Monitoring of Chemotherapy Response in Malignant Pleural Mesothelioma Using Fluorodeoxyglucose Positron Emission Tomography

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Abstract

We report a 56-year-old man who underwent monitoring of the response to chemotherapy of malignant pleural mesothelioma (MPM). 18F-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) and computed tomography (CT) were performed prior to chemotherapy and after the first and second courses of chemotherapy. The tumor lesion exhibited shrinkage on CT and a decrease in the standardized uptake value (SUV) max after the first course of chemotherapy, but exhibited size enlargement and an increase in SUV max after the second course of chemotherapy. These findings suggest that results of quantification of metabolic response by FDG-PET are related to the objective response as determined by CT in patients with MPM.

Key words: FDG-PET, mesothelioma, SUV, response

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Introduction

Malignant pleural mesothelioma (MPM) is an insidious neoplasm usually associated with asbestos exposure, with findings of malignant unilateral pleural effusion or increase in pleural thickness (1, 2). Currently, imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) are widely used for the evaluation of the effects of chemotherapy on thoracic tumors. However, it is sometimes difficult to evaluate the clinical response of MPM, since it exhibits a non-spherical growth pattern with irregular edges. On positon emission tomography (PET), altered glucose metabolism is visualized by the radiolabeled glucose analogue 18F-fluoro-2-deoxy-D-glucose (FDG). Evaluation of glucose metabolism using FDG-PET plays a critical role in early tumor diagnosis, staging, therapeutic strategy, and prediction of prognosis (3-6). FDG-PET imaging of responses to chemotherapy or irradiation has been found to be useful for patients with a variety of types of carcinomas (7, 8). However, few studies of MPM patients have been performed to assess the usefulness of FDG-PET for monitoring of responses to treatment (9, 10). We evaluated the role of FDG-PET in monitoring of responses to chemotherapy in a patient with MPM.

Case Report

A 56-year-old man non-smoker was referred to our medical center for further examination of massive pleural effusion in the right lobe on chest X-ray. He had complained of dyspnea on effort for the past 6 months, and had been diagnosed with tuberculous pleuritis. He had been treated with tuberculous drugs without improvement. His height was 162 cm and body weight 63.5 kg, and he had experienced no loss of body weight over the preceding 6 months. He had worked as a bus driver for 30 years without known asbestos exposure. Results of physical examination were nearly normal, without weakness of breath sounds in the right lung. Results of full hematological and biochemistry testing were all within normal limits, except for γGTP of 67 IU/L due to fatty liver. No elevation of CRP was found, and the tumor

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markers CEA, NSE, and pro-GRP were all within normal ranges, while CYFRA 21-1 was elevated to 6.7 ng/mL. A biopsy specimen obtained at admission from the chest wall revealed biphasic-type MPM. Thoracic drainage of pleural effusion was performed, and pleurodesis with OK-432 was performed. Pleural thickening was noted in the upper right hemithorax on chest computed tomography (Fig. 1a).

FDG-PET scanning was performed as a part of a study of the usefulness of functional imaging of MPM at Osaka City University Hospital (Osaka, Japan) (11) FDG-PET imaging and CT scanning were performed prior to chemotherapy, as well as after the first and second courses of chemotherapy, with written informed consent. FDG-PET images were compared with the corresponding CT images, permitting accurate identification of tumors by anatomical landmarks. For quantitative evaluation, a region of interest (ROI) (circle 6 mm in diameter) was placed on the area of maximum FDG uptake within the lesion. A background ROI was then placed on a non-tumorous region of the lung. The standardized uptake value (SUV), a quantitative measurement of activity in the ROI, was determined using the following formula:

\[
SUV = \frac{\text{Radioactivity Concentration in ROI (Bq/mL)}}{\text{Injected dose (Bq)/body weight (g)}}
\]

He received chemotherapy with cisplatin and irinotecan. Severe diarrhea then developed due to irinotecan, and he received a different chemotherapy regimen including cisplatin and docetaxel as a second course. The tumor lesion exhibited shrinkage on CT and a decrease in SUV max after the first course of chemotherapy (Fig. 1b), but size enlargement and an increase in SUV max after the second course of chemotherapy (Fig. 1c). The progression-free survival and the overall survival were 90 days and 320 days, respectively.

| SUV max | Modified RECIST |
|---------|----------------|
| 3.78    | 10.38          |
| 2.47    | 6.45           |
| 3.67    | 10.08          |

**Figure 1.** CT and PET monitoring prior to chemotherapy (a), after the first course of chemotherapy (b), and after the second course of chemotherapy (c). Arrows show the target lesions.

**Discussion**

This case shows some technical problems to measure sizes of tumors in determining the response to chemotherapy. Cross-sectional CT or MR images seem to be inappropriate to measure the size of these nonspherical tumors such as mesothelioma. Response evaluation criteria in solid tumor (RECIST) criteria determine the method of measuring the longest diameter of tumor (12), but it has not been determined whether these methods are appropriate or not. Recently, modified RECIST criteria were reported (13). Modified RECIST criteria determine the method of measuring tumor thickness perpendicular to the chest wall or mediastinum in these nonspherical tumors. The present findings suggest that the results of quantification of metabolic response by FDG-PET may be related to objective response as determined by modified RECIST in patients with MPM.

FDG-PET studies have been performed to assess various types of tumors after treatment (7, 8). These studies reported that SUV can be used to predict the eventual response to a particular therapeutic regimen. A correlation between SUV and prognosis has also been demonstrated. FDG-PET imaging is now highly accurate and reliable in differentiating malignant from benign pleural effusion and/or involvement (14). With a SUV cutoff of 2.0 to differentiate malignant from benign disease, a sensitivity of 91% and specificity of 100% were achieved, although the activity in some epithelial mesotheliomas tended to be close to this threshold (15). In our study, a total of 11 patients with MPM were treated, with a median overall survival time of 6.4 months. The mean pretreatment SUV of lesions was 3.71±1.49 SD. When the SUV cut-off was set at 2.0, sensitivity was 93.9%. Interestingly, the SUVs of 12 lesions of 4 patients, which exhibited no change in size, were significantly decreased from
Because tumors have heterogeneous biological activity in single tumors, SUV max indicates the metabolic activity of the most malignant part of the tumor. There is no evidence that SUV max represents the biological nature of whole tumor and the clinical utility of SUV max as a monitoring method for the response to chemotherapy. It is necessary to conduct clinical studies with a large number of patients in order to determine the usefulness of FDG-PET as a monitoring method of response to chemotherapy. A few studies in patients with MPM have been performed to assess the usefulness of FDG-PET for monitoring the response to treatment (9, 10). One of the differences between them and the present study is the timing of FDG-PET assessments after chemotherapy to evaluate metabolic responses. Steinert et al performed assessments after three cycles of chemotherapy, and reported that total lesion glycolysis (TLG), defined as (SUV max) × (Vol), more accurately identified patients responding or not to chemotherapy, and that PET and CT examinations may play important roles in the management of patients with MPM. Ceresoli et al measured CT and PET responses after two cycles of chemotherapy, and found that the early metabolic response was significantly correlated to the median time-to-tumor progression, and tended to be associated with a longer overall survival. Thus, the best time for early evaluation of metabolic response by FDG-PET in patients with MPM remains to be clearly determined.

Our findings have certain limitations. Three-dimensional volume measurement method may be required to determine the correct volume of the tumors in each situation. It is difficult to obtain cytological and histological materials from patients with MPM from multiple lesions at multiple time points with histological confirmation of metabolic response. In addition, FDG-PET has been reported to yield false-negative results for lesions smaller than 1 cm and false-positive results for lesions with inflammatory change (8). With the current state of technology, it is impossible to detect small clusters of tumor cells that will cause a clinically detectable recurrence of disease in the future (16). It also is important to realize that SUV are not strictly quantitative and repeated biopsies are sometimes required (17). The information derived from FDG-PET during treatment may need to be assessed based on standard follow-up procedures. The final interpretations of images are based on total analysis and not the SUV alone (18).

In conclusion, we have presented the use of FDG-PET for the monitoring of the response to chemotherapy in a patient with MPM. These findings suggest that FDG avidity, which reflects tumor activity, is related to the chemotherapy response determined by CT in patients with MPM.

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