# What Is Your Diagnosis?

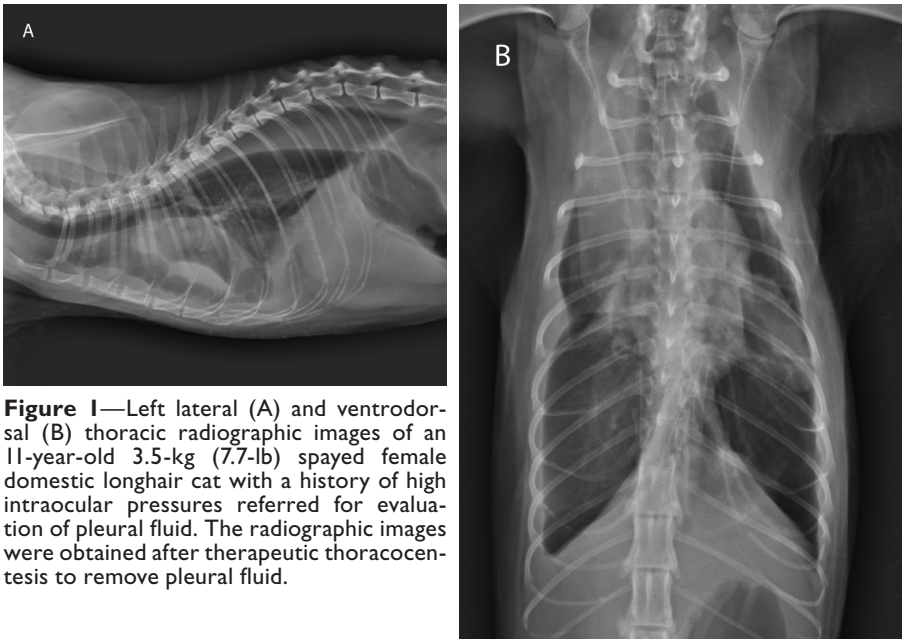


**Figure 1**—Left lateral (A) and ventrodorsal (B) thoracic radiographic images of an 11-year-old 3.5-kg (7.7-lb) spayed female domestic longhair cat with a history of high intraocular pressures referred for evaluation of pleural fluid. The radiographic images were obtained after therapeutic thoracocentesis to remove pleural fluid.

## History

An 11-year-old 3.5-kg (7.7-lb) spayed female domestic longhair cat was referred for evaluation of pleural fluid, which was discovered (thoracic radiography followed by thoracocentesis) at an emergency center on the previous day when the cat was examined because of a 1-day history of respiratory distress characterized by open-mouth breathing. Two weeks previously, the cat had been evaluated by the referring veterinarian because the owner noticed that the cat had decreased activity and seemed to show signs of discomfort in the areas of its pelvis and tail base. Tramadol was prescribed, laser treatment was performed on 3 separate days, and the cat was given an injection of methylprednisolone on the third day. In addition, on the third day of laser treatment, the cat's left eye was noticed to have been discolored and weeping; therefore, a fluorescein stain test was performed but revealed no uptake of stain. The cat was prescribed a course of 0.1% dexamethasone eye drops. Five days later, the cat had not improved and was returned to the referring veterinarian. The cat's intraocular pressure measurements were 36 mm Hg (reference range, 15 to 20 mm Hg) in both eyes, and 0.5% timolol ophthalmic solution was prescribed.

On referral examination, the cat was obtunded, laterally recumbent, and moderately dehydrated (approx 7% to 8% on the basis of a prolonged skin tent and tacky mucous membranes). The cat had a heart rate of 200 beats/min, respiratory rate of 24 breaths/min, and rectal temperature of 37.3°C (99.1°F; reference range, 36.7°C to 39.1°C [98.0°F to 102.4°F]). A grade 3/6 left sternal systolic heart murmur was detected on thoracic auscultation, and femoral pulses felt clinically normal to slightly weak bilaterally. The cat's left eye had a moderate amount of mucopurulent discharge and a corneal rupture ventromedially with the iris protruding. Abnormal results on a CBC and serum biochemical analyses included lymphopenia (665 lymphocytes/µL; reference range, 1,500 to 7,200 lymphocytes/µL), thrombocytopenia (96,000 platelets/µL; reference range, 200,000 to 700,000 platelets/µL), anemia (PCV, 28%; reference range, 30% to 48%), hyponatremia (143.7 mmol/L; reference range, 148 to 159 mmol/L), hypochloremia (107.7 mmol/L; reference range, 114 to 127 mmol/L), hyperglycemia (232 mg/dL; reference range, 70 to 160 mg/dL), hypermagnesemia (3.3 mg/dL; reference range, 1.9 to 2.6 mg/dL), hypoproteinemia (6.1 g/dL; reference range, 6.5 to 8.4 g/dL), high BUN concentration (47 mg/dL; reference range, 10 to 40 mg/dL), high total bilirubin concentration (0.6 mg/dL; reference range, 0.1 to 0.5 mg/dL), high creatine kinase activity (285 U/L; reference range, 50 to 225 U/L), and an albumin-to-globulin ratio (A:G) of 0.6 (suspicion for feline infectious peritonitis [FIP] is heightened when A:G is < 0.8[1]). Thoracocentesis yielded approximately 40 mL of straw-colored fluid, and a sample of the collected fluid was submitted for analyses. Our primary differential list for the pleural fluid included exudate, chyle, modified transudate, neoplastic effusion, and transudate. Thoracic radiography was performed **(Figure 1)**.

**Formulate differential diagnoses and treatment strategies from the history, clinical findings, and Figure 1—then turn the page →**

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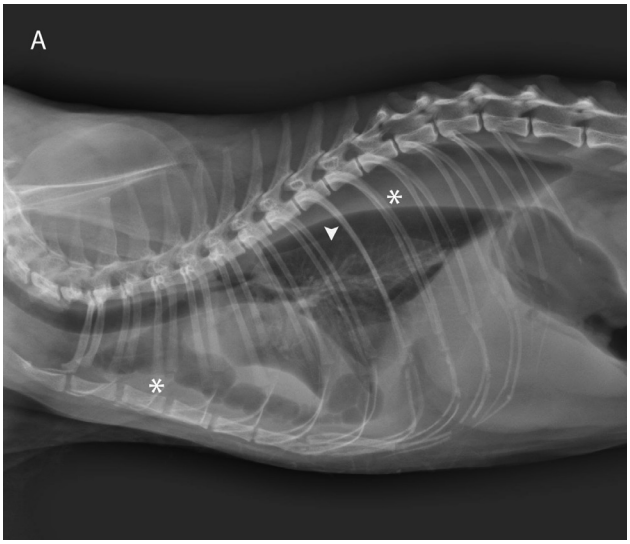


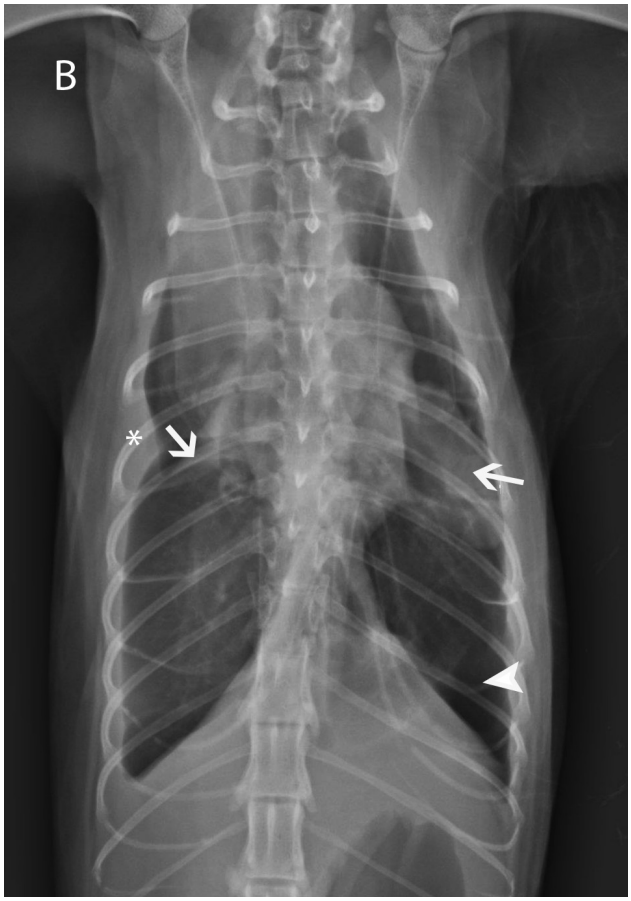


**Figure 2**—Same radiographic images as in Figure 1. Pleural fluid (asterisks) is evident bilaterally. Free gas is also present bilaterally in the pleural space (more severe on the left), and there is retraction of lung lobes from the thoracic wall (arrowheads). In the mid regions of the thorax bilaterally, there are multiple areas of homogeneous soft tissue opacity (arrows; B), consistent with atelectasis, trapped pleural fluid, or a multifocal alveolar pulmonary pattern.

## Diagnostic Imaging Findings and Interpretation

Thoracic radiography revealed a moderate volume of free gas bilaterally within the pleural space but more severe on the left **(Figure 2)**. There was also a moderate volume of pleural fluid causing border effacement of the cardiac silhouette and diaphragm bilaterally. The lung lobe margins were retracted from the thoracic wall. There was a focal region of homogeneous soft tissue opacity that caused focal border effacement of the cardiac silhouette in the right and left mid thoracic regions. These focal regions of homogeneous soft tissue opacity may have been caused by atelectasis secondary to pleural fluid and pneumothorax, trapped pleural fluid, or multifocal alveolar disease from bronchopneumonia, pulmonary edema, or neoplasia. Pneumothorax was likely secondary to the recent thoracocentesis.

Following radiography, results of pleural fluid analyses were received and indicated a predominantly neutrophilic exudate. Given the combination of physical, radiographic, ocular, and clinicopathologic findings, the primary diagnosis was the wet form of FIP. Ascites and less likely pleural effusion with a yellow-tinged fluid that has high protein concentration and low cellularity are considered pathognomonic for FIP.[1,2] Three-view abdominal radiographs (not shown) were obtained to assess whether there was abdominal evidence of FIP and revealed diffuse hepatomegaly, consistent with hepatitis, hepatic lipidosis, or neoplasia.

Echocardiography was performed to assess cardiac function and to rule out underlying cardiac disease as a cause for pleural fluid. Although echocardiography was difficult because of reverberation artifact caused by gas in the pleural space, mild thickening of the left ventricular free wall and interventricular septum was identified. Consideration for this mild thickening was given to pseudohypertrophy secondary to hypovolemia or mild hypertrophic cardiomyopathy. Because of the cat's unstable condition, CT was not performed at this point.

## Treatment and Outcome

Results of pleural fluid analysis indicated an exudate with primarily nondegenerate neutrophilic inflammation and a lower number of macrophages. Erythrophagocytosis was occasionally seen. No atypical cells or etiologic agents were found. A Grocott methenamine silver stain was used to evaluate the fluid, and no filamentous bacteria or fungi were seen. With this result added to all the previous findings, FIP was the working diagnosis. Because of the poor prognosis associated with FIP, the owners elected euthanasia and necropsy for the cat.

On necropsy, the superficial cervical lymph nodes were markedly enlarged, and a well-demarcated, pale, firm nodule (approx 3 X 2 X 2 cm) was identified in the left quadriceps muscle. The pleural space contained approximately 50 to 75 mL of red-tinged, clear, watery

fluid. There were fibrinous attachments between the visceral and parietal pleura, and there were multifocal to coalescing, widely disseminated, raised, pale white nodules present along the parietal and mediastinal pleurae. The caudal subsegment of the left cranial lung lobe was pale and firm and had a dark red center that sank in neutral-buffered 10% formalin. The remainder of the lung fields were dark red with small, multifocal nodules, through several of which the cut edge of the submitted sample transected.

On histologic examination, most cells in the lungs were anaplastic; however, some more differentiated neoplastic cells were present. Anaplastic neoplastic cells of similar appearance were also noticed on the parietal pleura, in the cerebrum, left ventricle of the heart, and anterior portion of the left eye, extending from the drainage angle through the cornea and Descemet membrane. The final histologic diagnosis was pulmonary bronchial adenocarcinoma with pleural carcinomatosis and metastases to the brain, muscles, lymph nodes, and left eye.

## Comments

Pulmonary bronchial adenocarcinoma may be suspected when there is radiographic evidence of a mass-like structure in the lung fields; however, cytologic or histologic examination is needed to confirm the diagnosis.[3–6] In the cat of the present report, there were no distinct pulmonary masses or nodules on thoracic radiographic examination, making antemortem diagnosis difficult. Adenocarcinoma accounts for 70% to 80% of all primary pulmonary tumors in dogs and cats.[3,7,8] Often, clinical signs relate to lameness associated with metastatic disease; however, dyspnea, coughing, or exercise intolerance can also occur,[4] as with the cat of the present report. Lung-digit syndrome occurs when a primary pulmonary adenocarcinoma metastasizes to a digit,[6,9,10] and lameness may be the first clinical sign, with discovery of a pulmonary mass on subsequent thoracic radiographic examination. Fine-needle aspiration of the lung mass and digital swelling, collection of thoracic fluid, or bronchoalveolar lavage can be performed to help obtain a diagnosis. Typically, once cats show clinical signs or bronchial adenocarcinoma is diagnosed, the mean survival time ranges from several weeks to several months, depending on tumor differentiation.[4,7,9] The mean survival time following surgical removal of the tumor may be approximately 115 days, if the tumor is diagnosed and treated early.[4,6,9] Treatment options that might prolong the life of affected cats are typically limited to surgical or medical intervention, with poor results owing to the declining health of the patient.[4,6] Surgical removal of the tumor burden can be attempted, but some portions of the tumor may be left behind if it is located too close to the hilus or if margins would be difficult to obtain.[3,9] Often, micrometastases will have already occurred before a large mass is observed, and these micrometastases are left behind when the large mass is surgically removed.[4,6,9] Computed tomography may be useful in determining prognosis because it is more sensitive for identifying metastasis than is radiography.[11] Although lymphatic micrometastases are common in certain types of pulmonary neoplasia in humans,[12] the incidence in cats is unknown; however, tracheobronchial lymph node enlargement with metastatic disease has been reported in cats.[4,8,13] Radiation therapy can be used when surgical removal of pulmonary adenocarcinoma is not attempted or is ill-advised for the patient.[9] The mainstay of treatment for people with non–small cell lung carcinoma is radiation and chemotherapy with or without surgical intervention.[14] Chemotherapy is better at limiting the spread of the tumor burden than reducing the size of the original tumor but can be used alone or for palliative treatment in cats when radiation therapy is not used.[9] Combination treatment with multiple chemotherapeutic drugs can be used and may yield higher response rates than use of a single chemotherapeutic drug protocol, but prolonged survival time may not be achieved.[9]

Thoracic radiographic findings of abnormal soft tissue opacities, as seen in the cat of the present report, can create a high index of suspicion for a primary pulmonary tumor; however, further evaluation is needed to rule out atelectasis, bronchopneumonia, thromboembolism, or a primary tumor of a different location.[6,8,11] Pulmonary adenocarcinoma is most commonly found in the caudal lung fields,[4,5,13] which was not the case in the cat of the present report. In addition, because of metastatic disease, signs of other conditions (eg, ocular disease and lameness) may develop.[3,6,10] The cat of the present report exemplified this because it was examined for clinical signs associated with pleural fluid, respiratory difficulties, and ocular changes. Thoracic radiographic examination was essential in identifying abnormal soft tissue opacities and pleural fluid in the cat of the present report; however, cytologic examination of a sample of the pleural fluid did not reveal carcinomatosis but a predominant neutrophilic exudate. In addition, the cat's A:G was 0.6, and A:G values < 0.8 are suggestive of FIP.[1] Thus, our working diagnosis prior to necropsy was the wet form of FIP.

Pleural effusion, as radiographically evident in the cat of the present report, occurs in 35% to 65% of cats with pulmonary adenocarcinoma and is a negative prognostic indicator.[8,9,11,13,15] Pleural effusion is typically present when the tumor has invaded the blood or lymphatic vessels associated with the pulmonary system or through the pleural surface of the lung and into the pleural cavity.[1] Pleural carcinomatosis is difficult to diagnose by cytology, as we encountered with the cat of the present report, because the neoplastic cells typically resemble either reactive mesothelial cells or epithelial cells with cytoplasmic basophilia, and substantial inflammation associated with the tumor can cause mesothelial cells to become dysplastic. Characteristics of pleural fluid in cats with FIP are typically diagnostic of the disease, and the cat

of the present report had pleural fluid with characteristics (ie, having a high protein concentration and with nondegenerative neutrophils with occasional macrophages present) similar to those typical with FIP.[1,2] Findings in the cat of the present report are interesting because, although the final histologic diagnosis was pulmonary bronchial adenocarcinoma with pleural carcinomatosis and metastases to the brain, muscles, lymph nodes, and left eye, the clinical signs and results of diagnostic evaluations mimicked those of FIP. Although results of ancillary diagnostic procedures pointed toward FIP, radiography identified pulmonary changes that were later identified on necropsy as pulmonary bronchial adenocarcinoma.

## Acknowledgments

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## References

1. Rebar AH, Thompson CA. Body cavity fluids. In: Raskin RE, Meyer DJ, eds. *Canine and feline cytology.* 2nd ed. St Louis: Saunders Elsevier, 2010;171–191.
2. Pedersen NC. An update on feline infectious peritonitis: diagnostics and therapeutics. *Vet J* 2014;201:133–141.
3. Moulton JE, von Tscharner C, Schneider R. Classification of lung carcinomas in the dog and cat. *Vet Pathol* 1981;18:513–528.
4. Hahn KA, McEntee MF. Prognosis factors for survival in cats after removal of a primary lung tumor: 21 cases (1979–1994). *Vet Surg* 1998;27:307–311.
5. Petterino C, Guazzi P, Ferro S, et al. Bronchogenic adenocarcinoma in a cat: an unusual case of metastasis to the skin. *Vet Clin Pathol* 2005;34:401–404.
6. Sandmeyer LS, Cosford K, Grahn BH. Metastatic carcinoma in a cat. *Can Vet J* 2009;50:95–96.
7. Langlais LM, Gibson J, Taylor JA, et al. Pulmonary adenocarcinoma with metastasis to skeletal muscle in a cat. *Can Vet J* 2006;47:1122–1123.
8. Nunley J, Sutton J, Culp W, et al. Primary pulmonary neoplasia in cats: assessment of computed tomography findings and survival. *J Small Anim Pract* 2015;56:651–656.
9. Clements DN, Hogan AM, Cave TA. Treatment of well-differentiated pulmonary adenocarcinomas in a cat with pneumonectomy and adjuvant mitoxantrone therapy. *J Feline Med Surg* 2004;6:199–205.
10. Gottfried SD, Popovitch CA, Goldschmidt MH, et al. Metastatic digital carcinoma in the cat: a retrospective study of 36 cats (1992–1998). *J Am Anim Hosp Assoc* 2000;36:501–509.
11. Aarsvold S, Reetz JA, Reichle JK, et al. Computed tomography findings in 57 cats with primary pulmonary neoplasia. *Vet Radiol Ultrasound* 2015;56:272–277.
12. Verhagen AF, Bulten J, Shirango H, et al. The clinical value of lymphatic micrometastases in patients with non-small cell lung cancer. *J Thorac Oncol* 2010;8:1201–1205.
13. Ballegeer EA, Forrest LJ, Stepien RL. Radiographic appearance of bronchoalveolar carcinoma in nine cats. *Vet Radiol Ultrasound* 2002;43:267–271.
14. Osmani L, Askin F, Gabrielson E, et al. Current WHO guidelines and the critical role of immunohistochemical markers in the subclassification of non-small cell lung carcinoma (NSCLC): moving from targeted therapy to immunotherapy. *Semin Cancer Biol* 2018;52:103–109.
15. Maritato KC, Schertel ER, Kennedy SC, et al. Outcome and prognostic indicators in 20 cats with surgically treated primary lung tumors. *J Feline Med Surg* 2014;16:979–984.

**Correction: A minimally invasive surgical technique for ureteral ostioplasty in two fillies with ureteral ectopia**

In the article "A minimally invasive surgical technique for ureteral ostioplasty in two fillies with ureteral ectopia" (*J Am Vet Med Assoc* 2018;253:1467–1472), a reference was omitted in the first sentence of the seventh paragraph of the Discussion section. The sentence should read as follows: Ureteral ostioplasty performed in dogs involves cystoscopy-guided laser ablation of the tissue separating the intramural portion of the ureter from the urethra and bladder[24,25,38] because the size of the urethra prohibits introduction of additional laparoscopic instruments. The omitted reference is reference 38 and should read as follows:

38. McCarthy TC. Transurethral cystoscopy and diode laser incision to correct an ectopic ureter. *Vet Med* 2006;101:558–559.