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CASE REPORT
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Pulmonary Nodule in a Bitch - ^{18}FDG-PET/CT for Discriminating the Origin and Malignancy of the Lesion

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ABSTRACT

***Background*:** Lung cancer is the leading cause of cancer-related deaths in humans. In dogs and cats, lung cancer is also a notable cause of death, with metastatic lung cancer being more common than primary lung cancer in dogs. Differentiating benign from metastatic lung nodules is important because treatment plans can differ. Metastatic tumors are typically treated medically, whereas primary cancers and benign lung nodules are managed surgically. Advanced imaging techniques, such as ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography, enhance the detection and diagnosis of lung nodules. This case report aimed to describe the role of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography in identifying the origin of a lung nodule in a bitch.

***Case*:** A 11-year-old intact bitch Golden Retriever was referred for evaluation and surgical resection of a splenic mass. Ultrasonography identified a well-demarcated, round mass measuring 7.6 × 6.9 cm at the splenic tail, suggesting a malignant splenic tumor owing to its size and remarkable change in splenic contour. ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography was performed to assess the malignancy and metastasis of the splenic tumor, revealing a pulmonary nodule with increased ^{18}F-fluorodeoxyglucose uptake indicative of metastasis, which had not been detected on radiography. The maximum mean standardized uptake value of the abnormal lesions were as follows: splenic tail mass, 2.91 and 2.17; mammary gland mass, 5.22 and 3.81; and pulmonary nodule, 4.16 and 3.37, respectively. These results suggest possible inflammatory or malignant lesions in the mammary gland mass and pulmonary nodule. Based on the ^{18}F-fluorodeoxyglucose-positron emission tomography/computed tomography findings, if the pulmonary nodule resulted from metastasis, its origin was more likely to be a mammary gland mass rather than a splenic mass. Histopathology following splenectomy and mammary gland resection were performed at the owner's request, and the bitch was diagnosed with splenic hematoma and high-grade mammary basaloid ductular carcinoma with focal lymphatic vessel invasion, respectively. The animal died of dyspnea 4 months post-surgery.

***Discussion*:** This case report highlights the utility of ^{18}F-fluorodeoxyglucose- positron emission tomography/computed tomography for defining the origin of pulmonary lung nodules in dogs. The ^{18}F-fluorodeoxyglucose- positron emission tomography/computed tomography results provided critical information that influences diagnostic and treatment approaches. This case demonstrates the potential of ^{18}F-fluorodeoxyglucose- positron emission tomography/computed tomography as a diagnostic tool for providing information on tumor malignancy and origin. In addition, the integration of ^{18}F-fluorodeoxyglucose- positron emission tomography/computed tomography with computed tomography provides both anatomical and functional information, providing a comprehensive assessment superior to that provided by computed tomography alone. Future perspectives include further evaluation of ^{18}F-fluorodeoxyglucose- positron emission tomography/computed tomography in larger cohorts of veterinary patients to establish its role in routine clinical practice for diagnosing the origin and malignancy of canine lung lesions.

Keywords: metastatic lung cancer, ^{18}F-FDG, positron emission tomography, mammary gland tumor, splenic mass, canine mammary glands.

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INTRODUCTION

Although lung cancer is the principal cause of cancer-related deaths in humans, primary lung cancer is relatively rare in dogs and cats, with metastatic lung cancer being more common in veterinary medicine [16]. Differentiating benign lung nodules from metastatic lung tumors is critical [7]. Lung masses can be abscesses, granulomas, hematomas, septic emboli, parasitic granulomas, or metastatic tumors [14]. Benign lung nodules or primary lung tumors do not necessarily present as solitary masses, but can appear as multiple masses or in a disseminated form, making it difficult to differentiate them from metastatic lung cancer [9,10]. Metastatic lung tumors are usually treated using a medical approach, whereas primary lung cancers and benign lung nodules are treated by surgical excision [7]. Therefore, it is important to diagnose the origin and type of lung nodules. Diagnostic imaging, such as computed tomography (CT), can be used to evaluate nodules in more detail to determine the treatment plan [9]. However, the utility of CT is limited as it only provides anatomical details [5].

Recently, positron emission tomography (PET)/CT, an imaging modality that uses ^{18}F-fluorodeoxyglucose (FDG), has been widely applied in humans [3]. By combining CT and PET, integrated PET/CT is a promising tool for detecting small lung metastases [3]. Furthermore, PET/CT was used to determine malignancy based on the standardized uptake value (SUV) in a case that described a dog with multiple lung nodules [7].

This case report aimed to describe a case in which FDG-PET/CT was used to provide information on the origin of a lung nodule.

CASE

A 11-year-old intact bitch Golden Retriever was referred for evaluation and surgical resection of a splenic mass. No clinical signs were observed in the dog, and the dog's heart rate (105 beats/min), respiratory rate (36 breaths/min), rectal temperature (38.2°C), and systolic blood pressure (110 mmHg), as measured by Doppler, were normal. Two years prior to the examination, a mass of 2.8 × 2.2 cm in the left 5th mammary gland was 1st detected and was still confirmed in physical examination.

Complete blood cell counts revealed eosinopenia (0.02×10^3/μL, reference interval [RI] = $0.06\text{-}1.23 \times 10^3$/μL) and mild lymphocytopenia (0.95×10^3/μL, RI = $1.05\text{-}5.10 \times 10^3$/μL). Concurrent biochemical analysis revealed increased levels of alanine aminotransferase (150 U/L, RI = 21-102 U/L) and alkaline phosphatase (367 U/L, RI = 29-97 U/L).

Thoracic radiography revealed a mild-to-moderate bronchial pattern and bronchial mineralization (Figure 1A). On abdominal radiography, a round-shaped abdominal mass with a size of 8.7 × 8.9 cm was found (Figure 1B). Based on anatomical location, the mass was suspected to have developed in the spleen. Abdominal ultrasonography revealed a well-demarcated, round mass at the level of the splenic tail (Figure 1C). The mass deformed the contour of the spleen, and the parenchyma was moderately homogenously hyperechoic compared with the normal spleen. The mass measured at approximately 7.6 × 6.9 cm. Owing to its large size, changes in the contour of the spleen, and solitude, a malignant splenic tumor was highly suspected. Blood distribution in the mass could not be examined using abdominal ultrasonography because of poor patient compliance.

To identify metastasis and malignancy, a PET/CT (Discovery-72STE)[1] scan was performed under general anesthesia, and major vital signs were measured at 5-min intervals. FDG (0.14 mCi/kg)[2] was intravenously injected into the cephalic vein. Before PET, CT images (pre- and post-contrast) were obtained after FDG injection. PET scans were performed approximately 60 min after FDG injection. A commercially available image analysis program (OsiriX MD v10.0)[3] was used to analyze PET images. The mean and maximum SUVs (SUVmean and SUVmax, respectively) were used to quantitatively analyze FDG uptake. The following formula was used to calculate SUV: SUV = average tissue concentration of FDG (MBq/mL)/total injected dose (MBq)/body weight (g).

SUV was measured to determine splenic malignancy. The size of the mass was 8.5 × 7.5 cm, and the SUVmean and SUVmax were 2.17 and 2.91, respectively (Figure 2A-C). These values were above the RI of the normal spleen (SUVmean, 1.16 ± 0.22; SUVmax, 1.56 ± 0.27) [2]; however, these results alone were insufficient to determine the malignancy of the splenic mass. In the left inguinal region, where the mass in the mammary gland was identified, a lesion measuring 3.9 × 1.8 cm with an SUVmean of 3.81 and an SUVmax of 5.22 was detected (Figure 2D-

F). These 2 SUVs were higher than the RI of normal mammary gland (SUVmean, 0.92 ± 0.16; SUVmax, 1.35 ± 0.27) [2]. The combined information on the size and SUVmax of the mammary gland mass indicated the possibility of a malignant mammary gland tumor (MGT). In addition, a 1.1 × 1.1-cm lung nodule with an SUVmean of 3.37 and an SUVmax of 4.16 was confirmed through the FDG-PET/CT scan (Figure 2G-I). These metabolic values were above the RI of normal lung parenchyma (SUVmean, 0.43 ± 0.06; SUVmax, 0.96 ± 0.16) [2]. Lung nodules, which had not been previously observed on radiography, had FDG uptake suggestive of inflammatory or malignant neoplasia.

Splenectomy and mammary gland resection were performed to prevent splenic rupture and mammary gland mass metastasis. Histopathological examination of the splenic mass revealed an acute-to-subacute hematoma with no evidence of malignancy (Figure 3A), whereas an intermediate-to-high-grade mammary basaloid ductular carcinoma with focal lymphatic vessel invasion was observed in the mammary gland (Figure 3B).

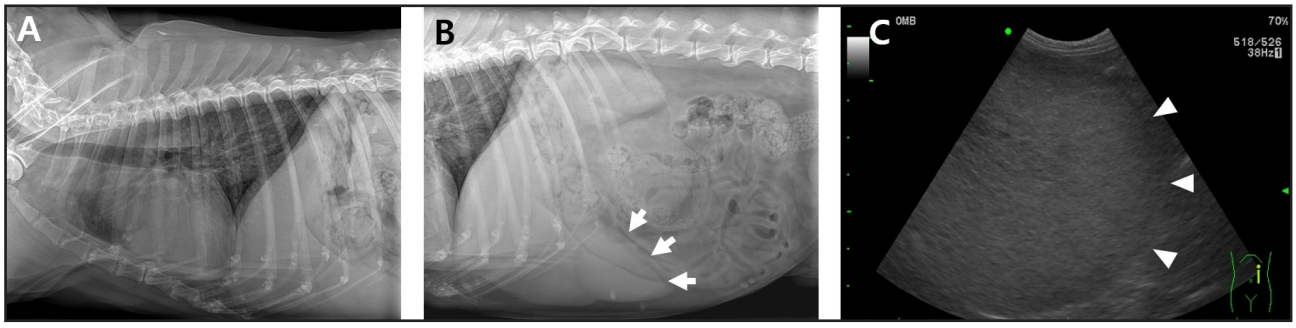

Figure 1. Radiographic findings of the lung and splenic mass are shown. A- Thoracic radiography revealed mild-to-moderate bronchial pattern and bronchial mineralization. However, no remarkable sign of lung nodule was found. B- In addition, splenic mass (arrows) can be observed in the left lateral view of the abdomen. C- An ultrasonographic view of the mass at the splenic tail is shown. On abdominal ultrasonography, a well-demarcated round-shaped mass was observed at the splenic tail level (arrowheads). Compared with a normal spleen, the spleen had moderately homogenously hyperechoic parenchyma. The large size and deformed contour of the mass suggested the presence of a malignant splenic tumor.

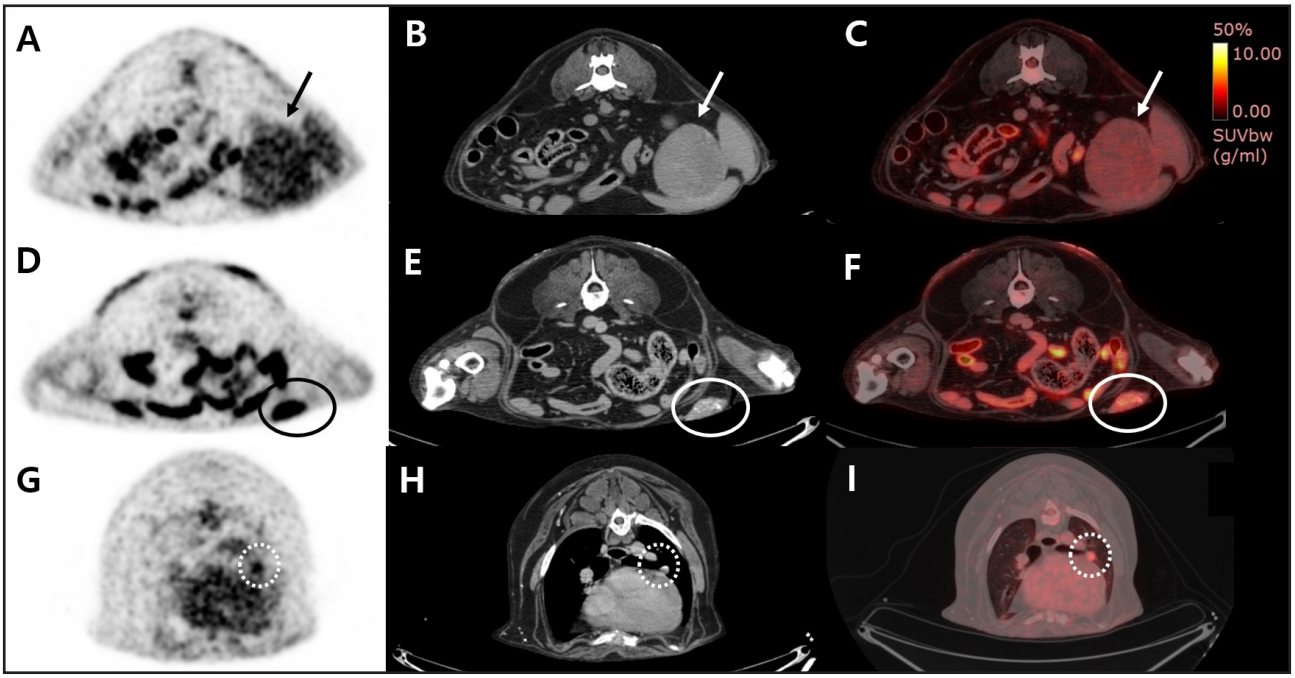

Figure 2. Representative images of positron emission tomography [PET] (A, D & G), computed tomography [CT] (B, E & H), and PET/CT fusion images (C, F & I) in a bitch with splenic mass (A-C), mammary gland mass (D-F), and lung nodule (G-I). On PET-CT fusion image, increased FDG uptake is shown in yellow, whereas low uptake is shown in black to red. The mean and maximum standardized uptake values of the splenic mass (arrows), mammary gland mass (circles), lung nodule (dotted circle) are 2.17 and 2.91, 3.81 and 5.22, and 3.37 and 4.16, respectively.

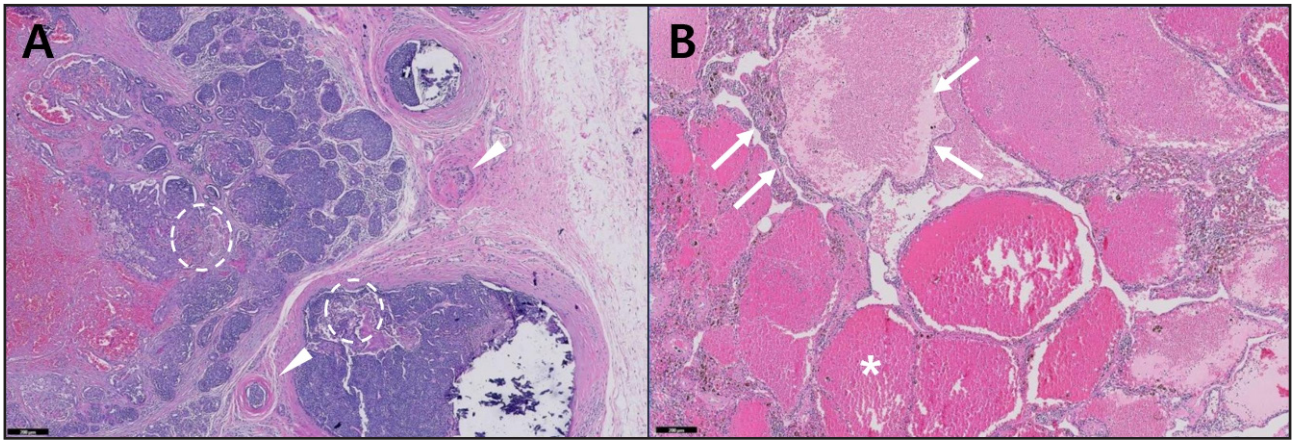

Figure 3. Histopathological evaluations of the mammary mass and splenic mass (hematoxylin & eosin). A- Moderate to marked hemorrhage was noted focally within the red and white pulp of the spleen, with some foci of mild thrombosis. Lymphoid hyperplasia, consisting of lymphoid follicles (dotted circles) and perivascular aggregates (arrow heads) of pleocellular lymphohistiocytic cells, was noted in the splenic mass, indicative of splenic hematoma (200×). B- Intermediate to high-grade mammary basaloid ductular carcinoma with focal lymphatic vessel invasions was found in the mammary gland mass. Neoplastic proliferation involved forming ducts (arrows) and solid formations (star). The mass was unencapsulated and exhibited stromal invasion (200×).

Two weeks after the surgery, the bitch exhibited respiratory distress, right front limb lameness, and pain. Additionally, thoracic radiography revealed that although there was no increase in the size of the lung nodule, a 1.6 × 1.5-cm round-shaped nodule appeared at the level of the 8th and 9th thoracic vertebrae, and the bronchial pattern worsened. It was challenging to differentiate whether the respiratory distress was owing to right front limb pain, lung metastasis, or pulmonary edema. Butorphanol[4] [0.2 mg/kg, IV] was injected to resolve front limb pain.

Four months after the surgery, the bitch showed symptoms of vomiting, respiratory distress, and a mild increase in temperature upon physical examination. At the time of presentation, the bitch's condition had notably worsened. Based on previous thoracic radiographic results, where lung metastasis and pulmonary edema were suspected, symptomatic treatment of furosemide[5] [1 mg/kg, IV] was administered based on previous thoracic radiographic result. The following day, the bitch's condition deteriorated, leading to respiratory arrest and ultimately death.

DISCUSSION

This report describes a case in which FDG-PET aids in the identification of lung nodule and the differentiation of primary lung lesion in a bitch. Radiography revealed an enlarged splenic mass. Several diseases can affect the spleen. The prevalence of malignant versus benign splenic lesions is 50%, and that of malignant disease is one-third of the likelihood of hemangiosarcoma [12]. On the CT scan, the size of the splenic mass was large, 8.5 × 7.5 cm, and changes in spleen's contour and solitude were detected. Therefore, considering the high prevalence of splenic hemangiosarcoma, large size, and changes in the splenic contour on CT, malignant splenic tumor was highly probable. However, the actual diagnosis was difficult until histopathological analysis was performed for a definite diagnosis. Generally, FDG-PET/CT can be used to differentiate between malignant and benign lesions [6]. With a threshold value of 2.3, the SUVmean in human patients, it is possible to differentiate between benign and malignant focal splenic lesions with sensitivity, specificity, positive predictive value (PPV), and negative predictive value of 100% [1]. Because the SUVmean of the spleen was 2.17 in this case, the splenic mass was suspected to be benign based on the threshold in humans [11]. On both ultrasound and CT imaging modalities, the splenic lesion appeared malignant owing to its large size and irregular contour; however, histological examination revealed hematoma, a benign lesion.

However, the possibility of lung metastases from MGT remains unclear. In one study involving canine cancer patients, tumor size of > 1.5 cm and SUVmax > 2 had a specificity and PPV of 100% for malignant tumors [13]. The FDG-PET/CT scan of the

present case met the malignancy criteria established in prior research, and the malignancy of the MGT was further confirmed through histopathological analysis. Consequently, FDG-PET/CT is a valuable tool for evaluating canine MGT. As malignant MGT tends to spread to the lungs, lung metastasis from the mammary glands seems highly likely in this case.

The pulmonary lesion was not identified on radiography but was detected using FDG-PET/CT. Pulmonary nodules may have been overlooked because of their small size or location [4,15]. It has been previously found that over 12% of dogs and cats with pulmonary tumors diagnosed by necropsy had seemingly normal pulmonary radiographs [14]. In the present case, the size of the pulmonary nodule was 1.1 × 1.1 cm and the SUVmax was 4.16, which is significantly higher than 0.96 ± 0.16, the SUVmean value of dogs without a history of lung disease [2]. In a study involving 57 human patients with pulmonary nodules < 1.5 cm in diameter, FDG-PET manifested higher diagnostic accuracy than CT [5]. Specifically, the diagnostic accuracy of FDG-PET/CT was 82%, whereas that of CT was 43% [5]. It is apparent from this study that FDG-PET/CT could be effective in diagnosing pulmonary lesions of unknown origin.

An FDG-PET/CT scan confirmed that the lung nodule had elevated FDG uptake. This uptake indicates the potential malignancy of the pulmonary nodule and raises the suspicion of metastasis originating from the highly malignant mammary gland. However, alternative diagnoses, including inflammatory pulmonary lesions and primary lung tumors, need to be considered [8]. FDG-PET/CT results served as the basis for determining whether the tumor was benign or malignant. Although the mammary gland and splenic masses were evaluated histologically, the lungs were not assessed. Notably, the lungs were not excised for evaluation during surgical intervention. In the absence of a microscopic examination of the lung mass, an accurate diagnosis of the lung tumor could not be established. However, given the high SUV uptake in the mammary gland and lung nodule on the FDG-PET scan, the histological confirmation of MGT, and the patient's poor prognosis, the lung nodule might have been a malignant lesion resulting from metastasis of the MGT.

In conclusion, this case highlights the utility of FDG-PET/CT in identifying the origin of a pulmonary nodule in a dog. Although a specific type of lung cancer was not identified, the pulmonary nodule was preliminarily diagnosed as malignant based on FDG-PET/CT results. Moreover, FDG-PET/CT provides crucial information on lung nodules that is not available through other diagnostic methods. Therefore, FDG-PET/CT has the potential to be a useful diagnostic tool for providing information regarding the malignancy and origin of a tumor. Further studies are necessary to use FDG-PET/CT as a diagnostic tool for discriminating the origin and malignancy of lung lesions in dogs.

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