ORIGINAL ARTICLE

There is a difference in degree of FDG uptake between lung metastasis from colorectal cancer and primary lung cancer on PET/CT

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Abstract

Purpose This study aimed to assess whether there is a difference in degree of F-18 fluorodeoxyglucose (FDG) uptake between lung metastasis (LM) from colorectal cancer (CRC) and primary lung cancer on PET/CT.

Materials and methods Nineteen patients with LM from CRC (80 nodules) , 84 patients with primary lung adenocarcinoma (PLA) (84 nodules), and 11 patients with primary lung squamous cell carcinoma (PLS) (11 nodules) were studied retrospectively. All nodules were 11 ~ 30 mm in size. Of the 84 PLAs, 51 were well-differentiated PLA and 33 were moderately ~ poorly differentiated one. All nodules were graded visually, and classified into the following five grades, grade 0: no accumulation, grade 1: lower than the mediastinal blood pool activity, grade 2: similar to the mediastinal blood pool activity, grade 3: higher than the mediastinal blood pool activity and lower than the brain activity, grade 4: similar to the brain activity. The frequency of each grade was evaluated and was compared between LM from CRC and primary lung cancer.

Results The most common grade of LM from CRC was grade 3. The grade of well differentiated PLA was widely distributed, and the most common grade was grade 2. In contrast, the most common grade of moderately ~ poorly differentiated PLA was grade 4. The most common grade of PLS was also grade 4. The frequency of each grade of LM from CRC was significantly different from that of well differentiated PLA

($p<0.0001$) or moderately ~ poorly differentiated one ($p<0.0001$).

Conclusion There was a significant difference in degree of FDG uptake between LM from CRC and PLA on PET/CT. FDG uptake of LM from CRC tended to be lower than that of moderately ~ poorly differentiated PLA.

Keywords PET ; FDG ; Lung metastasis ; Colorectal cancer ; Primary lung adenocarcinoma

Abbreviations

FDG Fluorodeoxyglucose

LM Lung metastasis

CRC Colorectal cancer

PLA Primary lung adenocarcinoma

PLS Primary lung squamous cell carcinoma

Introduction

Recently, incidence and mortality of colorectal cancer (CRC) have substantially increased in Japan (1). CRC is a common malignancy with a high incidence of relapse (1). The lung is the second most common site of recurrence after curative resection of CRC (1).

CT scans have a greater capacity to detect lung metastasis (LM) from CRC than F-18 fluorodeoxyglucose (FDG) PET/CT. When a pulmonary nodule is detected in patients with CRC, differentiation between primary lung cancer and LM can be crucial for treatment planning and predicting prognosis in clinical practice. Moreover, surgical strategies for treating primary lung cancer and LM are quite different (2). In general, the treatment of choice for LM is minimally invasive surgical resection in order to preserve as much healthy lung parenchyma as possible in case repeat operation is needed. In contrast, complete surgical resection with lobectomy and mediastinal lymph node dissection is the gold standard for primary lung cancer. Quantitative CT features and clinical characteristics of solitary pulmonary nodule in patients with CRC could help differentiate between primary lung cancer and solitary LM (3). However, primary lung adenocarcinoma (PLA) with intestinal differentiation is occasionally reported to mimic

LM (4). Therefore, it is sometimes difficult to determine whether a pulmonary nodule is a PLA or a LM. Image-guided needle biopsies may be useful for distinguishing between PLA and LM before surgical planning. However, it is difficult and risky to perform needle biopsies in some cases, especially for those with small lesions.

Recurrence of CRC can be accurately and conveniently diagnosed by FDG PET/CT (5, 6). Assessment with FDG PET/CT has a significant impact on the management of CRC patients with LM (5, 6). In oncological patients, FDG PET/CT provides good diagnostic performance for ruling in the malignancy in pulmonary nodules detected during follow-up (7). However, it is not confirmed whether there is a difference in degree of FDG uptake between LM from CRC and primary lung cancer on PET/CT. The aim of this study is to assess whether there is a difference in degree of FDG uptake between LM from CRC and primary lung cancer on PET/CT.

Materials and methods

Patients

Nineteen patients with LM (80 nodules) from CRC and 84 patients with PLA (84

nodules), and 11 patients with primary lung squamous cell carcinoma (PLS) (11 nodules) were studied retrospectively. Pathological type of all colorectal cancers was adenocarcinoma. All 84 PLAs and 11 PLMs were proven pathologically after PET study. LM from CRC were established by histopathological evaluation (n=6) or radiological follow-up (n=74). Patients who received chemotherapy before PET study were excluded.

The size of the nodules was measured on CT. The nodules 11 ~ 30 mm in size were included in this study.

It was reported that FDG uptake of PLA was affected by the cell differentiation (8). FDG uptake of moderately ~ poorly differentiated PLA was higher than that of well differentiated one (8). In the PLA, cell differentiation was estimated by an experienced pathologist. Of the 84 PLAs, 51 were well-differentiated PLA and 33 were moderately ~ poorly differentiated one.

FDG PET/CT imaging

PET images were fused with 4/slice multi-detector computed tomography system images (Discovery ST PET/4 slice CT fusion system; General Electric Medical Systems,

Milwaukee, WI, USA). Full width at half maximum (FWHM) of this system was 5 mm. All of the patients in the study fasted for 5 hrs before injection of FDG. Blood glucose level was measured, and the data were recorded. Patients with blood glucose levels above 130 mg / dl were excluded from this study, because brain and blood pool activity are affected by the blood glucose level on FDG PET/CT (9, 10).

FDG was administered intravenously. FDG was purchased via the delivery system. The average injection activity of FDG was 185 MBq. After a 60 minute uptake period, an emission scan was acquired. Three-dimensional acquisition was used. The combination of Fourier rebinning (FORE) and the ordered subsets expectation-maximization (OSEM) methods was used for reconstruction. Five iterations of OSEM with 32 subsets were used.

The strength of FDG uptake was estimated visually by an experienced nuclear medicine physician, and classified into the following five grades, grade 0: no accumulation, grade 1: lower than mediastinal blood pool activity, grade 2: similar to mediastinal blood pool activity, grade 3: higher than mediastinal blood pool activity and lower than brain activity, grade 4: similar to brain activity. This method is a modification of that reported previously (11, 12).

The frequency of each grade was evaluated, and was compared between LM from

CRC and PLA or PLS.

Statistical analysis

All statistical analyses were performed with SPSS for Windows (version 11.5; SPSS, Inc.). Statistical significance was determined by the chi-square test (Fisher's exact test). Probability values of less than 0.05 were considered statistically significant.

Results

Clinical characteristics of LM from CRC, PLA and PLS enrolled in this study are summarized in Table 1, 2, and 3.

The frequency of each grade of LM from CRC, PLA, and PLS were shown in Figure 1.

The most common grade of LM from CRC was grade 3 (Fig. 1 A). The grade of well differentiated PLA was widely distributed, and the most common grade of well differentiated PLA was grade 2 (Fig. 1B). In contrast, the most common grade of moderately ~ poorly differentiated PLA was grade 4 (Fig. 1C). The most common grade

of PLS was also grade 4 (Fig. 1D). The frequency of each grade of LM from CRC was significantly different from that of well differentiated PLA ($p<0.0001$) or moderately ~ poorly differentiated one ($p<0.0001$). There was no significant difference in the frequency of each grade between LM from CRC and PLS, while this result may be due to small number of PLS cases.

There was a significant difference in degree of FDG uptake between LM from CRC and PLA on PET/CT. FDG uptake of LM from CRC tended to be lower than that of moderately ~ poorly differentiated PLA.

Discussion

Kaira. et al. (13) reported that FDG uptake (tumor to mediastinum ratio) of LM was significantly lower than that of non-small cell lung cancer. In the study of Kaira et al. (13), however, other than CRC was included as the primary focus of LM, and cell differentiation of non-small cell lung cancer was not considered. The range of tumor size was 6 ~ 100 mm. In the current study, only CRC was included as the primary focus of LM, and cell differentiation of PLA was considered. Furthermore, only nodules as large as 11~30 mm were included in this study. In the current study, the most common

grade of LM from CRC was grade 3. In contrast, the most common grade of moderately ~ poorly differentiated PLA was grade 4. The most common grade of PLS was also grade 4. These results are consistent with that of Kaira et al.. However, the most common grade of well differentiated PLA was grade 2. LM from CRC showed FDG uptake with an intermediate strength between well differentiated PLA and moderately ~ poorly differentiated one on FDG PET/CT.

The strength of FDG uptake was estimated visually, and Semi-quantitative methods such as SUV value were not used. Visual interpretation is, however, sufficient for characterizing solitary pulmonary nodules, and semi-quantitative analysis does not improve the accuracy (7, 14, 15). SUV value is also affected by many factors, for example acquisition method and reconstruction method, and the SUV value is not suitable for use as a reference value when using in multiple facilities. In contrast, visual assessment is used as a reference value, for example Deauville 5-point scoring system in patients with malignant lymphoma (16, 17). In the Deauville 5-point scoring system, mediastinal blood pool and liver activity are used. In the current study, mediastinal blood pool and brain activity were used as reference values.

The nodules only 11~30 mm in size were included in this study. The strength of FDG uptake is affected by partial volume effect (PVE). PVE strongly depends on the

size of the tumor. The smaller the tumor, the greater the underestimation of the uptake value (18). As a result, different tumors with exactly the same uptake value but with different sizes yield tumor images with different degrees of brightness and hence different estimated uptake values. It was reported that LM from CRC can be accurately and conveniently diagnosed by PET/CT, when nodules are more than 9 mm (19). It was also reported that a reduced sensitivity of FDG PET has to be considered for lesions smaller than 11 mm in diameter (20). Almost all LMs were diagnosed when the nodules were less than 30 mm in size (1). Because of these reasons, nodules 11~30 mm in size were included in this study.

Study limitations

First, sample number of PLS cases were only 11, and were too few to estimate the statistical significance. Recently, the frequency of PLS is lower than that of PLA in Japan (21). In the current study, there was no significant difference in degree of FDG uptake between LM from CRC and PLS. This result may be due to small number of PLS cases. Additional study with numerous PLSs is warranted. It was reported that FDG uptake of PLS was significantly higher than that of PLA (22). In the current study,

many PLSs were FDG avid, and the most common grade of PLS was grade 4 (Fig. 1D). This result is compatible with the previous study (22).

Second, location of pulmonary nodule was not considered. FDG uptake of pulmonary nodules near the diaphragm may be underestimated due to respiratory movement (23).

Third, other than CRC was not included as the primary focus of LM. LM from other than CRC may show a different degree of FDG uptake.

Fourth, Kaira et al. (13) reported that FDG uptake in metastatic pulmonary tumors correlated significantly with the expression of Glut-1, hypoxia, phosphorylation of glucose, and angiogenesis. These biological factors were not compared between LM from CRC and PLA in the current study. Obviously, additional biological study is warranted.

Conclusion

There was a significant difference in degree of FDG uptake between LM from CRC and PLA on PET/CT. FDG uptake of LM from CRC tended to be lower than that of moderately ~ poorly differentiated PLA.

Compliance with ethical standards

Conflict of interest All authors have no financial disclosure. All authors have no conflicts of interest.

Ethical approval The study protocols for this retrospective analysis were approved by our institutional review board.

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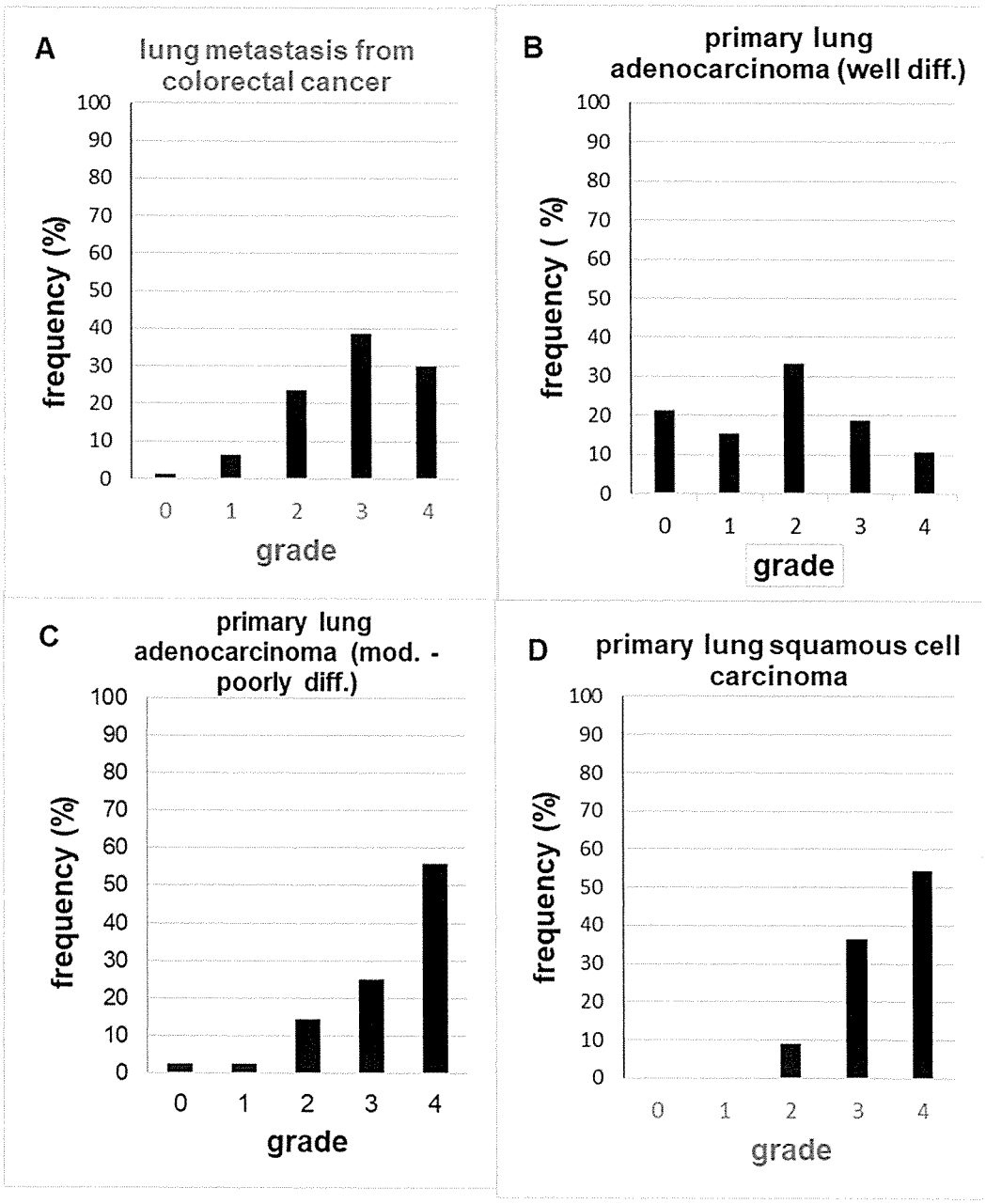
Figure Legend

Figure 1: The most common grade of LM from CRC was grade 3 (Fig. 1 A). The grade of well differentiated PLA was widely distributed, and the most common grade of well differentiated PLA was grade 2 (Fig. 1B). In contrast, the most common grade of moderately ~ poorly differentiated PLA was grade 4 (Fig. 1C). The most common grade of PLS was also grade 4 (Fig. 1D). FDG uptake of LM from CRC tended to be lower than that of moderately ~ poorly differentiated PLA.

diff.: differentiated, mod.: moderately


A
lung metastasis from colorectal cancer
frequency (%)
100
90
80
70
60
50
40
30
20
10
0
0 1 2 3 4
grade
B
primary lung adenocarcinoma (well diff.)
frequency (%)
100
90
80
70
60
50
40
30
20
10
0
0 1 2 3 4
grade
C
primary lung adenocarcinoma (mod. - poorly diff.)
frequency (%)
100
90
80
70
60
50
40
30
20
10
0
0 1 2 3 4
grade
D
primary lung squamous cell carcinoma
frequency (%)
100
90
80
70
60
50
40
30
20
10
0
0 1 2 3 4
grade