma, malignant mesothelioma, and metastatic ovarian carcinoma.

The 13 dogs with higher imaging modalities had either echocardiography or thoracic ultrasonography performed. Both imaging modalities were not performed in any 1 dog, so the sensitivity of the 2 imaging modalities could not be compared. Thoracic ultrasonography was performed in the 3 dogs with inconclusive imaging results. Because CT was unavailable at the time these 3 dogs were presented for evaluation, no conclusions could be made regarding thoracic CT use in the diagnosis of hemothorax. The dog that had a CT performed had a thoracic wall mass identified on thoracic ultrasound before CT evaluation. No additional intra-thoracic findings were documented on the CT scan.

Thoracocentesis was performed in all 16 dogs. In 8 dogs, the volume of effusion removed from the thoracic cavity was recorded in the medical record. The median volume of effusion collected was 5.3 mL/kg (range 0.91–26.6 mL/kg). However, record examination did not indicate the purpose of the thoracocentesis (e.g., diagnostic versus therapeutic). Three cases had multiple thoracocenteses performed with no more than 1 thoracocentesis within a 24-hour period. Cytologic examination of the pleural fluid did not identify the etiology of the hemothorax in any of the dogs. The median PCV of the pleural effusion was 27% (range 8–35%). The median ratio between pleural effusion PCV to the peripheral blood PCV was 0.70 (range 0.27–1.46).

Ten of 16 dogs received supplemental oxygen therapy. Of the 10, only 1 had an arterial blood gas on room air performed that revealed hypoxemia (PaO$_2$ = 59.9 mmHg; reference interval, PaO$_2$ > 60 mmHg on room air) and hypocapnia (PaCO$_2$ = 28.3 mmHg; reference interval, PaCO$_2$ = 35–45 mmHg). All 9 dogs with tachypnea received supplemental oxygen therapy. The final dog presented with an increased respiratory effort. Despite supplemental oxygen therapy, tachypnea persisted in 7 of 9 dogs. These 10 dogs received supplemental oxygen therapy until euthanasia (n = 5), discharge (n = 3), or surgery (n = 2).

Three of 16 cases received packed red blood cell transfusions for treatment of anemia. Seven dogs had surgery for control of hemorrhage and definitive therapy of the underlying cause. One dog was euthanized intraoperatively because of strong suspicion of widespread neoplastic disease that was confirmed on histopathologic examination as a malignant mesothelioma. Another dog experienced cardiopulmonary arrest from which resuscitation efforts were unsuccessful. This dog was subsequently diagnosed with pulmonary carcinoma. Five dogs survived the perioperative and postoperative period and were ultimately discharged. Surgical procedures performed on these 5 dogs included rib resection (n = 2), lung lobectomy (n = 2), and thoracic wall mass biopsy (n = 1). Histopathologic diagnoses from these 5 dogs were rib osteosarcoma (n = 2), hemangiosarcoma or suspected hemangiosarcoma (n = 2), and lung lobe torsion (n = 1).

Survival data were available for 3 of the 5 cases that survived surgery and were subsequently discharged. One dog with rib osteosarcoma was euthanized 70 days post discharge for collapse of secondary to hemobdome. The etiology of the hemoabdomen was not determined; however, coagulation studies (PT/PTT) were within the reference interval. This dog did not receive any adjunctive radiation or chemotherapy. The other case of rib osteosarcoma received single-agent cisplatin protocol every 3 weeks for a total of 3 treatments. No data were available for this case after its 3-month re-check. The case of hemangiosarcoma presented to the emergency room dead on arrival 18 days following discharge. This dog also did not receive any adjunctive radiation or chemotherapy. No data were available for the case of suspected hemangiosarcoma after its 1-month re-check. The dog with the lung lobe torsion and subsequent lung lobectomy was euthanized 18 months post discharge at their local veterinary hospital for persistent respiratory disease, characterized by a severe cough.

Seven dogs with thoracic cavity masses did not undergo surgical intervention. Ultrasound-guided aspiration of a consolidated lung lobe was performed in 1 dog. Pulmonary carcinoma was diagnosed via cytology and the dog was euthanized. Two additional dogs were discharged for palliative care with no medications dispensed in either case. Survival time for these dogs was 1 and 14 days after hospital discharge. The remaining 4 dogs were euthanized after identification of an intrathoracic mass in association with hemothorax. The rationale for euthanasia was due to poor long-term prognosis related to suspected neoplasia.

One dog was euthanized in the hospital despite no abnormalities identified on thoracic radiographs or thoracic ultrasonography. The rationale for euthanasia documented was a suspected underlying neoplastic process causing the hemothorax. Necropsy was performed on this dog and metastatic ovarian carcinoma was diagnosed.
The dog with severe pancreatitis was treated medically for pancreatitis, hemotherax, and hemoabdomen. Thoracic radiographs 2 weeks post discharge showed almost complete resolution of the hemothorax.

The most common cause of non-coagulopathic spontaneous hemothorax in dogs was neoplasia, which was identified in 14 patients. Seven dogs had a histologic diagnosis and neoplasms identified included hemangiosarcoma (n = 1), malignant mesothelioma (n = 1), metastatic ovarian carcinoma (n = 1), rib osteosarcoma (n = 2), and pulmonary carcinoma (n = 2). Seven dogs did not have a histopathologic diagnosis; however, an intrathoracic mass was visualized in each dog. Thoracic wall masses involving the ribs (n = 4) and sternabrae (n = 2) were identified in 6 dogs. In the final dog, a right atrial mass, judged most consistent with hemangiosarcoma, was identified with echocardiography. Pancreatitis and lung lobe torsion were each identified in 1 dog and survival time was 6 years and 18 months, respectively. In all, the median survival time of the 4 dogs diagnosed with neoplasia with available survival data was 16 days (range 1–70 days).

Discussion

Neoplasia was the most common diagnosis associated with non-coagulopathic spontaneous hemothorax in this study. The cause of hemothorax due to neoplasia is likely multifactorial. Pulmonary parenchymal neoplasia has been postulated to cause hemothorax by direct invasion of pulmonary vessels, compression, or ischemic necrosis of adjacent lung tissues by tumor, tumor-induced angiogenesis, or rupture of a well-vascularized tumor.13–15

In this study, 50% of the cases had thoracic wall masses. In previous reports, hemorrhagic pleural effusion occurred in 10–40%16,17 of dogs with thoracic wall masses. The most common thoracic wall tumor types reported in dogs were osteosarcoma and chondrosarcoma, with fibrosarcoma and hemangiosarcoma occurring less commonly.16–20 Proposed mechanisms of hemothorax due to thoracic wall neoplasia in dogs include direct invasion of intercostal vessels or tumor necrosis and secondary pleural hemorrhage.16 Prognosis for thoracic wall tumors is dependent on histopathologic results. Surgical therapy may be curative or result in a lengthy remission,16–20 while conservative management is typically ineffective. Median survival time reported for conservative management is 15 days19 for rib osteosarcomas and 5 weeks18 for rib sarcomas.

Lung lobe torsion has been uncommonly reported to cause hemorrhagic effusion in dogs21,22 and even more rarely associated with hemothorax with only one case identified in 2 retrospective studies on lung lobe torsion.21,22 Similar to previous reviews, only 1 case of lung lobe torsion causing a hemothorax was identified at our institution during the 12-year study period. The proposed mechanism of pleural effusion formation due to lung lobe torsion is a twisting of the bronchus and pulmonary vessels at the hilus. The thin-walled pulmonary vein collapses easily, while the more muscular artery continues to allow some flow into the lung. This leads to congestion and consolidation as fluid moves into the interstitial tissue and airways and eventually to the pleural space.23

Pancreatitis was diagnosed in one dog with hemothorax. Pancreatitis has been associated with pleural effusion in dogs.24 In pancreatitis, active pancreatic enzymes and inflammatory mediators are released into pancreatic tissues and blood vessels. Trypsin, which converts proelastin to elastase, is an important mediator in this process. Elastase subsequently digests elastic fibers in pancreatic blood vessels transforming pancreatitis from an edematous to hemorrhagic form.25 Trypsin also releases bradykinin, which produces a profound local vasodilation and increased vascular permeability further permitting escape of red blood cells into body cavities.25 Systemic release of elastase and bradykinin may have precipitated the hemothorax that developed in this dog. This dog was diagnosed with concurrent hemothorax and hemoabdomen due to the pancreatitis. Despite the severity of the pancreatitis, the dog was discharged from the hospital and was euthanized 6 years later from unrelated disease.

Complex diagnostic imaging such as ultrasonography, echocardiography, or computed tomography was utilized in 88% of cases to establish a diagnosis. Computed tomography, which has been gaining popularity in recent years, may be the most helpful imaging modality as it is more sensitive in detecting pulmonary parenchymal neoplasia than radiographs.26 CT will provide a detailed image of the ribs, and may be useful for surgical and oncologic planning. Although CT did not provide additional information in this study, it is difficult to draw conclusions regarding the sensitivity of CT in canine hemothorax cases on the basis of 1 case. As such, CT is accepted as the most accurate imaging technique for detection of pulmonary lesions and is an essential imaging tool of several pulmonary conditions in humans.27 Magnetic resonance imaging (MRI) was not utilized in any dog in this study; however, it may present an alternative imaging modality for canine hemothorax patients in hospitals without CT capability. MRI has been utilized in human medicine for the imaging of rib tumors28 and was found to be as sensitive as CT in detection of pulmonary metastases.29

Despite hemorrhaging into the thoracic cavity, only 3 dogs received blood transfusions and only 1 dog had...
hypoalbuminemia. This may be related to the short duration of hospitalization because 5 dogs were euthanized or discharged within 24 hours of admission. Of the remaining dogs, all 11 were hospitalized for at least 48 hours with 2 receiving a packed red blood cell transfusion. This suggests that the rate of blood loss into the pleural cavity was slow or the red cell regeneration was able to compensate. However, a reticulocyte count was only performed in 1 case, and thus the role of regenerative anemia cannot be determined. Another hypothesis is that intrathoracic hemorrhage increases intrapleural hydrostatic pressure, preventing further bleeding and also contributing to the lack of transfusion requirements.

None of the cases were managed preoperatively with thoracostomy tube placement and continuous suction as is the recommendation in human medicine for the management of hemothorax. Thoracostomy tube drainage is recommended because it allows for monitoring bleeding rate, relieves respiratory distress, and may decrease subsequent fibrosis. In addition, accumulated blood can serve as a nidus for infection and the development of subsequent empyema. The lack of emergent thoracostomy tube placement in our patients may be attributed to several reasons. Most importantly, only 3 dogs underwent multiple thoracocenteses and none had multiple thoracocenteses within a 24-hour period. In contrast to human medicine, the bleeding rate appears less catastrophic as only 3 dogs received packed red cell transfusions. Finally, autotransfusion occurs rapidly from the pleural cavity via the diaphragmatic lymphatics, resulting in near resolution of hemothorax within days. Therefore, it may only be necessary to remove that volume of effusion that relieves respiratory distress.

In human medicine, emergency thoracotomy is recommended in cases with hemodynamic instability or if thoracostomy tube drainage produces a large volume of blood. The rate of bleeding in humans at which thoracotomy should be performed varies among authors but generally ranges from 150 to 500 mL/hr. None of the dogs in this study had an emergency thoracotomy performed. However, it is difficult to draw conclusions regarding the optimal management strategy for non-coagulopathic spontaneous hemothorax in dogs based on a retrospective study with a small sample size.

Limitations of this study are inherent in its retrospective design. In addition, nearly half of the cases lacked a histopathologic diagnosis, which precludes assessment as to the tumor type most likely to cause a hemothorax. In this study, tests of primary hemostasis (e.g., buccal mucosal bleeding time) were not performed in any dog. However, it is unlikely that a primary hemostatic defect caused the hemothorax in any of these cases. The lowest platelet count of any dog included in this study was 72,000 cells/μL, and therefore not at a level typically associated with spontaneous bleeding. Bleeding into a body cavity such as the thorax is typically associated with a defect in secondary (e.g., factor deficiency/inactivation) hemostasis and not primary hemostasis. None of the dogs displayed clinical symptoms of a primary hemostatic defect noted on physical examination such as petechiation, ecchymoses, or epistaxis. Finally, a more likely underlying cause (e.g., mass, pancreatitis, or lung lobe torsion) was identified in all dogs.

In conclusion, the diagnosis of non-coagulopathic spontaneous hemothorax in a dog warrants a high index of suspicion for neoplasia, in particular thoracic wall neoplasia. Other differentials should include lung lobe torsion and pancreatitis, although they appear to occur less commonly. The attending clinician should initiate the diagnostic work-up with thoracic radiographs. However, advanced imaging modalities such as echocardiography, ultrasonography, or CT are typically required. While recommended in human medicine, thoracostomy tube placement may not be as imperative for management of veterinary patients. However, the clinical condition of the animal, the volume of the effusion removed, and the frequency of thoracocentesis should dictate thoracostomy tube placement. For a great proportion of dogs diagnosed with this condition, survival time appears short.

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References