A 5-year-old sexually intact male Giant Schnauzer was brought to the emergency service because of signs of lethargy, difficulty breathing, and left pelvic limb swelling. Eighteen months previously, the patient had had intermittent left pelvic limb swelling, but the owner declined further testing at that time.

Clinical Findings—Physical examination revealed severe pitting edema of the left pelvic limb and prepuce and muffled heart sounds on thoracic auscultation. Results of thoracic radiography and thoracocentesis were consistent with chylothorax, and CT imaging of the thorax and abdomen revealed a mass involving the whole left sublumbar area.

Treatment and Outcome—In an attempt to treat the chylothorax, pleural omentalization and pericardectomy were performed. Histologic evaluation of several biopsy specimens harvested in the abdominal and thoracic cavities revealed disseminated lymphangiosarcoma. The patient recovered well from surgery, and mitoxantrone chemotherapy was administered. As of 10 months after surgery, the dog was clinically normal except for mild pelvic limb edema.

Clinical Relevance—The combination of clinical signs, multiple imaging features, surgical findings, and histologic examination findings enabled the final diagnosis of lymphangiosarcoma. Clinical management that included medical and surgical treatments and chemotherapy resulted in improved quality of life and extended survival time in a dog with metastatic lymphangiosarcoma. (J Am Vet Med Assoc 2012;241:1639–1644)
extending from the caudal sublumbar region caudally to the left kidney cranially (Figure 1). This mass measured up to 7 cm at its largest axis. Lymphangiography was achieved by ultrasound-guided contrast medium injection in the left popliteal lymph node (1 mL/kg [0.45 mL/lb]; total volume of 35 mL, with approx 15% to 20% leakage in the subcutaneous space). Lymphatic vessels in the area of the thigh were abnormally numerous and tortuous. Cranially, the contrast medium did not reach the cisterna chyli and the thoracic duct. Injection of contrast medium was also attempted in the right popliteal lymph node. Although the needle tip was visible in the lymph node, severe leakage (approx 70% to 80%) occurred and no uptake was seen in the lymphatic vessels of the right pelvic limb.

Skin biopsy specimens were harvested from the erythematous inguinal lesions and from the edematous left tarsus. Prior to this procedure, prothrombin time and partial thromboplastin time were determined and were within reference limits. Microscopically, an atypical vascular lesion within the dermis was seen and was composed of spindle cells that were lining small irregular vascular spaces and clefts among the bundles of dermal collagen. The vascular spaces were largely empty, although some contained a few scattered erythrocytes. The spindle cells had hyperchromatic nuclei with mild anisokaryosis and no discernible mitotic figures. This vascular lesion was widespread within the dermis, toward the deeper aspect of the dermis. In the superficial dermis there was moderate dermal edema with mild perivascular dermatitis with lymphocytes, plasma cells, and eosinophils. These findings were consistent with a benign vascular lesion of lymphatic origin such as lymphangioma, lymphangiomatosis, or lymphatic malformation; however, a well-differentiated lymphangiosarcoma could not be ruled out.

In an attempt to treat the chylothorax, and to confirm the diagnosis by obtaining and histologically examining additional biopsy specimens, a surgical procedure was elected. After induction of general anesthesia, a midline ventral celiotomy was performed. On inspection of the abdominal cavity, a mass was observed in the left retroperitoneal region, surrounding the dorsal aspect of the left kidney cranially and extending to the sublumbar region caudally. The intestinal lymphatic vessels were visible and seemed enlarged throughout the entire jejunum. The rest of the abdomen appeared normal. An incisional biopsy of this mass was performed, and some chylous fluid flowed from the biopsy site. The retroperitoneal space was closed with a continuous suture pattern via a 3-0 absorbable suture material. The omentum was dissected as described by Stewart and Padgett, and a 1.5-cm incision was made into the pars costalis of the right side of the diaphragm. Approximately 1 L of thoracic chylous fluid drained from this incision and was aspirated. The augmented omentum was inserted into the diaphragmatic incision, and its base was tacked to the diaphragm with a 3-0 absorbable suture. The abdomen was thoroughly flushed with warm sterile saline (0.9% NaCl) solution and routinely closed. A right thoracotomy was performed at the level of the eighth intercostal space. A subphrenic pericardectomy was performed. The pericardium appeared thickened, and a moderate amount of effusion was present in the pericardial cavity. To allow a better observation of the caudal portion of the thoracic duct region, a second thoracotomy was performed at the level of the 10th intercostal space. A small irregular mass was seen in the dorsal aspect of the mediastinum along the aorta and the vagosympathetic trunk.

The latter mass measured approximately 1 cm in thickness and 2 cm in width; its length could not be assessed because only limited dissection was performed. Its macroscopic appearance was similar to the retroperitoneal mass. After dissection, the thoracic duct was not seen and seemed to be included with the abnormal tis-

![Figure 1](image-url)

**Figure 1**—Postcontrast lymphangiography transverse CT images of the abdomen obtained at the level of the left kidney (A) and urinary bladder (B) of a 5-year-old sexually intact male Giant Schnauzer evaluated because of lethargy, difficulty breathing, and left pelvic limb swelling; on thoracocentesis, pleural fluid was obtained that had cytologic and biochemical characteristics indicative of chylothorax. Notice the irregular mass (dashed line) that surrounds the left kidney (LK) and displaces the colon (C) ventrally. Notice the presence of contrast medium (arrows) in the renal pelvis, ureters, and urinary bladder (UB). Ao = Aorta, L = Left, VC = Caudal vena cava.
Three vascular clips were placed in this region, and the previously dissected area was closed with 3-0 absorbable suture. A 24F thoracic drain was placed. The thorax was lavaged with warm sterile saline solution, and both thoracotomy sites were closed routinely. After the surgery, the patient was hospitalized for 2 weeks, and no major complication occurred. Fentanyl (4 to 6 µg/kg/h [1.8 to 2.7 µg/lb/h], IV) and medetomidine (0.5 to 1 µg/kg/h [0.23 to 0.45 µg/lb/h], IV) constant rate infusions were used to provide an adequate analgesia. The thoracic drain was left in place throughout hospitalization, and the thorax was drained daily until hospital discharge. For 5 days following surgery, 2 L of serosanguineous fluid was withdrawn daily from the thoracic cavity. This amount decreased to 500 mL every other day at approximately 1 week after surgery and until drain removal. Electrolyte imbalances, hypoproteinemia, and hypovolemia caused by the frequent chest tube drainage were corrected by the administration of isotonic crystalloids and colloids. The abdominal mass, the thoracic mass, and the pericardium were sent for histologic examination. Histologically similar to the changes within the deep dermis of the skin, there were numerous spindle to cuboidal cells lining irregular small vascular spaces and clefts among the bundles of collagen (Figure 2). Neoplastic cells had mild cellular pleomorphism (anisocytosis and anisokaryosis), and no mitotic figures were observed. The vascular channels contained rare erythrocytes. Neoplastic cells had positive cytoplasmic immunoreactivity for both factor VIII-related protein and CD31 protein (Figure 3). On the basis of the histologic findings, immunohistochemical findings, and multicentric nature of the disease (cutaneous, abdominal, and thoracic involvement), the lesions were most consistent with a disseminated lymphangiosarcoma. The presence of chylothorax and pitting edema also strongly supported the diagnosis.

Three weeks after surgery, a chemotherapy protocol was started with IV administration of mitoxantrone at the initial dosage of 5 mg/m². The dose was subsequently decreased to 4.8 mg/m² because of the development of neutropenia (1.4 × 10⁹ neutrophils/L; reference range, 3 × 10⁹ neutrophils/L to 11.5 × 10⁹ neutrophils/L) that was detected a week after the first treatment and quickly resolved. Six treatments every 3 weeks were performed. The hematologic parameters were monitored before each treatment. Since the thoracic drain removal, no thoracocentesis was deemed necessary. Thoracic radiography was performed 2 months after the surgery and revealed a mild pleural effusion. However, the patient’s respiratory pattern was normal. Follow-up physical examinations were performed on a regular basis, but the owners declined recheck thoracic radiography. At 10 months after the surgery, the patient was still alive and did not have any abnormal clinical signs except for mild, persistent left pelvic limb and inguinal edema.

**Discussion**

Lymphangiosarcoma is a rare malignant tumor involving the lymphatic endothelial cells of humans²⁻⁵.
and domestic animals.6–11 In dogs, the clinical signs associated with this tumor are moderate to severe lymphedema, most frequently seen in the limbs, the ventral portion of the abdomen, or the neck.6,12–14 The presence of a subcutaneous mass has also been described in some reports.6,13,15 In a large proportion of the cases, dyspnea and exercise intolerance secondary to various degrees of pleural effusion are also seen as a reason for initial evaluation.6,9 Medium and large breeds seem to be affected more often, even if a breed predisposition has not been clearly identified.6,7,10–12,16

The differential diagnosis for this type of swelling includes both primary and secondary lymphedema. Secondary lymphedema could be associated with infection, trauma, neoplasia, foreign body, arteriovenous fistula, or any other type of secondary lymphatic or venous obstruction.6,10,11 On the other hand, primary lymphedema occurs as a result of a lymphatic dysplasia, resulting in poor lymphatic drainage. Patients with primary lymphedema have dilated nonfunctional lymphatic vessels and sometimes absent or hypoplastic popliteal lymph nodes.10,11,13 Although this is a congenital disease, clinical signs can arise relatively late in life.5,13

The biological behavior of lymphangiosarcoma has not been clearly understood in veterinary patients.7 In most of the cases reported, the tumor develops in the areas having been lymphedematous for a long period of time.9,12,13 This suggests that the presence of a protein-rich chylous fluid, the chronic mechanical pressure on the lymphatic endothelium, or a combination of both may be a trigger for neoplastic transformation.6,11 In humans, lymphangiosarcoma appears to be an aggressively malignant tumor, with an overall prognosis considered poor to extremely poor.2–5 In dogs, the tumor is considered a highly malignant tumor, with an overall prognosis considered poor to extremely poor.2–5,12,13

In human patients, lymphangiosarcoma is known to arise secondary to chronic lymphedema, especially in the axillary region after radical mastectomy in women (Stewart-Treves syndrome).2–7,10,11 Some veterinary reports9,12,13 describe the presence of a chronic lymphedema lasting for long periods before the diagnosis of lymphangiosarcoma is made. In the dog of the present report, pelvic limb lymphedema was observed 18 months before the acute onset of dyspnea and eventual diagnosis, leading us to believe that lymphangiosarcoma developed secondary to chronic lymphedema. Although the primary cause of the pelvic limb swelling was originally not investigated at the first evaluation, a primary lymphedema was highly suspected. Moreover, the tortuous aspect of the lymphatic vessels identified on CT strongly supports this hypothesis. One report described an acute onset of edema in a patient with lymphangiosarcoma. This suggests that the lymphedema could be in fact secondary to the tumor.6 Therefore, it is not always clear whether the edema is a cause or a consequence of the tumor in affected dogs.6

Final diagnosis of lymphangiosarcoma can be made on the basis of histologic examination of skin biopsy specimens taken from the edematous area6,9 or from any other abnormal tissue found during surgical exploratory or necropsy.7,9 Histologic evaluation of skin biopsy specimens has been proven to be an effective diagnostic tool for this type of tumor.2,4,5 It should therefore be considered in the evaluation of dogs with acute or chronic lymphedema.

Histologically, it can be difficult to differentiate tumors arising from the lymphatic endothelium from those arising from vascular endothelium such as hemangiosarcoma. The presence of neoplastic endothelial cell–lining channels, stromal edema, and lymphocytic proliferation with lack of erythrocytes within the vascular spaces seem to be consistent features of lymphangiosarcoma.5–9,12,17 Immunohistochemical staining can be used to confirm the endothelial origin of the tumor cells. The factor VIII–related antigen and CD31 protein are commonly used, and the distribution and intensity of the stain are evaluated. When immunohistochemistry with factor VIII–related antigen is performed, neoplastic lymphatic endothelium usually will have a light to moderate staining intensity, and the distribution will be patchy, whereas neoplastic vascular endothelium will have a more intense and uniform staining pattern. Neoplastic lymphatic endothelial cells usually maintain expression of CD31 protein similar to neoplastic vascular endothelium. Recently, monoclonal antibodies against vascular endothelial growth factor receptor-3 have been used in human medicine as a new specific marker for lymphatic endothelial cells.7 In the near future, this medical advance could help in the distinction between lymphatic and vascular cells in affected dogs. In some reports,12,13 lectin histochemical staining has also proved beneficial in the phenotypic characterization of cells. In the dog of the present report, histologic findings, positive immunoreactivity for factor VIII–related protein and CD31 protein, and clinical characteristics of the disease led to diagnosis of lymphangiosarcoma. Further immunohistochemical testing was not considered necessary.

In affected humans, because of the rarity of the tumor, no therapeutic guidelines have been established. The treatment is usually based on radical ablative surgery, chemotherapy, radiotherapy, or a combination of these.2–5 Because most dogs with lymphangiosarcoma are euthanized because of the guarded prognosis, only limited information about treatment options are available. Waldrop et al12 described a pulmonary lymphangiosarcoma associated with a chylothorax, which failed to respond to medical management and was treated with thoracic duct ligation; the patient was euthanized 6 days after surgery because of lack of clinical improvement. In another report,7 surgical excision of a localized mass, in conjunction with doxorubicin administration (20 mg/m2, IV, over 45 minutes, q 3 wk, repeated 4 times), was an effective treatment of lymphangiosarcoma in a dog; no recurrence or distant metastases were seen for 10 months after remission. Surgical excision of a single subcutaneous lymphangiosarcoma without chemotherapy has also been described in a dog, and no recurrence was seen 8 months after surgery.13 However, as opposed to the dog of the present report, both tumors described in the other reports8,13 were localized, thus making them best suitable for a surgical resection.
Adjuvant chemotherapy was used in the dog of the present report because of the metastatic nature of the tumor. Mitoxantrone is a synthetic antitumor antibiotic, which has been successfully used in dogs and cats. Its tolerability in dogs is good at the recommended dosage, and the main adverse effects of this drug are myelosuppression and gastrointestinal disorders. Unlike doxorubicin, mitoxantrone also seems to be free of cardiotoxic effects.6,22,24 Some tumors like lymphoma and tumors of epithelial origin respond to this chemotherapy agent, and it has also been described for the treatment of some sarcomas in dogs.23–25 To our knowledge, only 2 cases of lymphangiosarcoma in dogs treated with chemotherapy have been described for the veterinary literature. These 2 reports18,17 described a doxorubicin or doxorubicin derivative protocol for the treatment of localized lymphangiosarcoma, incompletely excised in surgery. No recurrence or distant metastases were seen for 9 months after remission in one dog,9 and the other dog17 also had substantial clinical improvement. Although a good response to treatment of lymphangiosarcoma with doxorubicin has been described for humans2 and dogs,6,17 doxorubicin has the potential to cause tissue damage with extravasation.20 Because the dog of the present report continued to have a degree of pleural effusion and subcutaneous edema, mitoxantrone appeared to be a safer choice; the only adverse effect observed was moderate neutropenia, which only required minor adjustment of the dosage.

Chylothorax is the accumulation of chylous fluid in the pleural cavity. Even if it was initially thought to occur as a result of a traumatic thoracic duct tear, leakage of chyle through an intact but dilated duct seems to be more frequently seen in veterinary medicine.16,20 Various etiologies have been described and include heart disease (pericardial effusion, heartworm, and cardiomyopathy), neoplasia (involving the thoracic wall, the lymphatic vessels, or the mediastinum), lung lobe torsion, fungal granuloma, or venal cava thrombosis. In most cases, even with a complete diagnostic workup, the cause remains unknown, and the chylothorax is considered idiopathic.1,16,26–29 Chylothorax has previously been described for affected dogs with disseminated lymphangiosarcoma.27 Although the surgical treatment of idiopathic chylothorax usually consists of thoracic duct ligation and pericardectomy, with or without adjunctive procedures such as pleural ontalization,1,17–20,31–33 it is not known whether such procedures could be an effective method for the treatment of a chylothorax associated with lymphangiosarcoma. However, it is the authors’ feeling that the dog of the present report benefited from surgery. The corrosive effect of the chyle on the pericardial sac could eventually lead to the development of a restrictive pericarditis. An increase in venous pressure could result from this and then worsen the accumulation of chyle into the pleural cavity.31 Pericardectomy is performed as a means to break this vicious circle. In the dog of the present report, the pericardium appeared thickened, and the echocardiography revealed collapse of the right atrium. Moreover, the myocardial motility appeared subjectively improved after pericardectomy. The role of pleural omentalization in the treatment of chylothorax is unclear. According to some authors,1,20 the omentum could serve as a physiologic drain to prevent further chyle accumulation, and it also could be a source of neovascularization helping in thoracic duct healing. For the dog of the present report, surgery was used as both a diagnostic and a therapeutic tool. Indeed, it allowed the harvesting of several biopsy specimens and also apparently helped in treating the chylothorax. Although accurate thoracic duct ligation was impossible because of the presence of a mediastinal mass, pericardectomy and pleural omentalization were most likely helpful in preventing chylous effusion recurrence.

References