Lung cancers in dogs involve various paraneoplastic syndromes such as hypertrophic osteopathy, hypercalcemia, and multiple neuropathy [12]. In human lung cancers, marked leukocytosis, especially with neutrophilia and monocytosis, has been reported as a paraneoplastic syndrome. In dogs, several reports have been published on paraneoplastic leukocytosis. In this case, various examinations were conducted on a dog with extreme neutrophilic leukocytosis diagnosed via a blood test at first admission. A huge pulmonary mass was detected, which was surgically removed. The tumor was diagnosed as papillary adenocarcinoma of the lung by histopathology. The number of neutrophils recovered to normal after surgery, and the dog was diagnosed as paraneoplastic syndrome due to lung cancer.

Key word: dog, leukocytosis, lung cancer, paraneoplastic syndrome

Primary Lung Carcinoma with Paraneoplastic Leukocytosis in a Dog

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Abstract

In human lung cancers, marked leukocytosis, especially with neutrophilia and monocytosis, has been reported as a paraneoplastic syndrome. In dogs, several reports have been published on paraneoplastic leukocytosis. In this case, various examinations were conducted on a dog with extreme neutrophilic leukocytosis diagnosed via a blood test at first admission. A huge pulmonary mass was detected, which was surgically removed. The tumor was diagnosed as papillary adenocarcinoma of the lung by histopathology. The number of neutrophils recovered to normal after surgery, and the dog was diagnosed as paraneoplastic syndrome due to lung cancer.

Key word: dog, leukocytosis, lung cancer, paraneoplastic syndrome

Lung cancers in dogs involve various paraneoplastic syndromes such as hypertrophic osteopathy, hypercalcemia, and multiple neuropathy [12]. In human lung cancers, marked leukocytosis, especially with neutrophilia and monocytosis, has been reported as a paraneoplastic syndrome that occurs due to the production of granulocyte-colony stimulating factor (G-CSF) and/or granulocyte macrophage-colony stimulating factor (GM-CSF) from the cancer cells [3, 4, 6-8, 11, 14]. In dogs, there have been several reports published on paraneoplastic leukocytosis [1, 5, 9, 10, 13, 15, 16].

This report describes a case of a dog having lung adenocarcinoma with possible paraneoplastic leukocytosis. The patient was an 11-year-old male Shetland sheepdog. The chief complaint was coughing, but its appetite and activities were normal. Radiography and complete blood count (CBC) revealed a large single mass in the left thoracic cavity and severe neutrophilic leukocytosis. The patient received antimicrobial therapy with an anti-inflammatory drug for 2 months, but clinical signs did not improve.

The patient was referred to the Veterinary Teaching Hospital, at Azabu University. Upon admission, transient hematuria and diarrhea were observed, but they soon disappeared. Thoracic radiography revealed a large mass in the left caudal lung area that compressed and shifted the enlarged heart to the right (Fig. 1). Thoracic CT was not permitted by the client. Abdominal radiography showed an enlarged prostate, which appeared homogenous on ultrasonography and appeared to be benign prostatic hyperplasia without cystic formation. Auscultation revealed cardiac murmur of Levine 5/6 level. The echocardiography then revealed expansion of the left atrium and thickening of the mitral valve.

The results of CBC and blood chemistry are shown in Tables 1 and 2. At first admission, white blood cell (WBC) count was 112,000/μl and the neutrophil count was 106,070/μl (Fig. 2) with a slight increase in the monocyte count (3,250/μl). The blood urea nitrogen (BUN) level was elevated (75.7 mg/dl), but other parameters, including serum creatinine level,
were all within normal ranges. According to these results, we surmised that the elevated BUN level was prerenal secondary to cardiac insufficiency.

Based on these clinical data, the cause of the cough and the neutrophilia were considered to possibly be related to the thoracic mass. In order to improve the cough, thoracotomy was performed.

The patient underwent surgery through the intercostal approach on the 15th day after first admission. The 5th rib of the patient was removed due to the large size of the mass. The mass involved the left caudal lung lobe and adhered to the pleura of the mediastinum and diaphragm. The pericardium was not involved in the mass. Blunt dissection of the mass from the pleura of the mediastinum caused some bleeding. After blunt dissection from the adhered sites, the left lung lobe was totally removed with the mass. Swelling of the tracheobronchial lymph nodes was not observed.

The patient recovered from surgery without any events and showed good healthy conditions. The WBC count decreased to the normal range 2 weeks after surgery (Table 3) and was normal for 21 weeks after surgery. The patient’s cough disappeared after surgery, and the respiratory function of the patient was recovered. Furthermore, cardiac function was maintained well with the simultaneous administration of digoxin and an angiotensin converting enzyme inhibitor for cardiac insufficiency. However, cardiac function worsened, and 4 months after surgery, the patient had an increased BUN level. The patient showed collapse/syncope due to cardiac failure and died 5 months after surgery. Autopsy was not permitted by the client.

Histopathological examination of the pulmonary mass revealed that the tissue consisted of multiple neoplastic foci divided by various amounts of fibrous septa. The neoplastic foci were characterized by papillary or glandular structures that were lined by cuboid to cylindrical epithelial cells. Some tumor cells showed a goblet-cell appearance, while some had cilia on their cell surface. These proliferating neoplastic cells showed moderate cellular atypia, and the mitotic figure index was 2–3 per high-power magnification (×400) field. The tumor cells invaded the lymph vessels of the surrounding tissues. Multifocal necrotic areas were also observed within the neoplastic foci. In the interstitial areas, there were moderate infiltrations of lymphocytes and macrophages, deposition of calcium, and occasional ossification. The pleurae were
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Based on these findings, the mass was histopathologically diagnosed as a papillary adenocarcinoma of the lung. The vessels were invaded by tumor cells, and the margin at the pleural dissection site was not clear.

Lappin [9] reported that WBC count of his case decreased after surgery and returned to normal level within 1 week, and in our case, the neutrophil count drastically decreased to normal levels from the 2nd to the 21st week after surgery. In contrast, in a case with metastasis the WBC count did not decrease to normal level, in spite of surgery [15].

The clinical course and blood examination data revealed no bacterial or fungal infection, and the dog also had no coexisting hematological findings indicative of primary bone marrow disease. The prostate was enlarged, but that may have been due to benign hyperplasia.

Therefore, we tentatively diagnosed that this neutrophilic leukocytosis was of paraneoplastic origin.

In humans, paraneoplastic leukocytosis has been reported in various types of tumors [3, 4, 6–8, 11, 14]. However, only seven cases, including metastatic fibrosarcoma, rectal adenomatous polyps, renal adenocarcinoma, renal transitional cell carcinoma and papillary adenocarcinoma of the lung, have been reported in dogs [1, 5, 9, 10, 13, 15, 16].

In cats, lung squamous cell carcinoma and dermal tubular adenocarcinoma have been reported in two cases [2, 15]. In those cases, the relationship between G–CSF and GM–CSF production in tumor cells was discussed, but a direct demonstration was not performed. In humans, paraneoplastic leukocytosis may be used as a marker for assessing the effect of treatments and recurrence after complete remission [17].

Unfortunately, we were not able to demonstrate the presence of the factors described in the previous reports. However, we suggest that the extreme leukocytosis in this case was due to the lung tumor. This case had an unclear surgical margin, and recurrence may have been diagnosed based on the neutrophil count, if that could have been used as a recurrence marker. However, we could not demonstrate it due to the early death of the patient.

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<th>Table 1. Complete blood count results</th>
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<td><strong>RBC (/μl)</strong></td>
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<td><strong>Hb (g/dl)</strong></td>
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<td><strong>MCH (pg)</strong></td>
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<td><strong>PLT (/μl)</strong></td>
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<th>Table 2. Blood chemistry results</th>
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<td><strong>TP (g/dl)</strong></td>
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<td><strong>ALT (U/l)</strong></td>
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<td><strong>TCho (mg/dl)</strong></td>
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<th>Table 3. Change in CBC</th>
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<td><strong>First admission</strong></td>
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<tr>
<td><strong>WBC (/μl)</strong></td>
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<td><strong>Band (/μl)</strong></td>
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<td><strong>Seg (/μl)</strong></td>
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<td><strong>Eos (/μl)</strong></td>
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<td><strong>Bas (/μl)</strong></td>
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<td><strong>Others (/μl)</strong></td>
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References


腫瘍随伴性白血球増加症がみられた犬の肺癌の1例

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■ 和文要約

人の肺癌では、腫瘍随伴症候群として好中球増加症や単球増加症を伴う白血球増加症が報告されている。しかしながら、犬では腫瘍随伴性白血球増加症の報告は少ない。今回、初診時の血液検査にて好中球を主体とした白血球増加症を示した犬に対し、種々の検査を行った結果、巨大肺腫瘤を認め、肺腫瘤の摘出術を行った。術後の病理組織検査にて肺腺癌と診断されたが、腫瘍の摘出とともに劇的な好中球数の回復がみられ、肺癌による腫瘍随伴性白血球増加症と診断した。

Key word: dog, leukocytosis, lung cancer, paraneoplastic syndrome

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