Hemidiaphragmatic reconstruction with a transversus abdominis muscle flap after resection of a solitary diaphragmatic mesothelioma in a dog

Julius M. Liptak, BVSc, MVetClinStud, DACVS; Nicholas S. Brebner, DVM

A 2-year-old 19-kg (41.8-lb) female Siberian Husky was evaluated for a 2-week history of coughing and gagging and decreased appetite and activity level. Clinical Findings—Radiography, surgery, and immunohistochemical examination revealed a solitary sclerosing mesothelioma extending from the left thoracic diaphragmatic surface that was adherent to the pericardium and the caudal mediastinum.

Treatment and Outcome—The tumor was resected along with most of the left hemidiaphragm, and the left transversus abdominis muscle was used to reconstruct the diaphragm. The 13th rib formed the base of the muscle flap. The muscle flap was transposed into the diaphragmatic defect so that the mesothelium-lined surface faced the thoracic cavity and the deep aspect of the muscle formed the abdominal surface of the diaphragm. To minimize risk of adhesions, the exposed raw aspect of the abdominal surface was covered with porcine small intestinal submucosa. Recovery was uneventful, and the dog’s appetite and activity level soon returned to normal. Evaluation 54 days after surgery revealed 2 subcutaneous masses on the thorax and masses in the liver and both kidneys; histologic and immunohistochemical analyses revealed metastasis of the original tumor. The dog was euthanatized.

Clinical Relevance—Hemidiaphragmatic reconstruction with a transversus abdominis muscle flap after resection of a diaphragmatic tumor was successful. The muscle flap was easily harvested and transposed into the diaphragmatic defect. (J Am Vet Med Assoc 2006;228:1204–1208)

From the Department of Clinical Studies, Ontario Veterinary College, University of Guelph, Guelph, ON N1G 2W1, Canada. The authors thank Drs. Margaret Stalker, B. E. Powers, and E. J. Ehrhart for histologic and immunohistochemical evaluation of the tumor. Address correspondence to Dr. Liptak.

ABBREVIATIONS

SIS Small intestinal submucosa

10^9 cells/L) and mild monocytosis (1.3 × 10^9 cells/L; reference range, < 1.1 × 10^9 cells/L) and lymphopenia (0.7 × 10^9 cells/L; reference range, 0.8 × 10^9 to 5.1 × 10^9 cells/L). Serum biochemical abnormalities were mild and included hyperproteinemia (50 g/L; reference range, 53 to 74 g/L), hypobulbilinemia (28 g/L; reference range, 29 to 43 g/L), hypocholesterolemia (2.9 mmol/L; reference range, 3.6 to 10.2 mmol/L), high alanine aminotransferase activity (126 U/L; reference range, 19 to 107 U/L), and low BUN concentration (1.9 mmol/L; reference range, 3.5 to 9.0 mmol/L). Prothrombin time was mildly prolonged (15.5 seconds; reference range, 9.0 to 15.0 seconds), but activated partial thromboplastin time and activated clotting time were within reference limits. Results of urinalysis were unremarkable.

Thoracic radiography revealed a large space-occupying multilobulated soft tissue mass in the left hemithorax extending into the right hemithorax (Figure 1). The mass silhouetted the heart and left crus of the diaphragm. The mass also displaced the heart to the right, and the left caudal lung lobe was compressed.

Differential diagnoses included diaphragmatic hernia, primary lung tumor, lung lobe torsion, or diaphragmatic mass. Diaphragmatic hernia was considered the most likely diagnosis, but there was no known history of trauma, and the fairly acute onset of clinical signs was not consistent with a congenital diaphragmatic hernia.

The dog was premedicated with oxymorphone (0.40 mg/kg [0.18 mg/lb], IV). General anesthesia was induced with a combination of diazepam (0.25 mg/kg [0.11 mg/lb], IV) and propofol (1.85 mg/kg [0.84 mg/lb], IV) and maintained with isoflurane and oxygen. Intraoperative analgesia consisted of a continuous rate infusion of fentanyl (20 µg/kg/h [9.1 µg/lb/h]). A venital midline celiotomy revealed no evidence of a diaphragmatic hernia, but the surface of the left hemidiaphragm was firm and lobulated. No other abdominal abnormalities were detected. The ventral midline celiotomy was extended into a median sternotomy from sternbrae 2 to 8. Exploration of the thoracic cavity revealed a large mass (19 × 14 × 12 cm) extending from the left diaphragmatic surface cranially into the left hemithorax and adherent to the pericardium and caudal mediastinum (Figure 2). There was no gross evidence of other intrathoracic lesions. Intraoperative cyto-
logic examination of a fine-needle aspirate revealed findings consistent with a soft tissue sarcoma, possibly a rhabdomyosarcoma, with a large population of monotypic spindle cells and occasional straplike spindle cells. The diaphragmatic mass was resected with 3-cm margins of grossly normal tissue, including the pericardium and mediastinal tissue, because of the high suspicion of a soft tissue sarcoma. This resulted in resection of most of the left hemidiaphragm lateral to the esophageal hiatus, including the phrenic nerve.

The left transversus abdominis muscle was used to reconstruct the diaphragm. The 13th rib formed the base of the transversus abdominis muscle flap. The ventral border of the muscle flap was created by incising its fascial attachment to the linea alba for approximately 20 cm caudally from the 13th rib. The caudal border of the muscle flap was created by incising through the transversus abdominis muscle in a ventral-to-dorsal direction to the most dorsal aspect of the transversus abdominis muscle. The dorsal border of the muscle flap was created by incising the transversus abdominis muscle from the caudal border in a caudal-to-cranial direction to the 13th rib and parallel to the ventral border. The muscle flap was mobilized by separating the deep aspect of the transversus abdominis muscle from the underlying internal abdominal oblique muscle via blunt dissection, cautering perforating abdominal vessels, and transecting perforating nerves. The transversus abdominis muscle flap was then transposed into the diaphragmatic defect from its cranial base so that the mesothelium-lined surface faced the thoracic cavity and the deep aspect of the transversus abdominis muscle formed the abdominal surface of the diaphragm. The muscle flap was sutured under moderate tension to the remaining diaphragm and central tendon with a simple continuous pattern of 3-0 polydioxanone suture material (Figure 3). To minimize the risk of adhesion formation after surgery, the exposed raw abdominal surface (deep aspect) of the transversus abdominis muscle flap was covered with porcine SIS.

Intraoperative complications included blood loss and hypotension. Blood loss occurred during tumor resection and not during harvesting of the muscle flap. The dog was treated for hypotension with boluses of an isotonic polyionic IV fluid (20 mL/kg), typed and matched whole blood transfusion (25 mL/kg/h [11.4 mL/lb/h]), and a continuous rate infusion of dopamine (7 µg/kg/min [3.2 µg/lb/min]).

After placement of a left-sided thoracostomy tube, the median sternotomy was closed with No. 2 polypropylene suture material and the remainder of the abdominal and thoracic incisions were closed routinely. An epidural catheter was inserted for postoperative analgesia.
Postoperative management included analgesia with a continuous rate infusion of fentanyl (2 to 4 µg/kg/h [0.9 to 1.8 µg/lb/h]), epidural administration of morphine (0.03 mg/kg/h [0.012 mg/lb/h], q 6 h), and oral administration of meloxicam (0.1 mg/kg [0.05 lb/kg], q 24 h); supplemental oxygen (1.5 to 4.0 L/min, intranasal); and monitoring of blood gases, blood pressure, urine output, and thoracic fluid volume and character. Plasma was administered for treatment for hypoproteinemia (2.6 g/L). Otherwise, the postoperative recovery was uncomplicated. The thoracostomy tube was removed after 46 hours because respiratory rate and pattern were normal, fluid production was minimal (468 mL [0.54 mL/kg/h [0.24 mL/lb/h]]) with no evidence of continuous hemorrhage (thoracic fluid PCV, < 5%), and blood gas results were acceptable for a dog receiving supplemental oxygen (oxygen saturation, 98.8%; PaCO₂, 41.3 mm Hg; PaO₂, 140 mm Hg).

Histologically, the mass consisted of sheets of epithelial cells forming tubules and clefts in a nonsecretory cavernous arrangement, multiple blood-filled sinuses lined by normal endothelium, and regions of fibrin and collagen with variable numbers of fibroblasts. The neoplastic epithelial cells had a low mitotic rate (1 to 2 mitotic figures/hpf) with moderate anisocytosis, anisokaryosis, and apoptosis. A carcinoma of thoracic origin was suspected, but a definitive diagnosis could not be made on the basis of the histologic characteristics of the tumor. There was no evidence of tumor cells at the inked margins.

Immunohistochemical staining with vimentin and cytokeratin AE1/AE3 was performed to further characterize the tumor type. The tumor stained positively for vimentin and cytokeratin AE1/AE3 markers, but the staining pattern was atypical for a carcinoma because vimentin staining was more diffuse and prominent than was staining with cytokeratin AE1/AE3. This
immunohistochemical staining pattern was consistent with a sclerosing mesothelioma,1,2 although other mesenchymal tumors, such as nephroblastoma and teratoma, could not be excluded.

The dog’s appetite and activity level returned to normal after surgery, but the dog was reevaluated 54 days after surgery because of a 5-day history of anorexia, somnolence, hematochezia, and hematuria. Two 3-cm-diameter subcutaneous masses were evident bilaterally on the thoracic wall. Ultrasonographic examination of the abdomen revealed multiple mixed-echogenic lesions ranging in size from 0.9 × 1.0 cm to 2.7 × 5.6 cm in the liver and both kidneys. Three-view thoracic radiography revealed 2 pulmonary lesions and an intact left diaphragm with no evidence of local tumor recurrence (Figure 4). Metastatic disease was suspected, and the dog was euthanatized. The owners declined a necropsy but permitted needle-core biopsies of the skin, hepatic, and renal lesions. The histologic and immunohistochemical staining characteristics of these lesions were similar to the diaphragmatic mass, with strong positive staining for vimentin and weak and inconsistent staining for cytokeratin AE1/AE3 and CD10. On the basis of these findings, metastatic sclerosing mesothelioma was diagnosed.

Primary tumors of the diaphragm are rare in dogs. To the authors’ knowledge, only 1 case of a solitary diaphragmatic tumor, a peripheral nerve sheath tumor, has been reported in the veterinary literature.3 Primary diaphragmatic tumors are also rare in humans, with < 150 cases described.4 Lipomas are the most common benign tumors, and mesenchymal tumors, such as liposarcoma, rhabdomyosarcoma, and leiomyosarcoma, are the most frequently reported malignant tumors.4 Diaphragmatic involvement is more common with extension of tumors of the lungs or gastrointestinal junction into the diaphragm or diffuse neoplastic diseases of the thoracic or abdominal cavities, such as malignant mesothelioma.5

Mesothelioma is a tumor that diffusely involves the mesothelial surfaces of the pleura or peritoneum.1,5 An association between direct or indirect exposure to silicate minerals in asbestos fibers, particularly crocidolite and amosite, and the development of pleural mesothelioma has been detected in dogs and humans.5,6 Flea repellants, urban environments, and genetic susceptibility are also etiologic factors in dogs with pleural or peritoneal mesothelioma.7 The dog described here had no known direct or indirect exposure to asbestos, but was relatively young and lived in an urban environment. A genetic susceptibility cannot be excluded, considering the age of the dog and the characteristics of the tumor and clinical signs, such as the large size of the tumor and acute onset of clinical signs.

Pleural mesothelioma is characterized by pleural thickening with multifocal nodules and pleural effusion.1 In the dog of this report, the mesothelioma was a solitary mass arising from the thoracic surface of the diaphragm with no intraoperative evidence of multifocal or diffuse mesothelial involvement or metastatic disease in the abdominal or thoracic cavities. Solitary mesotheliomas are very rare in human medicine and have not been reported in the veterinary literature.4,10 A soft tissue sarcoma was originally suspected on the basis of intraoperative cytologic interpretation. Interestingly, the major differential diagnosis for localized malignant mesothelioma in human medicine is a mesenchymal neoplasm called solitary fibrous tumor. These 2 tumors cannot be differentiated histologically, and immunohistochemical analysis is required for definitive diagnosis, as was necessary in the dog reported here.5,9

Histologically, mesotheliomas may have epithelial, mesenchymal, or mixed morphologic features.4 The epithelial form is the most common in dogs, and although rare, mesenchymal mesothelioma, which is also known as sclerosing mesothelioma, has been reported in dogs.1,11,12 Histologically, the tumor in the dog reported here was a primitive and anaplastic epithelial tumor. Sclerosing mesothelioma was diagnosed on the basis of the immunohistochemical staining pattern, which, unlike the histologic appearance of the tumor, suggested a mesothelioma with mesenchymal morphologic features because of consistent and strong vimentin staining and weak cytokeratin AE1/AE3 staining.5,9 In humans, treatment options for pleural mesothelioma are usually limited to palliative care because of the diffuse nature of the disease.5 Other than thoracoscopic pleurodesis for palliation for symptomatic or recurrent pleural effusion, surgical treatments (such as extrapleural pneumonectomy or pleurectomy and decortication) are associated with high mortality rate, high rate of local tumor recurrence, and no substantial improvement in survival.1 Surgical resection was performed in the present case because the mass was solitary and localized, and resection was possible with appropriate surgical margins without compromising vital structures, such as the caudal vena cava and both phrenic nerves.

Autogenous and prosthetic techniques have been described for the reconstruction of large diaphragmatic defects in dogs.13,14 Most studies are experimental with dogs being used as a model for human diseases, such as congenital agenesis of the hemidiaphragm. Autogenous techniques include a thoracoabdominal muscle flap and fascia lata.13,15 Muscle flaps that have been used successfully in humans include the reverse latissimus dorsi muscle flap alone or in combination with the serratus anterior and the combined external abdominal oblique flap and transversus abdominis muscle flap.17,18 The transversus abdominis muscle flap has been described in 2 dogs with chronic diaphragmatic hernia.13 The outcome was excellent in 1 dog, and 1 dog was euthanatized because of complications caused by obstruction of the caudal vena cava by the muscle flap.13

The transversus abdominis muscle satisfies the criteria for use as a muscle flap: the muscle should be of suitable size and thickness to cover the defect, within the arc of rotation for local transfer, and easily accessible; donor-site damage should be minimal; and muscle function must be either unimportant or maintained by a synergistic muscle.10 The transversus abdominis muscle flap was easily harvested and, with the base of the flap along the ventrodorsal length of the costal arch, was transposed into the diaphragmatic defect. An autogenous muscle flap was preferred in this case because of the immediate availability of a suitable muscle flap and the theoretical concerns of infection and adhesion formation with prosthetic materi-
als. However, prosthetic materials could have been used because no difference in long-term clinical function and outcome was detected in an experimental study that compared prosthetic (silastic sheeting and polytetrafluoroethylene) and autogenous techniques (thoracoabdominal muscle flap) for repair of large diaphragmatic defects in puppies. Polytetrafluoroethylene is the preferred prosthetic material for reconstruction of diaphragmatic defects in children, but was not readily available for the dog reported here.

Porcine SIS has been successfully used as a prosthetic material for reconstruction of diaphragmatic defects in rats, but has not been reported for this purpose in dogs or humans. The rationale for using porcine SIS was to minimize adhesion formation between abdominal organs and the deep exposed surface of the transversus abdominis muscle flap, which formed the abdominal side of the reconstructed hemidiaphragm. Porcine SIS was not used with the intention of supplementing the transversus abdominis muscle flap and subjectively did not appear to provide additional structural support to the reconstructed hemidiaphragm. Porcine SIS was not sutured over the thoracic side of the transversus abdominis muscle flap because adhesion formation between the mesothelial-lined peritoneal surface of the muscle flap and lungs was considered unlikely.

On the basis of clinical and radiographic findings, use of the transversus abdominis muscle flap was successful for reconstruction of the left hemidiaphragm. Transection of the left phrenic nerve during resection of the tumor would have resulted in unilateral diaphragmatic paralysis. Even with preservation of the phrenic nerve, paradoxical diaphragmatic motion has been observed for up to 8 weeks after diaphragmatic reconstruction with thoracoabdominal muscle flaps in puppies. However, unilateral diaphragmatic paralysis and paradoxical diaphragmatic motion do not adversely affect respiratory function, and there was no evidence of respiratory compromise in the present case. Necropsy was not permitted, but the reconstructed hemidiaphragm appeared intact via radiographic and ultrasonographic examination immediately prior to euthanasia. Similar results have been reported in children with hemidiaphragmatic agenesis and reconstruction of the defect with a combined internal oblique and transversus abdominis muscle flap, but herniation at the donor site of the muscle flap was a common complication. Herniation was not observed in the dog reported here, probably because the larger internal abdominal oblique muscle was preserved and the transversus abdominis muscle is unlikely to contribute substantially to the strength of the abdominal wall because of its size and location.

Adjunctive treatment options for malignant mesothelioma in humans include chemotherapy, radiation, and novel biologic and targeted therapies. Response rates to single- and multiple-agent chemotherapy protocols are usually < 20%. Chemotherapy has not been specifically investigated in the treatment of canine mesothelioma, but phase II trials of doxorubicin and mitoxantrone have revealed responses in a limited number of dogs with mesothelioma. Irradiation and alternative therapies have not been reported in dogs with mesothelioma. Adjunctive therapy was not attempted in the present case because of the solitary rather than diffuse distribution of the mesothelioma, rarity of distant metastasis in dogs with mesothelioma, and difficulty in establishing a definitive diagnosis.

References