Lymphadenopathy by Scrub Typhus Mimicking Metastasis on FDG PET/CT in a Patient with a History of Breast Cancer

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Abstract We report the case of a 60-year-old woman with left-sided breast cancer who showed lymphadenopathy mimicking metastatic lesions. She underwent surveillance ^{18}F -fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) after treatment. PET/CT demonstrated multiple lymphadenopathies with increased FDG uptake, most notably in the right axilla. She had an eschar on the right axillary area, and her serologic test was positive for anti-*Orientia tsutsugamushi* IgM antibody. Ten months after the treatment, follow-up FDG PET/CT and ultrasonography showed improvement in generalized lymphadenopathy.

Keywords ^{18}F -fluorodeoxyglucose · PET · Scrub typhus · Lymphadenopathy

Introduction

Tsutsugamushi disease (also known as scrub typhus) is a febrile illness caused by *Orientia tsutsugamushi*. The diagnosis of scrub typhus is based on the patient's history of exposure, clinical features, and serologic testing [1]. Scrub typhus occurs over a wide area of eastern Asia and the western Pacific region [2]. Patients with scrub typhus usually have lymphadenopathy with tenderness in the region of the eschar and generalized lymphadenopathy is a common finding [2]. Furthermore, chest radiographic abnormalities [1, 3] and inflammatory changes with spleen enlargement [2, 4] were also observed in a previous case of scrub typhus.

Here, we report the case of a breast cancer patient with scrub typhus who showed lymphadenopathies with increased ^{18}F -fluorodeoxyglucose (FDG) uptake on positron emission tomography/computed tomography (PET/CT) mimicking metastatic lesions. To the best of our knowledge, this is the first report of a false-positive finding on FDG PET/CT images in a patient with scrub typhus. This case report was approved by the institutional review board of our medical center.

Case Report

A 60-year-old woman underwent lumpectomy of the breast, followed by adjuvant chemotherapy and radiotherapy with tamoxifen treatment for invasive ductal carcinoma of the left breast. Initial FDG PET/CT for breast cancer staging showed only a focal mild FDG uptake around the known malignant lesion involving the left breast parenchyma. No other lesion with abnormal FDG uptake was detected in the scanned areas.

Six months after the surgical resection of breast cancer, a surveillance FDG PET/CT was performed (Fig. 1). Adjuvant treatment had been completed before 2 months. At the time of the FDG PET/CT scan, the

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Fig. 1 The 6-month follow-up FDG PET/CT images after the lumpectomy of left breast cancer. Multiple enlarged and hypermetabolic lymphadenopathies were shown in the cervical chains, right axilla, and pelvic cavity on maximal intensity projection image (a) and transaxial PET/CT images (b) and (c). Further, the spleen had relatively higher metabolic

activity than the liver parenchyma without focal lesion. The US finding (d) demonstrated oval shaped lymph nodes with even cortical thickening which contains fatty hilum and normal hilar vessels, suggesting reactive hyperplasia

patients had mild fever with general weakness. On FDG PET/CT images, lymphadenopathies with intensely increased FDG uptake [maximum standardized uptake value (SUV_{max}) of 10.9] were detected in the right axilla, and generalized lymphadenopathy with mild-to-moderately increased FDG uptake was also detected. Furthermore, the spleen showed diffusely increased FDG uptake which was more intense than that in the liver without any focal lesion. These findings on PET/CT images were interpreted as generalized lymphadenopathy due to an inflammatory response, but metastatic lymphadenopathies were also suspected.

After the PET/CT scan, ultrasonography (US) was performed for assessing the right axillary lymphadenopathy. The results of the US showed multiple lymph nodes with even cortical thickening and preserved fatty hilum, suggesting reactive hyperplasia. The chest radiographic finding in the patient showed no significant abnormalities. The patient was a farmer who worked in the fields. She had no significant past medical history except for breast cancer, and she had not travelled abroad recently. On physical examination, an eschar was found in her right axilla with mild rash on her upper trunk. Laboratory studies revealed mildly elevated serum levels of aspartate aminotransferase (AST) at 65 IU/L, of alanine aminotransferase (ALT) at 45 IU/L, and of lactate dehydrogenase (LDH) at 274 IU/L. Further, serologic testing revealed a positive anti-*Orientia tsutsugamushi* IgM antibody level. The patient was subsequently diagnosed as having scrub typhus and was treated with doxycycline.

Ten months after the treatment for scrub typhus, the patient showed improvement in lymphadenopathy on follow-up FDG PET/CT (Fig. 2) and her US was unremarkable.

Fig. 2 The 10-month follow-up FDG PET/CT images after the treatment for scrub typhus. Multiple lymphadenopathies with increased FDG uptake disappeared, and FDG uptake of the spleen decreased to within the normal range

Discussion

Scrub typhus is an acute febrile disease caused by *Orientia tsutsugamushi* and transmitted to humans through the bite of mite. The disease is endemic in eastern Asia including Korea with 1 million new cases annually [2]. Clinical manifestations and laboratory findings of tsutsugamushi disease are non-specific, such as fever, cough, gastrointestinal symptoms, leukopenia and abnormal liver function tests. Therefore, the differential diagnosis of an acute febrile disease in endemic areas and the detection of a typical eschar are important factors for making a timely diagnosis [2]. The diagnosis of scrub typhus is based on a history of exposure, clinical features, and serologic test. In most patients, an important diagnostic clue is the presence of an eschar at the site of the mite bite. Our patient lived in a rural area of South Korea, where scrub typhus is pandemic, and the diagnosis in the patient was based on the presence of an eschar in the right axillary area and a positive serum test for anti-*Orientia tsutsugamushi* IgM antibody.

Our case demonstrated that increased FDG uptake in lymphadenopathies caused by scrub typhus can be misleading and may mimic metastatic lesions in patients with underlying malignancy. Our patient showed intense FDG uptake in her right axillary lymph nodes, the contralateral side to the previously treated breast cancer. Although contralateral axillary lymph node metastasis is uncommon in patients with breast cancer, with an incidence of between 3.6 and 6 % [5], metastatic lymphadenopathies were suspected because of the intense FDG uptake in her right axillary lymph nodes. However, regional and generalized lymphadenopathy is a common findings in inflammatory disease including scrub typhus [2]. Hence, when a patient with malignant disease shows multiple lymphadenopathies with increased FDG uptake, false-positive inflammatory lymphadenopathies including those in scrub typhus should be considered, especially in scrub typhus endemic areas. Further diagnostic work-up studies such as US are usually needed to confirm the diagnosis.

In our case, lymph nodes around the eschar site in the right axilla were especially enlarged and showed more intense FDG uptake than lymph nodes at other sites, suggesting an active immune response to the bite of a mite. Furthermore, increased FDG uptake in the spleen rather than in the liver was demonstrated. In normal subjects, FDG uptake in the spleen is less than that in the liver [6, 7], and, theoretically, increased FDG uptake in the spleen can be observed in many inflammatory conditions, suggesting immune system activation [8]. Splenomegaly is also a common radiologic finding in scrub typhus [2, 9]; however, our patient did not show an enlarged spleen

on CT images. In patients who show generalized lymphadenopathy and relatively increased FDG uptake in the spleen with regional lymphadenopathy with intense FDG uptake, scrub typhus should be considered along with other inflammatory diseases.

In conclusion, we report the first case of a breast cancer patient with scrub typhus who showed generalized lymphadenopathy with increased FDG uptake, concerning for metastatic lesions. Scrub typhus should be considered in the differential diagnosis of lymphadenopathies with increased FDG uptake in endemic areas.

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Conflict of Interest Jeong Won Lee, Sang Mi Lee, Kyu Taek Lee, Sung Young Kim, Sun Wook Han, Shin Young Kim declare that they have no conflict of interest.

Informed Consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000. The study design and exemption of informed consent were approved by the Institutional Review Board of Sooncheonhyang University Cheonan Hospital.

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