Monitoring Therapeutic Response in a Case of Extrapulmonary Tuberculosis by Serial F-18 FDG PET/CT

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Abstract Due to the low yield of AFB smear and culture in extrapulmonary tuberculosis, therapeutic responses of patients with extrapulmonary tuberculosis are usually monitored clinically and/or radiographically. Such monitoring techniques, however, are not enough to provide effective diagnosis if a remnant lesion exists after treatment. Tuberculosis presents hypermetabolic activity on F-18 fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT) scanning. Reported herein is a case of extrapulmonary tuberculosis where the therapeutic response was assessed via serial F-18 FDG PET/CT scanning, which was useful for detecting the extent of extrapulmonary tuberculosis and for estimating the patient's therapeutic response.

Keywords Extrapulmonary tuberculosis · F-18 FDG PET/CT · Tuberculosis

Introduction

The treatment strategy of extrapulmonary tuberculosis is principally the same as that of pulmonary tuberculosis, and the treatment duration and decision whether to use steroid depend on the individual patient and the invaded organs [1]. For all types of tuberculosis, assessment of the treatment

response is required. In the case of extrapulmonary tuberculosis, clinical or radiographical assessment of the treatment response is generally performed, but those approaches serve a limited role if remnant lesion exists [1–3]. F-18 fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT), well known for usefulness in assessing malignant tumors, can yield positive results for inflammation sites such as those caused by tuberculosis [4]. The usefulness of F-18 FDG PET/CT in the assessment of the activity of extrapulmonary tuberculosis and of the patient's treatment response was recently reported [5, 6].

A 23-year-old female patient presented a palpable mass on her right flank, which occurred 1 month after the completion of treatment for tuberculous pleurisy. F-18 FDG PET/CT was used for the assessment of the extent of tuberculous abscess before the treatment and for completion of anti-tuberculous treatment. The details of the case are reported herein.

Case Report

A 23-year-old woman presented persistent cough and pain in her right chest, which began 1 month before her presentation. The patient had no particular predisposing factors or family history, and her vital signs measured at the time of presentation were stable: blood pressure, 120/80 mmHg; pulse rate, 88 bpm; body temperature, 36.5°C; respiratory rate, 18 breaths/min. The physical examination revealed no particular findings.

The blood test that was performed at the time of the patient's presentation showed no abnormal parameters. The chest radiography showed costophrenic angle blunting on the right side (Fig. 1). In the diagnostic test of the pleural fluid, the adenosine deaminase (ADA) and mycobacterium tuberculosis polymerase chain reaction (M.Tb PCR) tests could not be performed because the amount of pleural fluid was

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too small. The pleural fluid had an appearance of exudate, with pleural-fluid protein and LDH levels of 5.2 (normal range 1.0–3.0) and 492 IU/l, blood protein and LDL levels 7.5 (normal range 5.8–8.1) and 332 (normal range 233–497). The result of the tuberculin skin test was positive. After the clinical diagnosis with tuberculous pleurisy, a four-drug therapy consisting of anti-tuberculosis treatment (isoniazid, rifampin, ethambutol and pyrazinamide) was initiated. Six months later, the right-sided pleural effusion had disappeared (Fig. 1), and the treatment was completed.

Three weeks later, however, the patient presented again to an outpatient clinic with swelling on her right flank. There was a 10-cm palpable mass on the right flank. No heat sensation or flare was detected in the mass, which was softly but tenderly indented. Abdominal computed tomography (CT) was performed and revealed an approximately 20-cm-diameter, thick-walled septated fluid collection with invasion of the right psoas, right quadratus lumborum and right back muscles (Fig. 2). Ultrasonography-guided tube drainage was performed at the right flank site. The aspirated fluid showed that the ADA level was 428.6 U/l (normal range 5–23) and that M.Tb PCR was positive. The AFB culture result showed the *Mycobacterium* species. To examine the extent of disease, F-18 FDG PET/CT was performed using a PET/CT scanner (Discovery ST, General Electric Medical Systems, Milwaukee, WI). After the patient had fasted for at least 8 h, the approximate blood glucose level was checked (<140 mg/dl). Then the patient was injected with 5.18 MBq of FDG per kilogram of body weight, and images were acquired 50 min later. CT was performed for attenuation correction, and subsequently, emission scanning was performed from the skull base to the proximal thigh. Images were reconstructed using an iterative algorithm (ordered subset expectation maximization). To quantify FDG uptakes, standardized uptake values (SUVs) were calculated as follows: $SUV = [\text{decay-corrected activity (kBq)} / \text{milliliter of tissue volume}] / [\text{injected FDG activity (kBq)} / \text{body mass (g)}]$.

Fig. 1 Chest X-ray shows blunting of right costophrenic angle, suggesting pleural effusions (a), and follow-up chest X-ray shows improvement (b)

Fig. 2 Pre-treatment abdominal CT shows lobulated, margined, thick-walled fluid collection (longitudinal diameter: up to 20 cm) invading the right psoas and quadratus lumborum muscles as well as the entire right back muscle (a), and 6 months after treatment abdominal CT shows residual small-sized abscess pockets along right psoas muscle (b). Finally, 9 months after treatment, abdominal CT no longer shows cold abscesses along right psoas muscle but still shows shrunken residual skin track (c)

In PET/CT images, irregular increased FDG uptakes with maximum SUVs ranging from 6.8 to 9.0 were observed along the inside septum, including the wall of the lobule, and intense hypermetabolism with a maximum SUV of 10.5 was observed at the origin of the mass, the retrohepatic area. There was no specific FDG uptake in the right pleural space (Fig. 3). Since this occurred shortly after finishing standard anti-tuberculous treatment for the tuberculous pleurisy, second line anti-tuberculous treatment (amikacin, cycloserin, prothionamide, levofloxacin, pyrazinamide, ethambutol) was initiated considering the possibility of resistance to the prior treatment.

One month after the start of the treatment, the patient developed hearing impairment, which was confirmed by audiometry. According to the audiometry results, amikacin was discontinued, and the hearing impairment disappeared. The rapid mycobacteria drug susceptibility test of the aspirated fluid showed sensitivity to isoniazid and rifampin. Thus, isoniazid and rifampin were added to the previous regimen until the definite drug susceptibility test result could be obtained. However, the result of the definite drug susceptibility test did not become available because of the lack of growth of the referred mycobacterial colonies. Considering that the disease was responsive to the treatment and the result of the rapid drug susceptibility test, a switch to four-drug therapy (isoniazid, rifampin, ethambutol, and pyrazinamide) was made.

Fig. 3 Pre-treatment F-18 FDG PET/CT images show irregular increased FDG uptakes (arrowhead) with maximum SUVs ranging from 6.8 to 9.0 along the inside septum including the wall of the lobule in the lesion of the right back muscle. In the retrohepatic area

with the starting site of the tissue lesion, irregular and intense hypermetabolisms (arrow) with maximum SUV of 10.5 can be seen [(A) maximum intensity projection image of PET, and from (a) to (e) fused PET/CT images]

Six months after the start of the retreatment, abdominal CT was performed, which showed that most lesions, including those of the skin tract, had decreased but still remained (Fig. 2). Thus, a decision was made to extend the treatment for 3 months. At 9 months after the start of the retreatment, F-18 FDG PET/CT was performed again, and the regional hypermetabolisms previously revealed had disappeared (Fig. 4). The patient now leads a normal life, with no particular recurrence after the completion of the treatment.

Discussion

F-18 FDG PET/CT can be useful for early detection and determination of the extent of inflammatory disease. The active tuberculous lesion sometimes consists of epithelioid cells, Langhans giant cells and lymphocytes, and an active tuberculous lesion, and appears to be proliferating. These cells exhibit increased glucose metabolism and intense FDG uptake [7–9]. Yago et al. [10] reported two patients with tuberculous cold abscesses, which have moderate uptake in the capsule and low in the center by FDG PET; they found that FDG uptake in tuberculosis lesions may vary depending on the grade of inflammatory activity of the lesion. F-18 FDG PET/CT also can be useful in evaluating fever of unknown origin using the properties of the test, not only showing the anatomical change but also the pathological metabolic activity of the tissues [11, 12].

And it is useful for evaluating the therapeutic response. As some tuberculous lesions do not diminish and instead grow larger despite treatment, whether the initial treatment failed should be determined. As the degree of metabolism of a lesion may indicate the response to antibiotic treatment, the degree of FDG uptake can represent the scale of the

chemical effect of tuberculosis treatment [13]. A lower FDG uptake indicates that the metabolism of the lesion has decreased, which in turn can be interpreted as the lesion being responsive to treatment, enabling the continuation of the treatment. In contrast, increased FDG uptake indicates that the metabolism of the lesion is still high despite the treatment, meaning that the lesion is not responsive to the current treatment, and as such, the treatment method needs

Fig. 4 Post-treatment maximum intensity projection image of F-18 FDG PET/CT shows hypermetabolic foci have disappeared including shrunken residual skin track

to be changed [14, 15]. Demura et al. [6] reported that in patients with pulmonary tuberculosis, F-18 FDG PET/CT was useful for examining the activity of the tuberculosis and for assessing the treatment response, while Park et al. [5] reported that based on the case where a decrease in FDG uptake was observed after treatment, F-18 FDG PET/CT was useful for the assessment of the treatment responses of tuberculoma patients.

Additionally, F-18 FDG PET/CT may have usefulness for evaluating remnant lesions after standard treatment duration. There are several reports on evaluating remnant lesions after cancer treatment [13, 14, 16]. Just like the advantages of evaluation remnant lesion in malignancy, F-18 FDG PET/CT may be useful to determine the extension of treatment duration in tuberculosis.

In the case reported herein, assessment of the treatment response was required to choose drugs and set up the treatment duration for extrapulmonary tuberculosis occurring within a short time after the completion of the primary treatment. As such, F-18 FDG PET/CT was performed before and after the treatment of extrapulmonary tuberculosis, and the treatment was completed after the confirmation that the FDG uptake had decreased and had eventually disappeared.

The existing test has a limitation in the assessment of the treatment response of extrapulmonary tuberculosis, whereas F-18 FDG PET/CT is believed to be useful for such purposes. Due to its high cost, the F-18 FDG PET/CT scan, however, is currently not widely used for treatment response assessment, but when the treatment response is unclear, such as in cases where a remnant or a new lesion is found after the recommended treatment period, F-18 FDG PET/CT can be considered an assessment option.

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