

Usefulness of ^{18}F -FDG positron emission tomography/computed tomography for the diagnosis of pyothorax-associated lymphoma: A report of three cases

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Abstract. Pyothorax-associated lymphoma (PAL) is a unique and rare non-Hodgkin's lymphoma developing in the pleural cavity following a long-standing history of chronic pyothorax (CP). The development of F-18 2'-deoxy-2-fluoro-D-glucose (FDG) positron emission tomography combined with computed tomography (PET/CT) has contributed to the evaluation of lymphoma staging. However, only a few studies describing FDG-PET/CT findings in PAL have been published. This study reported three cases of PAL; all 3 patients had previously undergone artificial collapse therapy for pulmonary tuberculosis. Both the first case (an 84-year-old male) and second case (an 83-year-old male) complained of abdominal pain. An ultrasound scan revealed a mass shadow in the left chest wall without abnormal findings in the abdomen, and the CT and magnetic resonance imaging scans suggested malignant lymphoma of the left chest. FDG-PET/CT imaging showed extremely intense FDG uptake only in the left pleura and chest wall. Diagnosis was CP in the two patients, showing a high maximum standardized uptake value (SUV_{max}: early, 14.8 and delayed, 19.4 in the first case; early, 20.8 and delayed, 27.3 in the second case, respectively). Histopathological analysis of the specimens obtained by biopsy of the PET/CT-positive pleural mass showed non-Hodgkin's, diffuse large B cell lymphoma in the two cases. The third case was a 79-year-old male with relapse after right pleuropneumectomy for PAL (diffuse large

B cell lymphoma) 4 years earlier. PET/CT showed intense FDG uptake (SUV_{max}: early, 19.9 and delayed, 35.7) in the right pleura and chest wall. Diagnosis was CP, suggesting the recurrence of PAL. Furthermore, abnormal intense FDG uptake was noted in the hilar, mediastinal and supraclavicular lymph nodes, as well as in the spleen. In conclusion, FDG-PET/CT imaging is useful in the evaluation of the area of invasion in PAL.

Introduction

Pyothorax-associated lymphoma (PAL) is a unique and rare disease involving malignant lymphoma. PAL appears in the pleural cavity with chronic pyothorax (CP) following artificial collapse therapy for pulmonary tuberculosis (1,2). Lymphoma comprises Hodgkin's and non-Hodgkin's types. PAL is a non-Hodgkin's lymphoma developing in the pleural cavity after a long-standing history of CP, and is strongly associated with Epstein-Barr virus (EBV) infection (3). It has been reported that approximately 90% of the cases are diffuse large B cell lymphoma and that the 5-year survival rate is approximately 20% (1). It is crucial to evaluate the area of invasion in PAL, which may determine the appropriate treatment, such as surgery, chemotherapy, irradiation and best supportive care. However, conventional imaging modalities cannot provide sufficient information for an accurate diagnosis of PAL (4).

The development of the new modality of F-18 2'-deoxy-2-fluoro-D-glucose (FDG) positron emission tomography combined with computed tomography (PET/CT) has contributed to the evaluation of human cancer. Additionally, the usefulness of FDG-PET/CT for lymphoma staging is well established (5,6). However, few studies exist describing FDG-PET/CT findings in PAL (7). This study reported three patients with PAL, who had previously undergone artificial collapse therapy for pulmonary tuberculosis. The first two cases involved initial occurrences, and the last case showed recurrent disease following right pleuropneumectomy for PAL. FDG-PET/CT imaging revealed a unique intense uptake of FDG in the area of CP and in the lymphatic and systemic metastatic lesions.

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Therefore, the usefulness of FDG-PET/CT imaging to evaluate the area of invasion in PAL was examined.

Patients and methods

This study was performed with informed consent of the patients and with approval of the Ethics Committee of the Tokorozawa PET Diagnostic Imaging Clinic.

Case 1

An 84-year-old male complaining of abdominal pain consulted the M Clinic in Tokyo. An ultrasound study revealed a mass shadow in the left chest wall without abnormal findings in the abdomen. CT and magnetic resonance imaging scans suggested malignant lymphoma of the chest. A physical examination showed no apparently abnormal findings or signs of systemic lymphadenopathy other than a mass in the left chest wall. Blood analysis showed an elevated serum interleukin-2 receptor (IL-2R, 1,560 Ug/ml) without other abnormalities, including tumor markers such as carcinoembryonic antigen (CEA) and CA19-9. The patient had previously undergone left artificial collapse therapy for pulmonary tuberculosis at the age of 20.

¹⁸F-FDG PET/CT scans were obtained using a Biograph Duo (Siemens CTI) at the Tokorozawa PET Diagnostic Imaging Clinic, as described in our previous study (8,9). To determine semi-quantitative FDG uptake, regions of interest (ROIs) were placed over the lesion, including the highest uptake area (circular ROI, 1 cm in diameter), and the standardized uptake value (SUV) was calculated. Early PET/CT showed intense abnormal FDG uptake only in the left pleura and chest wall, suggesting CP (SUVmax, 14.8) (Fig. 1A and B). A delayed scan showed a more intense FDG uptake (SUVmax, 19.4) in CP. No areas, other than CP, showed an abnormal uptake of FDG. The PET/CT findings strongly suggested malignancy of the chest wall without lymphatic or systemic metastasis.

Histopathological examination was performed, and the biopsy specimens were obtained from the PET/CT-positive pleura. A microscopic examination showed a diffuse infiltrative growth of the large atypical lymphoid cells (Fig. 1C). The lymphoid cells contained irregular nuclei. Immunohistochemical analysis showed that the neoplastic cells were positive for LCA (CD45RO), CD79a (Fig. 1D), CD20 and BCL-2. The neoplastic cells were also positive for LMP-1, suggesting EBV infection. Histopathological examination confirmed the diagnosis as non-Hodgkin's, diffuse large B cell lymphoma. Due to poor general condition, the patient received best supportive care without chemotherapy or surgery despite the localized lesion of PAL.

Case 2

An 83-year-old male complaining of abdominal pain presented at the Tokorozawa Clinic in Saitama. An ultrasound study revealed a mass shadow in the left chest wall without abnormal findings in the abdomen. A physical examination showed no apparently abnormal findings or signs of systemic lymphadenopathy other than the mass of the left chest wall. Blood

analysis showed elevation of the serum IL-2R (634 Ug/ml) and neuron-specific enolase (58 ng/ml). The patient had previously undergone left artificial collapse therapy for pulmonary tuberculosis at the age of 24.

¹⁸F-FDG PET/CT scans were obtained in our PET clinic. Early PET/CT showed intense abnormal FDG uptake only in the left pleura and chest wall, suggesting CP (SUVmax, 20.8) (Fig. 2A and B). A delayed scan showed a more intense FDG uptake (SUVmax, 27.3) in the CP. No areas, other than CP, revealed an abnormal FDG uptake. The PET/CT findings strongly suggested malignancy of the chest wall without lymphatic or systemic metastasis. An MRI scan showed high signal-intensity on T2-weighted images in the left chest, suggesting CP, as well as moderate signal-intensity around the CP, which was consistent with malignant lymphoma (Fig. 2C).

Histopathological examination was performed on biopsy specimens obtained from the PET/CT-positive pleura. This examination confirmed the diagnosis as non-Hodgkin's, diffuse large B cell lymphoma. The patient received chemotherapy (R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) despite the localized lesion of PAL, following the patient's request for non-surgical treatment.

Case 3

A 79-year-old male complaining of chest pain presented at the Kyosai Tachikawa Hospital in Tokyo. He had previously undergone right artificial collapse therapy for pulmonary tuberculosis at the age of 24. Fifty years later, he was diagnosed with PAL, diffuse large B cell lymphoma and was treated with right pleuropneumectomy. At the present examination, a blood analysis showed elevation of the serum IL-2 receptor (2,360 U/ml), suggesting a relapse of PAL. Gallium-67 (⁶⁷Ga) scintigraphy showed a faint level of abnormal uptake in the chest (Fig. 3A). Histopathological examination of specimens obtained from the pleural mass showed diffuse large B cell lymphoma, and the patient was diagnosed as having a recurrence of PAL.

Early ¹⁸F-FDG PET/CT showed intense abnormal FDG uptake in the right pleura and chest wall, suggesting CP (SUVmax, 19.9) (Fig. 3B-E). Abnormal intense FDG uptake was also noted in the hilar, mediastinal, supraclavicular and abdominal lymph nodes, as well as in the spleen. A delayed scan showed a more intense FDG uptake (SUVmax, 35.7) in the CP. The patient received chemotherapy (R-CHOP) numerous times, but finally refused to receive further chemotherapy.

Discussion

PAL is a non-Hodgkin's lymphoma that develops in the pleural cavity following a long-standing history of CP. It is known that approximately 90% of PAL cases involve diffuse large B cell lymphoma, and that the 5-year survival rate is approximately 20% (1). Standard treatment for PAL has yet to be established, although the prognosis is poor. Certain studies have described PAL cases in which surgery was performed (10,11). It is essential that the area of invasion in PAL be evaluated, since it may determine the appropriate choice of therapy, including surgery, chemotherapy, irradiation and best supportive care. However, conventional imaging

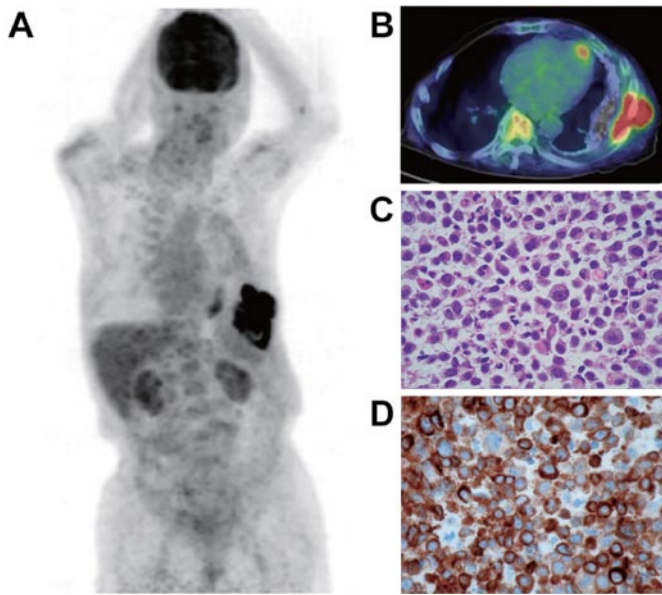


Figure 1. (A and B) PET/CT of case 1 shows intense abnormal FDG uptake only in the left pleura and chest wall, showing chronic pyothorax (SUVmax, 14.8). (C) Microscopic examination shows a diffuse infiltrative growth of large atypical lymphoid cells. The atypical lymphoid cells contain irregular nuclei. (D) Immunohistochemical analysis shows neoplastic cells positive for the CD79a antigen. Magnification, x100.

modalities cannot provide sufficient information for the accurate diagnosis of PAL (4).

The development of FDG-PET/CT contributes to the evaluation of human cancer staging. Moreover, the usefulness of PET/CT is well established for lymphoma staging (5,6). However, only one study on PET findings in PAL has been published, by Asakura *et al* (7). These authors reported a PAL case in which the FDG-PET finding determined the area of

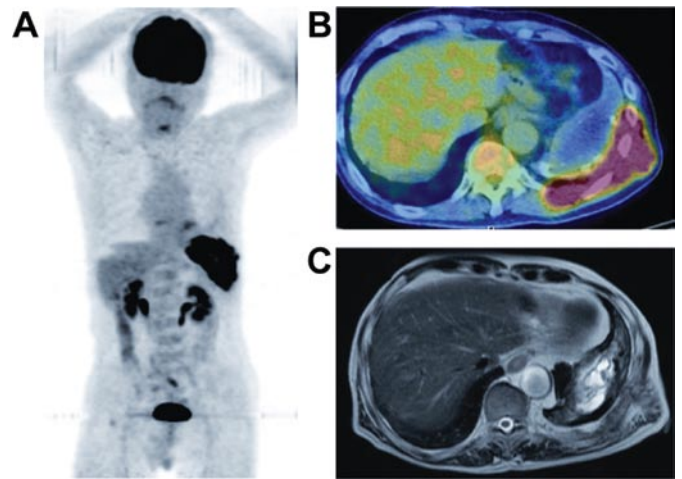


Figure 2. (A and B) PET/CT of case 2 shows intense abnormal FDG uptake in the left pleura and chest wall of chronic pyothorax (CD) (SUVmax, 20.8). (C) MRI shows high signal-intensity on T2-weighted images in the left chest, suggesting CP. A moderate signal-intensity on T2-weighted images around the CP is shown, which is consistent with malignant lymphoma.

PAL invasion and provided useful information for the planning of radiotherapy. We presented three cases of PAL, two of which showed initial occurrence and one recurrent case. The PET/CT scan showed intense FDG uptake only in the chest wall in the two cases showing initial occurrence of PAL. In these cases, the area of invasion determined by the PET/CT scan contributed to decisions regarding PAL treatment.

In the recurrent case of PAL, the PET/CT scan showed intense FDG uptake, not only in the chest wall, but also in the lymphatic and systemic metastatic lesions. On the other hand, ⁶⁷Ga scintigraphy showed a faint level of abnormal uptake

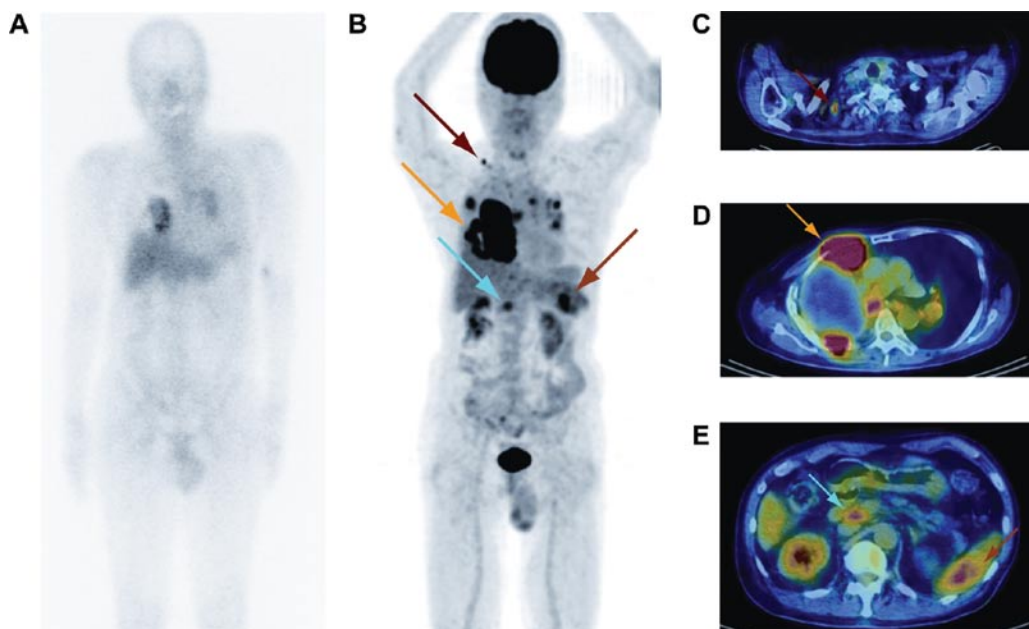


Figure 3. (A) Gallium-67 (⁶⁷Ga) scintigraphy of case 3 shows a faint level of abnormal uptake in the chest. (B-E) PET/CT shows intense abnormal FDG uptake in the right pleura and chest wall demonstrating chronic pyothorax (yellow arrow: SUVmax, 19.9). Abnormal intense FDG uptake is also noted in the hilar, mediastinal and supraclavicular (red arrow) and abdominal lymph nodes (blue arrow), as well as in the spleen (orange arrow).

only in the chest. Certain studies have shown the usefulness of ^{67}Ga scintigraphy in the diagnosis and assessment of the effects of treatment (4,12). However, our case showed that FDG-PET/CT imaging is a more reliable and sensitive method for staging and monitoring therapy as opposed to ^{67}Ga scintigraphy in cases of PAL, which is in agreement with Kostakoglu *et al* (13). Zinzani *et al* performed an extensive analysis of the reliability of PET after induction treatment in patients with Hodgkin's disease and aggressive non-Hodgkin's lymphoma. Findings of these authors showed that there were no false-negative results among 75 PET scans performed in that study (14).

PAL is a non-Hodgkin's lymphoma that develops in the pleural cavity following a long-standing history of CP, and is strongly associated with EBV infection. In our first case, histopathological analysis showed that the neoplastic cells were positive for LMP-1, suggesting an association with EBV infection. Takakuwa *et al* reported that the downregulation of EBV nuclear antigen-2 expression may be a selection pressure for the progression of PAL (3).

In conclusion, we report three cases of PAL that showed a high FDG uptake in the lesions of PAL on the FDG-PET/CT scan. FDG-PET/CT imaging is therefore useful in the evaluation of the area of invasion, facilitation of treatment planning, as well as the assessment of treatment response in PAL.

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