

LUNG ADENOCARCINOMA AS A CAUSE OF SPONTANEOUS PNEUMOTHORAX IN A CAT

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Abstract

A 15-year-old indoor/outdoor female, neutered, domestic European short haired cat was presented to our clinic with a history of neck-elongation and wheezing during inspiration/expiration. The first signs of respiratory disease occurred two weeks before the clinical presentation. After taking of clinical history, clinical examination and basic laboratory tests (complete blood count, blood smear, snap Feline Immunodeficiency Virus / Feline Leukemia Virus Combo test), a lung x-ray was performed showing the presence of left lung atelectasis and pneumothorax. The primary causes of lung atelectasis were not determined. Given that the general condition of the cat was very bad, she was put in an oxygen cage, thoracocentesis was performed, but the animal's condition did not improve, and 24 hours after clinical presentation, the cat died. Autopsy revealed the presence of a tumor mass on the caudal lobe of the right lung, tumor formation in the area of trachea bifurcation and changes in the liver in the form of four round structures of different sizes. Histopathologically, the existence of primary undifferentiated lung adenocarcinoma with metastases on the liver and trachea was determined.

Key words: cats, lung adenocarcinoma, metastasis, pneumothorax

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CASE PRESENTATION

A 15-year-old indoor/outdoor female, neutered, domestic short haired European cat, 3.55kg, irregularly vaccinated, was presented to the Small Animal Teaching Hospital at the Faculty of Veterinary Medicine University in Belgrade, Serbia with a history of shortness of breath, weight loss, intolerance to movement, and breathing with an outstretched neck and hiss. The first pronounced clinical signs of respiratory tract disease were noticed by the owner two weeks before clinical presentation, and pronounced weakness with suffocation appeared two days before presentation. No cough was noticed. Prior to the onset of the clinical signs of the disease, the cat was not ill. On clinical examination, the cat showed general weakness, depression, pale mucous membranes, prolonged skin tent time (5-6% dehydration), capillary refill time 2-3 sec, rectal temperature 37.7 °C, and difficult abdominal breathing with the neck outstretched during inspiration and expiration. Auscultation of the trachea registered a whistle and zero respiration on the left chest side. During the blood sampling, the cat went into respiratory distress, so the procedure was interrupted and the minimal amount of blood was taken for hematological examination.

Hematological analyses. Complete blood count (CBC) and blood smear examination revealed leukocytosis $23.38 \times 10^9/L$ (reference interval: $5.5-9.0 \times 10^9/L$) with neutrophilia and right shift $18.56 \times 10^9/L$ (reference interval $2.5-12.5 \times 10^9/L$). Mild microcytosis was present (RBC= $7.08 \times 10^{12}/L$ (RI= $5-10 \times 10^{12}/L$), HGB= $92g/L$ (RI= $80-150g/L$), HCT= 22.65% (RI= $24-45$), MCV= 32 fL (RI= $39-55\text{ fL}$)). There were no changes in platelet number or shape. The Snap FIV/FeLV (Feline Immunodeficiency Virus/Feline Leukemia Virus) Combo test (IDEXX®) was negative. After patient stabilization using the oxygen cage, and application of corticosteroids (prednisolone 1 mg/kg) and Ringer's solution, native thorax radiography was performed in two standard projections.

Radiological examination findings. On the radiograph of the latero-lateral (LL) projection of the thorax, a banded, sharply contoured, hypertransparent finger-width zone intersecting the caudal parts of the lung diaphragmatic lobes, following the flow of the diaphragm, was visible (Figure 1). The pulmonary parenchyma around the hilus and towards the diaphragm produced a segmental milky-white atelectasic shading of the tongue-like shape, with the base facing the diaphragm and the apex toward the hilus and from the dorsal side tangles the aortic arch. In the ventro-dorsal (VD) projection, the right hemithorax was enlarged and deepened due to unilateral air accumulation giving a wide hypertransparent field. In the narrowed left hemithorax, a homogeneous soft tissue zone was observed which, by giving the effect of mass, engaged the apical and cranial part of the diaphragmatic lobe, where linear shadows of dislocated interlobar sulci were poorly visible. In the left displaced mediastinum, the attraction of the hilus towards the atelectasic lobe and the peripherally positioned lungs gave the left hemithorax a soft-tissue shadow of uniform density that completely covered the silhouette of the heart.

Based on the x-ray, a diagnosis of secondary spontaneous pneumothorax (SSP) was made. Thoracocentesis was performed on the right side of the chest at the level of the 8th intercostal space (along the cranial edge of the 8th rib) and 45 ml of air was extracted, after which there was no improvement of the general condition. The cat was again put in an oxygen cage, but 24 hours after arriving at the clinic, the cat suddenly died. An autopsy was performed after the death.



Figure 1. X-ray views of pneumothorax in a 15-year-old cat. **A)** Latero-lateral view. Note the large volume of free gas and collapsed lung lobe; **B)** Dorsoventral view. Pneumothorax is worse on the right side.

Autopsy report. During the autopsy, 100 ml of clear, yellow fluid was found in the thoracic cavity and pleura, but no lesions or proliferation were observed. The left lung was grayish-yellow in color with a firm elastic consistency. At the intersection of the left lung, a lobular structure was observed from which a gelatinous yellow mass was displaced (Figure 2A). A white node 3 cm in diameter was observed on the surface of the right lung, with a firm elastic consistency on the caudal lobe (Figure 2B). The tracheal lumen in the area of bifurcation narrowed due to the existence of a neoplasm of gray color and firmly elastic consistency. A button probe could be inserted between the mucosa of the sulcus and the neoplasm in only one part of the jacket (Figure 2C). Four nodes of different size, white-gray in color, with a solid consistency clearly distinct from the liver parenchyma, were observed on the liver surface (Figure 2D).

Lung, tracheal and liver tissue specimens were used for histopathological examination. Tissue specimens 5 μ m thick were stained by the hematoxylin-eosin method. Tumor proliferation present in the tissue sections of the lungs and trachea corresponded morphologically to lung adenocarcinoma. Tumor proliferation was characterized by multiplied polymorphic cells of the glandular epithelium with frequent pathological mitoses (Figure 3). The tumor stroma was well developed and cholesterol crystal deposits were present in the tumor parenchyma. Tumor masses in the liver were clearly restricted from the liver parenchyma and indicated the adenocarcinoma in the liver was

a metastasis of the primary lung neoplasm. A purulent exudate composed of numerous neutrophil granulocytes and macrophages was also observed in the pulmonary alveoli.

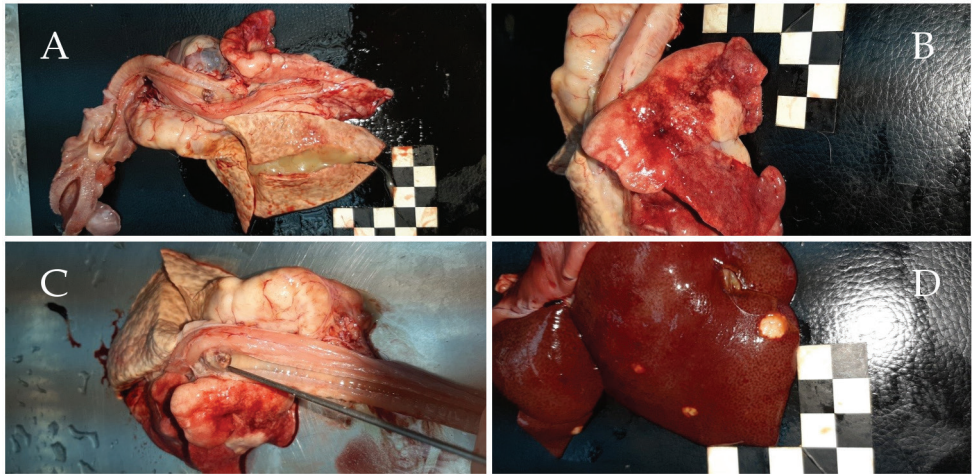


Figure 2. Lung of 15-year-old cat. **A)** gelatinic content at the intersection of the altered left lung; **B)** neoplastic node in the right lung; **C)** neoplasm on bifurcation of trachea; **D)** liver with neoplastic nodes in the parenchyma.

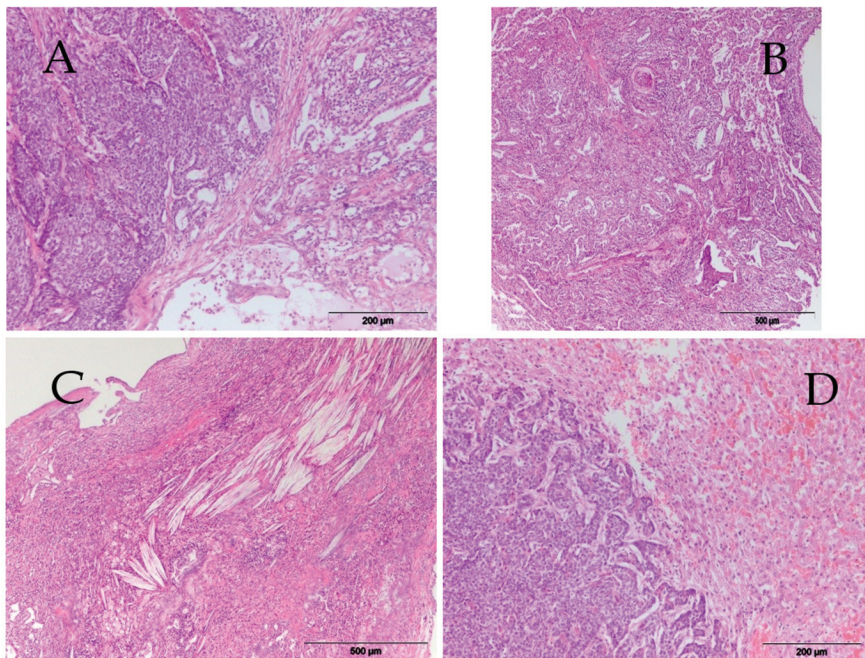


Figure 3. Tissue sections of adenocarcinoma (hematoxylin-eosin staining): **A)** in the left lung lobe; **B)** in the trachea; **C)** cholesterol crystal deposits in tumor mass; **D)** in the liver.

DISCUSSION

Cat lung adenocarcinomas are the most commonly isolated primary lung cancers in these animal species (Hahn and McEntee, 1997; Karl et al., 2014), but very rarely lead to spontaneous pneumothorax (SP). The greatest prevalence of primary lung adenocarcinoma was noted in elderly domestic European cats (Koblik, 1986; Hahn and McEntee, 1997; Nunley et al., 2015; Stacie et al., 2015), to which grouping our case also belonged. So far, only 10 cases of primary lung cancers leading to the occurrence of SSP in cats have been presented (Erin et al., 2012; Debra and Deborah, 2014; George et al., 2017) of which four were adenocarcinomas (Erin et al., 2012; George et al., 2017). In general, SP in cats is not a common finding, and to the authors' knowledge there are only three studies that have presented cases of cat pneumothorax (Erin et al., 2012; Debra and Deborah, 2014; George et al., 2017), and the rest are isolated cases. Pneumothorax is the accumulation of gas in the pleural space followed by the collapse of the lungs and can be classified as open or closed, and as traumatic, spontaneous or iatrogenic (Elisa, 2001; Erin et al., 2012). Traumatic pneumothorax is the most common cause of pneumothorax in dogs and probably in cats (Erin et al., 2012; Debra and Deborah, 2014). SP occurs in cases where there is no trauma in the patient history, but it remains of unclear pathogenesis, and can be primary (lung tissue is unchanged) or secondary (there is airways disease and or lung parenchyma). In cats, primary SP has not yet been documented (Debra and Deborah, 2014).

In this case, the cause of SSP was primary adenocarcinoma of the lung, which engulfed the entire left lung, and metastasis was observed on the caudal right lobe (the cat was in the terminal stage of the disease). Of the two reports showing cases of primary lung adenocarcinoma in cats with SSP, in one, the localization of adenocarcinoma was in the right lung (in one cat in the cranial and in the other in the medial right lobe) (George et al., 2017), while in the other report (Erin et al., 2012), the tumor localization was not described. Pulmonary adenocarcinomas are divided into undifferentiated and differentiated adenocarcinomas based on the histological differences and prevalence (Moulton et al., 1981), as undifferentiated adenocarcinomas are more common (Hahn and McEntee, 1997). Necrosis of the tumor mass with cholesterol clefts, calcification and secondary pneumonia are much more common in the undifferentiated form of adenocarcinoma (Hahn and McEntee, 1997), which was also observed in the current case. The undifferentiated form is much more aggressive and has a much greater tendency for metastasis, especially in the pleura and regional lymph nodes (Hahn and McEntee, 1997), toes (feline lung-digit syndrome) and other organs (Elizabeth et al., 2017; Yoko et al., 2018). In this case, metastases were registered intrathoracically, but on the right lung (caudal lobe) and trachea as well as extrathoracically on the liver. Based on the World Health Organization recommendation about the grading of primary lung tumors by the TNM system (Owen, 1981), this tumor was classified in the T2N0M1 category, indicating poor prognosis. The pronounced respiratory clinical signs lasted a relatively short time (two weeks) and the suffocation that was the main reason for the

clinical presentation was more related to the tumor metastasis in the trachea (causing obstruction of the tracheal lumen) than to the primary adenocarcinoma on the left lung. Such a relatively short course of disease in cats with primary lung adenocarcinoma is not uncommon, because clinical signs of lung disease usually occur at a late stage of the disease (Hahn and McEntee, 1998) or do not occur at all (Moore and Middleton, 1982; Nunley et al., 2015), so diagnosis of lung adenocarcinoma is usually made at autopsy, which was also the course of events in this case. Laboratory parameters (CBC and serum biochemical analyses) in the presence of a primary cat lung tumor may be unchanged (Hahn and McEntee, 1998), which was confirmed in this case as well, but there can be significant CBC and biochemical abnormalities (Hahn and McEntee, 1997). Pneumothorax can be the first clinical finding in lung cancer, and there are currently no molecular biomarkers for the prognosis of cat lung tumors (D'Costa et al., 2012). There was no evidence of an association between primary cat lung tumors and FIV and FeLV infection (Hahn and McEntee, 1997), which was also the status of our case. Also, we did not establish the existence of paraneoplastic syndrome, which corresponded with literature data (Hahn and McEntee, 1998; Erin et al., 2012; George et al., 2017). A disadvantage of this case report is the limited number of recommended diagnostic procedures (biochemical blood analyzes, bronchoalveolar lavage, CT examination) we conducted, because the patient was in a very bad general clinical condition that resulted in death 24 hours after clinical presentation.

Lung carcinomas in older cats can go unnoticed, as frequently, only general clinical signs occur (often attributed to age), so it is necessary to keep this in mind as part of the differential diagnosis to be taken into account in such cats. Statistics in cats with lung cancer indicate that cats in which a primary lung tumor was diagnosed prior to development of clinical signs were likely to have low -grade tumor and longer survival times (Karl et al., 2014). Also, in the case of x-ray findings of SSP in elderly animals, lung cancer should be differentially diagnosed, which involves the use of special testing methods (CT examination and alveolar lavage) if the clinical condition of the diseased cat permits. As the incidence of tumors increases, studies on the biomarkers of early diagnosis of lung cancer look promising in addressing this problem.

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Authors' contributions

NA, JFA data analysis and interpretation; manuscript writing; SN histological analysis and interpretation; NK radiological examination; data analysis and interpretation

Competing interests

The authors declare that they have no competing interests.

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ADENOKARCINOM PLUĆA KAO UZROK PNEUMOTORAKSA KOD MAČKE

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Kratak sadržaj

U ovom radu predstavljen je slučaj primarnog adenokarcinoma pluća kod domaće kratkodlake mačke stare 15 godina. Prvi znaci oboljenja respiratornog sistema pojavili su se dve nedelje pre dovođenja mačke na pregled, pri čemu su dominirali znaci disanja sa ispruženim vratom i šištanje tokom inspirijuma i ekspirijuma. Nakon uzimanja istorije bolesti, kliničkog i laboratorijskog ispitivanja (krvna slika, krvni razmaz, FIV/FeLV brzi dijagnostički test) urađen je rendgen pluća koji je pokazao postojanje atelektaze levog plućnog krila i pneumotoraks. Nije utvrđeno koji patofiziološki mehanizam je odgovoran za atelektazu pluća. S obzirom da je opšte stanje mačke bilo jako loše, stavljena je u kiseonički kavez, urađena je torakocenteza ali stanje se nije popravilo i 24h od dolaska na kliniku mačka je uginula. Na obdukciji je utvrđeno odstupanje od normalnog nalaza na levom plućnom krilu, postojanje promena na desnom plućnom krilu, tumorsna tvorevina u predelu bifurkacije traheje i promene na jetri u vidu četiri okrugle tvorevine različite veličine. Histopatološki je utvrđeno postojanje primarnog nediferentovanog adenokarcinoma pluća sa metastazama na već pomenutim organima.

Ključne reči: mačka, adenokarcinom pluća, metastaza, pneumotoraks