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A case of early stage lung cancer detected by repeated cancer screening with positron emission tomography

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Abstract. There has been an increase in the detection rate of small early lung cancer due to recent improvements in imaging technology. However, conventional imaging modalities such as computed tomography (CT) alone are not capable of differentiating small pulmonary nodules. New modalities such as F-18 2'-deoxy-2fluoro-D-glucose (FDG) positron emission tomography combined with CT (PET/CT) have contributed to the evaluation of lung cancer staging, although the differential diagnosis of pulmonary nodules showing ground-glass opacity (GGO) with PET/CT is controversial. In Japan, cancer screening with whole body FDG-PET has been available for asymptomatic individuals, and it has been reported that a wide variety of cancer types are detectable by FDG-PET at potentially curable stages. We present the case of a 62-year-old male with early lung cancer, which was revealed by repeated health screening. A PET/CT scan revealed definite intense FDG uptake (SUVmax 1.2) in the pulmonary nodules of the right upper lobe, while no definite FDG uptake was observed in the lesion in the previous annual screening. Right upper lobectomy was performed, and the pathological diagnosis was well-differentiated adenocarcinoma. Five-year survival has been noted since the thoracotomy, and the patient is doing well without recurrence. This is a significant case of early lung cancer with GGO lesions, which revealed intense FDG uptake during an annual repeated health screening with FDG-PET/CT.

Introduction

An increase has been noted in the rate of detection of small early lung cancers with recent improvements in imaging technology such as computed tomography (CT). In particular, since high-resolution computed tomography (HRCT) scans with low radiation dose were first applied for lung cancer screening during the late 1990s to 2000s (1-3), there has been a marked increase in the detection of ground-glass opacity (GGO) in peripheral lung lesions. GGO is a non-specific finding that may be caused by various diseases, including inflammation, fibrosis and cancer, while other studies have reported that GGO is related to bronchioalveolar carcinoma (BAC) (4).

Positron emission tomography (PET) with F-18 2'-deoxy-2fluoro-D-glucose (FDG) has been used to differentiate malignant from benign lesions due to the higher metabolic activity of malignant lesions indicated by high secondary isotope uptake. Numerous reports are available regarding the usefulness of FDG-PET in differentiating malignant pulmonary nodules from benign ones (5,6). In Japan, cancer screening with whole FDG-PET has been available for asymptomatic individuals, albeit with a high procedure fee. Moreover, it has been reported that a wide variety of cancer types are detectable by FDG-PET at potentially curable stages (7-9). New modalities such as FDG-PET combined with computed tomography (FDG-PET/CT) are now well-established for the evaluation of various cancer types (10-13). Clinically, PET/CT has contributed to the evaluation of lung cancer staging, while the usefulness of FDG-PET/CT for the differential diagnosis in small nodules showing GGO remains controversial (14-17).

We report a noteworthy case of early lung cancer with GGO lesions, which revealed definite intense FDG uptake during repeated health screening with a PET/CT scan.

Patient and methods

This study was performed with the patient's informed consent and with approval for the study from the ethics committee of Tokorozawa PET Diagnostic Imaging Clinic, Japan.

A 62-year-old man received health screening, including a PET/CT scan, in September 2005 at Tokorozawa PET Diagnostic Imaging Clinic. ^{18}F-FDG PET/CT scans were obtained with a Biograph Duo (Siemens CTI) as described in our previous study (11,18). To determine semi-quantitative FDG uptake, regions of interest (ROIs) were placed over the lesion, including the highest uptake area (circular ROI, 1 cm

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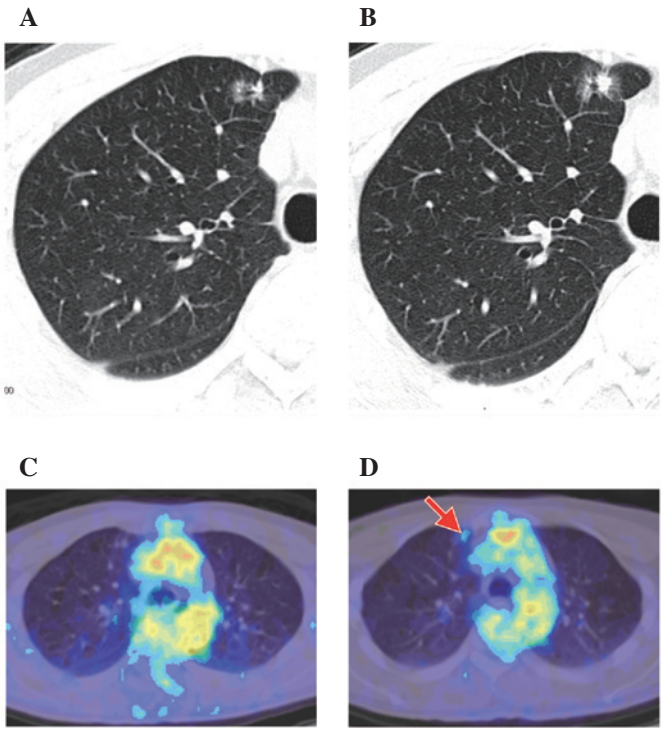

Figure 1. (A) A CT scan revealed a ground-glass opacity (GGO) lesion (10 mm) in the upper lobe of the right lung of a patient in September 2005. (B) A year later, the CT scan revealed an abnormal shadow of a larger size (15 mm) in the upper lobe of the right lung and GGO with a small solid area. (C) PET/CT revealed no abnormal F-18 2'-deoxy-2fluoro-D-glucose (FDG) uptake in the GGO lesion in September 2005. (D) PET/CT revealed abnormal FDG uptake in the GGO lesion with SUVmax 1.2 (arrow) one year later.

in diameter), and the standardized uptake value (SUV) was calculated. The CT scan revealed a GGO lesion (10 mm) in the upper lobe of the right lung (Fig. 1A). PET/CT revealed no abnormal FDG uptake in this GGO lesion (Fig. 1C), and also suggested no apparent malignant findings in the whole body. Physical examination revealed no apparent abnormal findings, and no abnormalities were revealed in the blood analysis, including tumor markers such as carcinoembryonic antigen (CEA) and CA19-9. The patient consulted a chest surgeon but no explanatory thoracotomy was performed at the patient's request. Three months later, the patient received another CT scan but no change was noted in the abnormal shadow of the right upper lobe. A year later, he again underwent health screening with a PET/CT scan. The CT scan revealed a larger size (15 mm) abnormal shadow in the upper lobe of the right lung, and a small solid area with pleural indentation was noted in the GGO lesion (Fig. 1B). PET/CT revealed abnormal FDG uptake in this GGO lesion with SUVmax 1.2 (Fig. 1D).

Results

Explanatory thoracotomy was performed and biopsy specimens were obtained at the National Defense Medical College Hospital, Japan. Frozen sections of the tumor revealed a growth of cancer cells. The patient underwent right upper lobectomy plus dissection of the hilar and mediastinal lymph nodes. Macroscopically, the tumor in the right upper lobe measured 13x13x10 mm in diameter, and the cut surface of the tumor was

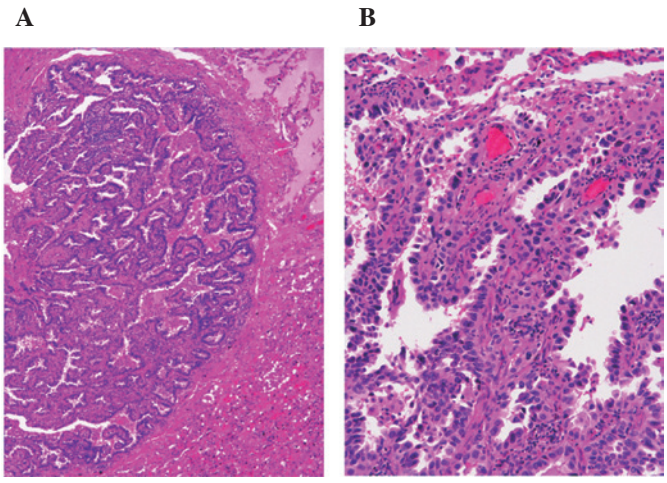

Figure 2. (A) Microscopic examination of the right pulmonary tumor lesion showed foci of tumor growth of atypical cells (magnification, x100). (B) Microscopic findings of the right pulmonary tumor on high power view revealed tumor cells with a glandular and papillary pattern with fibroblastic formation, a feature of well-differentiated adenocarcinoma; Noguchi classification type C (magnification, x500).

solid with a blue-white color. The microscopic findings revealed growth of atypical cells with a glandular and papillary pattern with fibroblastic formation, a feature of well-differentiated adenocarcinoma (Noguchi classification type C; pT1N0MO; Fig. 2). No metastatic lesions were observed in the dissected lymph nodes and the patient received no chemotherapy following the surgery. Five years after thoracotomy, PET/CT revealed no abnormalities and there were no signs of either recurrence or systemic metastasis in any other examinations.

Discussion

Low-dose HRCT scans were first applied for lung cancer screening between the late 1990s and early 2000s (1-3). In their study, Henschke *et al* reported that CT screening significantly reduced lung cancer mortality in a cohort of approximately 8,000 smokers (19). The development of FDG-PET/CT has contributed to the evaluation of human cancer staging, and the usefulness of PET/CT is well established for cancer staging. This imaging modality increases the otolaryngologist's and radiation oncologist's confidence when treating head and neck cancer patients, leading to appropriate management changes (20). We have reported that this modality was clinically useful for evaluating human cancers, including rare carcinoma cases (18,21-23). In the present study, we reported a lung cancer case with GGO, which revealed an increased intense FDG uptake by FDG-PET/CT during annual cancer screening, and the repeated FDG-PET/CT examinations were used to evaluate the pulmonary nodules with GGO.

In lung cancer screening with low-dose HRCT, there has been a marked increase in the detection of GGO in peripheral lung lesions. Computer-aided diagnosis (CAD) systems provide a useful second opinion in detecting pulmonary nodules when physicians carry out lung cancer screening with low-dose HRCT (24). Certain reports indicate that CT findings on GGO with a solid area are useful in differentiating between benign and malignant lesions (25). In our case, the CT scan revealed that

the pulmonary lesion with GGO had a slightly increased size with a solid area after a one year interval between screenings.

In Japan, cancer screening with whole FDG-PET has been available for use in asymptomatic individuals, albeit with high procedure fees, and it has been reported that a wide variety of cancer types are detectable by FDG-PET at potentially curable stages (7-9). Murano *et al* reported that FDG-PET cancer screening was beneficial to patients above the break-even age despite the exposure to radiation (26). In our PET center, we performed cancer screening by PET/CT with informed consent including that for radiation exposure, and 140 cases of cancer were detected by PET/CT and other modalities among 7,236 examinations in a period of approximately 5 years and 7 months between August 2005 and March 2011. A total of 140 cancer patients were pathologically diagnosed as having various cancers: 33 lung, 17 thyroid, 17 breast, 11 colon and 62 other cancer types, whereas PET/CT revealed no significant FDG uptake in 22 of the 140 patients. The total detection rate was 1.93%, and the detection rate with PET/CT was 1.55%.

In this study, we have reported a rare case of early lung cancer with GGO lesions. The patient underwent thoracotomy and at present is without recurrence. Thus, intense FDG uptake during an annual follow-up repeated health screening with FDG-PET/CT may prove useful in detecting such cancer types.

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