Case Report
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대한영상의학회지

Lessons Learned from a Negative Biopsy: Impact of Positron Emission Tomography/CT on Targeted Biopsy for Lung Cancer[1]

음성 생검 결과에서 얻은 교훈: 폐암 조준 조직생검(Targeted Biopsy)에서 Positron Emission Tomography/CT의 유용성[1]

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We introduce two cases in which positron emission tomography (PET)/CT delineated viable malignant tissue from nonmalignant areas and guided us to successful biopsies when conventional CT failed to do so. According to our experience, PET/CT appears to be helpful in deciding the adequate site for biopsy in patients with lung cancer, owing to its capability to delineate malignant from nonmalignant areas, and also to reflect the areas with the most aggressive behaviors, especially in the era of the personalized cancer therapy.

Index terms
Lung Cancer, Biopsy
Targeted Biopsy
False Negative
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INTRODUCTION

Lung cancer is a heterogeneous tumor composed of both malignant and nonmalignant components. CT scans can differentiate malignant areas from nonmalignant portions, such as necrosis, but may sometimes be less satisfactory in delineating these specific areas. Positron emission tomography (PET), a functional imaging technique reflecting the metabolic characteristics, can be helpful in delineating viable malignant areas from that of nonmalignant areas or differentiating malignant lesions from nonmalignant ones in cases with multiple nodules; and thus, helpful in deciding the adequate site for biopsy. We introduce two cases.

CASE REPORT

Case 1

A 53-year-old man visited our medical center in early March 2010 with an incidentally detected mass on a chest radiograph during a routine health examination. Chest CT showed a 61-mm-sized homogenously enhancing mass in the superior segment of the right lower lobe, and it was associated right pleural effusion (Fig. 1A). Fluoroscopy-guided percutaneous transthoracic lung biopsy for the mass in the right lower lobe was performed with the patient in a prone position. Pathologic report of the biopsy didn't reveal malignant cells, but only a core of fibrotic lung with necrosis (Fig. 1B). A 18F-fluorodeoxyglucose (FDG) PET/CT, performed on the following day, showed high FDG uptake, not in the entire tumor, but mostly in the deeper portion of the mass (Fig. 1C). Rebiopsy was conducted with more concerns to take a sample from a deeper area, which showed high FDG uptake under C-arm cone-beam CT (C-arm CBCT) guidance. We first tried to identify the target lesion on fluoroscopy and were assured that the lesion matched with that on preprocedural CT and PET-CT scans.

After the identification of the target lesion, the puncture area was cleaned with antiseptic solution, followed by subcutaneous injection of local anesthetic (1% lidocaine, Xylocaine, AstraZeneca, London, UK). Then, percutaneous transthoracic lung biopsy was performed by using an 18-gauge gun biopsy needle (Gunbiopsy, M. I. Tech, Seoul, Korea). After the appropriate needle pass, unenhanced C-arm CBCT was performed to confirm that the needle tip was located within the target nodule. The pathologic report, at this time, revealed pleomorphic carcinoma (Fig. 1D).

Case 2

A 44-year-old woman visited our institution in late May 2010 for the evaluation of multiple nodules on chest radiographs.

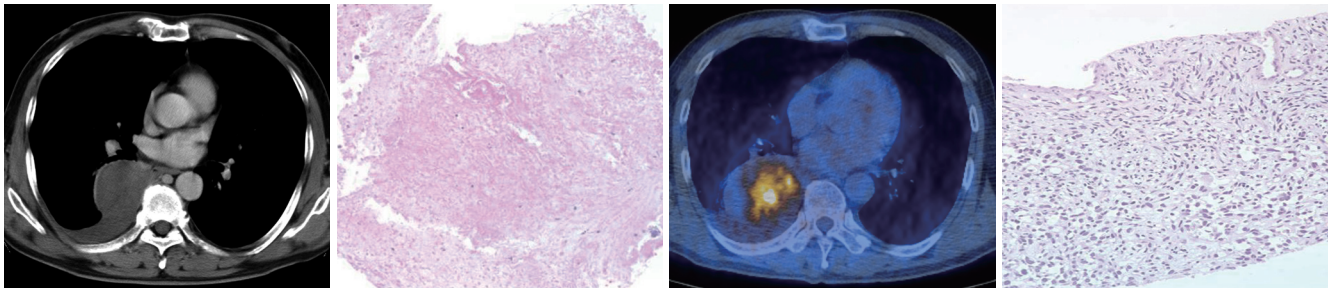

Fig. 1. A 53-year-old man with pleomorphic carcinoma.
A. Axial CT scan shows a homogeneously enhancing mass in the superior segment of the right lower lobe with right pleural effusion.
B. Photomicrograph from the first biopsy shows a core of fibrotic lung with necrosis (H&E, × 10).
C. PET-CT scan shows metabolic uptake, not in the entire tumor, but in deeper areas.
D. Photomicrograph from the rebiopsy shows malignant spindle cell tumor (H&E, × 40).
Note.—PET = positron emission tomography

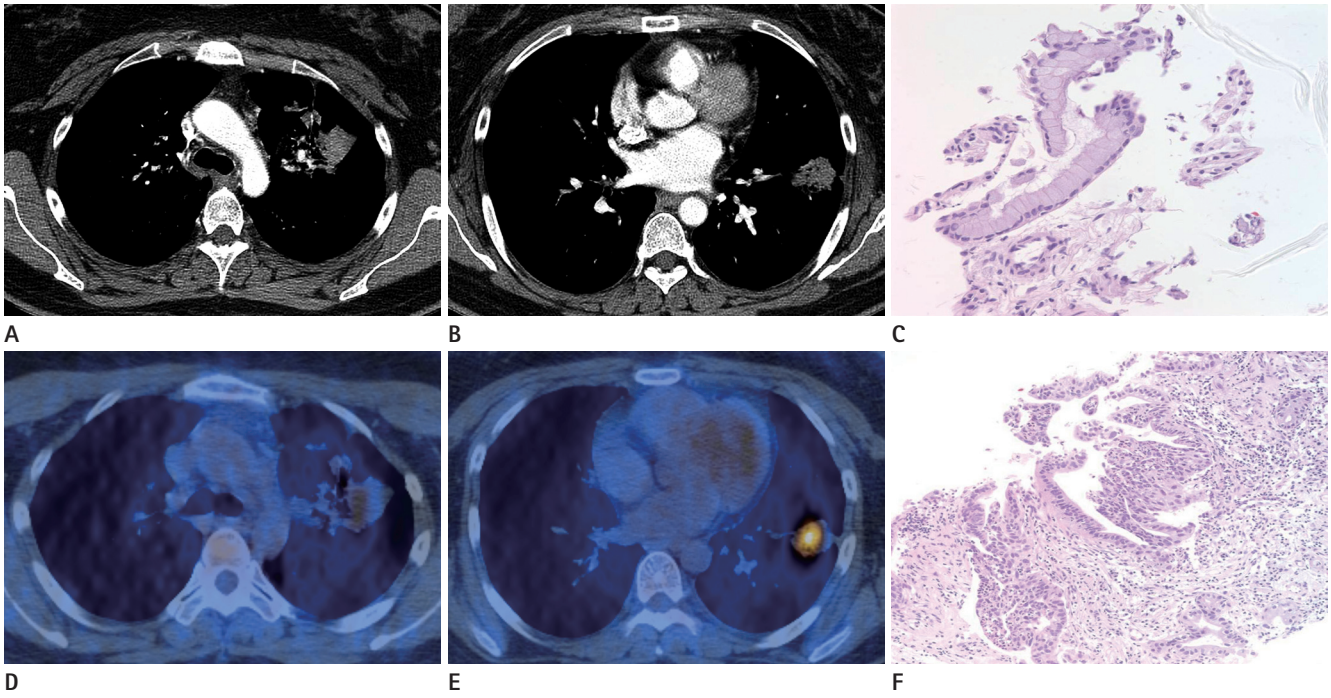

Fig. 2. A 44-year-old woman with adenocarcinoma.
A, B. Axial CT scans show multiple nodules with similar enhancements, including the largest one in the left upper lobe.
C. Photomicrograph from the first biopsy targeting the largest one of the left upper lobe shows only atypical columnar cells (H&E, × 40).
D, E. On the PET-CT scans, the lesion on the left upper lobes shows mild uptake; whereas the lesion in the left lower lobe shows strong uptake.
F. Photomicrograph from the rebiopsy targeting the lesion in the left lower lobe shows papillary adenocarcinoma with fibrovascular cores surrounded by malignant cells (H&E, × 40).
Note.—PET = positron emission tomography

Chest CT also showed multiple enhancing nodules or masses with similar morphologic characteristics on both lungs, with the largest one on the left upper lobe, measuring up to 4 cm in diameter (Fig. 2A, B). Fluoroscopy-guided biopsy was done on the largest lesion on the left upper lobe because it was relatively easy to access. Biopsy results showed no evidence of malignancy, but atypical columnar cells (Fig. 2C). At PET/CT performed the day after, only mild FDG uptake was noted in the lesion in the left upper lobe; whereas, strong FDG uptake was noticed for the lesion in the superior segment of the left lower lobe (Fig. 2D, E). Fluoroscopy-guided rebiopsy was performed for the lesion on the left lower lobe, not for the lesion on the left upper lobe. Biopsy results in this time revealed adenocarcinoma (Fig. 2F).

DISCUSSION

Lung cancer is a heterogeneous tumor, composed of malignant tissues, as well as other components, such as fibrosis, inflammation, or necrosis (1, 2). Moreover, lung cancer includes histologically different subtypes. According to the new classification of lung adenocarcinomas (3), there are five different subtypes, and each subtype shows rather different prognosis (4). For example, lepidic-growth predominant (former adenocarcinoma with a bronchioloalveolar carcinoma component) invasive adenocarcinomas virtually show little invasive features, whereas, micropapillary-predominant invasive adenocarcinomas show higher aggressiveness than other subtypes (4, 5). Thus, the location to perform a biopsy for lung cancer is important for securing positive biopsy results on a one-time trial.

The CT study, which is the most commonly used imaging modality to make a diagnosis of lung cancer and plan for its biopsy, defines malignant tumor based on its morphology and the degree of enhancement in a dynamic contrast enhancement study. In most cases, CT scans help differentiate the tumor portion harboring malignant cells from the nonmalignant portions, including the area of tumor necrosis; and thus, allows one to target the most aggressive areas during the biopsy procedure. But sometimes, as in our two cases, it may be less satisfactory in delineating these specific areas. Tissue sampling conducted in these nonmalignant regions may yield to false negative biopsy results (6), leading one to unnecessary repetitive trials of biopsy, and resulting in increased cost and risk for complications.

On the other hand, the extent of FDG uptake in tumors on PET scans is multifactorial, which is determined mainly by the glucose metabolic activities, but also by growth rate, regional hypoxia and Glut-1 concentration (7). In our first case, the area with different metabolic activity, which was unidentifiable on enhancement CT scans, was delineated by using the PET/CT study. This different FDG uptake was taken into account in the second biopsy, which led us to successful results. In the second case, nodules that seemed to show similar enhancement on CT scans had very different metabolic activities on PET scans, which guided us as to where to perform the biopsy.

The importance of considering metabolic activity during the lung tumor biopsy is more emphasized in unresectable lung cancer patients, since their pathologic descriptions are solely dependent on small specimens from biopsies, not from resected specimens (8). Approximately 80% of patients with lung cancer have unresectable tumor at the initial presentation. Therapeutic decisions for those patients are also likely to be made by depending solely on diagnostic biopsy samples, which are usually the only materials available for testing. Moreover, the coupling of advances in image-guided biopsy, microarray technology, and amplification techniques allows one to obtain significantly decreased tissue amount (like a core biopsy), which is required to perform microarray genetic analyses (9, 10). Therefore, targeted biopsy in areas that show the highest metabolic activities may be especially meaningful to inoperable patients who are planned for palliative treatment. This is because the most aggressive area could reflect better prognosis and be related more to a personalized therapy. Therefore, even though initial biopsy results may not reveal malignancy in patients highly suspicious for lung cancer, instead of delay or pause in the workup, acquisition of PET/CT may be helpful in yielding positive results. In summary, according to our experience, PET/CT appears to be helpful in deciding the adequate site for biopsy in patients with lung cancer, owing to its capability to delineate malignant from nonmalignant areas and also to reflect areas with most aggressive behaviors, especially in the era of the personalized cancer therapy.

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폐암 조직검사에 있어서 positron emission tomography (이하 PET)/CT가 악성 부위를 비악성 부위로부터 구별해 줌으로써 성공적인 조직생검 결과를 얻을 수 있었던 두 증례를 보고하고자 한다. 우리 경험에 의하면, PET/CT는 폐암 환자에게 있어서 악성 병변을 비악성 병변으로부터 구별해 냄으로써 최적의 생검 위치를 결정하는 데 도움이 될 뿐만 아니라, 가장 공격적 성향을 갖는 부위를 반영함으로써 개인 맞춤 암 치료 시대에 있어 특히 도움이 되리라 생각된다.

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