IV. 4. Mediastinal Tumors Studied with Positron Emission Tomography

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Introduction

Mediastinal masses include a wide variety of tumors, and remain an interesting diagnostic challenge for radiologists. Computed tomography (CT) has proved to be an excellent diagnostic tool for investigating the mediastinum\(^1,2\). The CT demonstration of fat, calcium or water attenuation in a tumor often suggests a specific diagnosis. However, the ability of CT in differentiating soft tissue mediastinal masses is limited due to a considerable overlap in the CT characteristics between malignant and benign tumors\(^3,4\).

Positron emission tomography (PET) has proved excellent in detecting malignant tumors of the central nervous system and non-CNS tumors\(^5\). Both 2-deoxy-2-fluoro-[\(^{18}\)F]-D-glucose (FDG) and L-[Methyl-\(^{11}\)C]methionine (Met) have been used with PET for the diagnosis of head and neck, breast, and lung cancers, while FDG has also been used in detecting liver tumors and pancreas cancer. To our knowledge, the use of FDG and Met in primary mediastinal tumors has not yet been evaluated. In order to predict the malignant nature of these tumors preoperatively, we performed PET studies using FDG or Met, and compared the results with the pathological diagnosis and the results of CT examination.

Materials and Methods

The study protocol was approved by the Ethics Committee for Clinical Research of Tohoku University and informed consent was obtained from each patient.

A total of 28 patients (mean age: \(48 \pm 20\) (\(\pm SD\)), range: 14-83, 16 women and 12 men) with mediastinal tumors were studied with PET imaging. Nineteen patients had anterior, 5 patients had middle, and four patients had posterior mediastinal tumors. None received chemo- or radiotherapy before the PET study. Histologic diagnosis was confirmed
in all patients after the PET study by surgical pathology (18 patients) or biopsy (10 patients), and the histological diagnosis was compared with results of the PET study.

Twenty-two patients were studied with FDG while Met was used in seven patients (one patient had both FDG and Met-PET studies). After fasting for five hours, the blood glucose level was measured before the injection of FDG or Met. PET scans were performed using PT931/04 scanner (Siemens-CTI, Knoxville, TN). After a transmission scan, a bolus dose of FDG or Met was injected intravenously. The mean dose of FDG was 4.3 ± 0.8 mCi (159.1 ± 29.6 MBq) while that of Met was 19.7 ± 7.0 mCi (728.9 ± 258.0 MBq). Dynamic images were obtained first, followed by a 10 min static image which was acquired 40-50 min after injection of FDG or 30-40 min of Met. The tumor ROI, including the highest radioactivity point, was set on the static image. To avoid contamination of the non-tumor area, the tumor ROIs were checked carefully by superimposing both on transmission images and on the early post injection images, which showed vascular structures.

Eight muscle ROIs, located in the tumor slice, were placed in the paravertebral muscles bilaterally, shoulder, lateral and anterior chest wall muscles, as described previously. The mean radioactivity per pixel within the tumor and muscle ROI was quantitatively analyzed by calculating the differential uptake ratio (DUR, synonym; standardized uptake value; SUV), as reported previously. This involved expressing the radioactivity concentration in ROI relative to the injection dose and body weight. We also calculated the tumor to muscle radioactivity ratio (T/M). Students’ t-test was used for statistical analysis.

Results

A high FDG uptake was clearly observed in nine of ten patients with malignancies, and also in one patient with sarcoidosis. A moderate level of FDG uptake was observed in benign thymomas, a myeloma and schwannoma, while a low FDG uptake was detected in a teratoma and various benign cysts. The mean FDG uptake was significantly higher in malignant tumors compared with that of benign tumor, using either DUR or T/M ratio (Table 1). However, the FDG uptake of muscle and blood glucose level in malignant tumors were not significantly different from those in benign tumors. Examples of typical PET images of thymic cancer (Figure 1) is presented.

Although the number of patients studied with PET and Met was small, the results of these studies were similar to those using FDG. Thus, malignant tumors showed a high Met uptake while benign tumors had a low Met uptake but statistically not significant. The muscle Met uptake and blood glucose levels in malignant and benign tumors were similar (Table 1).

The distribution of DUR in malignant and benign tumors with FDG and Met is shown in Figure 2. The use of FDG and Met enabled differentiation of most malignant tumors from benign tumors based on DUR analysis. However, an overlap between malignant and benign
tumors was evident. FDG tended to provide a better distinction between malignant and benign tumors compared with Met.

Our analysis demonstrated the presence of a significant linear correlation between the T/M ratio and DUR \((r=0.9896, p<0.001)\) (Figure 3). Although the mean DUR in muscles examined with FDG \((0.79 \pm 0.07, n=18)\) was slightly lower than that with Met \((0.90 \pm 0.06, n=7)\), the correlation between T/M ratio and DUR with FDG was not significantly different from that with Met.

**Discussion**

The major finding of the present study is that the distribution of FDG or Met uptake in malignant mediastinal tumors, revealed by PET, was significantly higher than that in benign tumors. These results are in agreement with those reported recently on the excellent diagnostic performance of PET in differentiating the malignancy of lung nodules using FDG-PET\(^6\). The present results are also consistent with FDG-PET studies of other tumors, including breast\(^7\) and pancreatic tumors\(^8\). These results suggest that the high uptake of FDG seems to be a general feature of a variety of cancers. Increased FDG uptake may reflect the high activity of hexokinase and glucose transport\(^9\).

Calculation of the glucose metabolic rate using FDG based on the Sokoloff's model has been applied to oncology PET, mostly to brain tumor studies\(^10\). However, such method requires arterial blood sampling and estimation of the lump constant. Determination of the latter in individual tumors is impossible in humans. More simple evaluation methods without blood sampling, such as DUR or tumor/normal tissue ratio, have been recently introduced. The clinical value of these parameters has been demonstrated in several oncology studies. The use of DUR and tumor/muscle radioactivity ratio in the present study confirmed the presence of a significant linear relationship between the two parameters in benign and malignant tumors.

The level of FDG uptake of tumors is related to the grade of malignancy in brain and soft tissue tumors\(^10,11\). Furthermore, it has also been used as a prognostic indicator of malignancy in gliomas\(^12\). The FDG uptake by the tumor also correlates with the cell density in gliomas of grade 2 and 3\(^13\). Results of experimental studies indicate that the uptake of FDG is related to the number of viable cancer cells in vitro\(^14\), and the amount of viable tissue in vivo\(^15\). FDG uptake varies also with the histologic differentiation of human abdominal tumors transplanted in nude mice\(^16\). In this regard, recent studies from our laboratory indicate that FDG uptake by cancer cells is higher in G\(_0\)/G\(_1\) and G\(_2\) phases of the cell cycle compared with the S and M phases\(^17\), and that tumor growth rates correlated with the FDG uptake of tumors\(^18\). These results suggest that the uptake of FDG by mediastinal tumors may represent a biological marker of the clinical behavior of these tumors.

In conclusion, PET, particularly in combination with FDG, seems to be useful in the evaluation of malignancy in primary mediastinal tumors.
Acknowledgement

The authors thank Mr. Sugawara for photography, Mr. Watanuki and Mr. Seo for PET operation, and to the staff of the Cyclotron and Radioisotope Center, Tohoku University, for their assistance. We also thank Dr. F. G. Issa (Word-Medex) for his assistance in reading and editing the manuscript. This work was supported by grants-in-aid (06454320, 06670899) from the Ministry of Education, Science and Culture, Japan.

References


Table 1. FDG or Met uptake by benign and malignant mediastinal tumors.

<table>
<thead>
<tr>
<th></th>
<th>Tumor DUR</th>
<th>Muscle DUR</th>
<th>T/M ratio</th>
<th>Glucose (mg/dl)</th>
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<tr>
<td><strong>FDG</strong></td>
<td></td>
<td></td>
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<tr>
<td>Malignant (10)*</td>
<td>7.15±2.27†</td>
<td>0.85±0.10‡</td>
<td>8.34±2.47†</td>
<td>101±9‡</td>
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<tr>
<td>Benign (12)</td>
<td>1.80±1.24</td>
<td>0.81±0.14</td>
<td>2.31±1.75</td>
<td>97±15</td>
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<tr>
<td><strong>Met</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Malignant (4)</td>
<td>6.31±2.33‡</td>
<td>0.89±0.05‡</td>
<td>7.19±2.93‡</td>
<td>95±10‡</td>
</tr>
<tr>
<td>Benign (3)</td>
<td>2.93±0.97</td>
<td>0.90±0.08</td>
<td>2.97±1.41</td>
<td>86±15</td>
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Mean±s.d. *: number of patients. Glucose: blood glucose level.
†: p<0.001 compared to benign tumors.
‡: not significant compared to benign tumors. (Students' t-test)
Fig 1. A typical FDG-PET image (a) and CT (b) of a thymic cancer. Forty to fifty min after injection of 4 mCi (148 MBq) of FDG, showing an increased FDG uptake by tumor (DUR: 7.22).

Fig 2. The distribution of DUR of FDG (left column) and Met (right column) in malignant (circle) and benign (triangle) primary mediastinal tumors. The standard deviation of muscle uptake of each tracer is shadowed in the graph.
Fig 3. The correlation of tumor DUR and tumor/muscle ratio using FDG (open symbol) and Met (closed symbol) in primary mediastinal tumors. The tumor/muscle ratio increased linearly with DUR (Y=1.08x+0.51, r=0.968, n=29, p<0.001).