Hypermetabolic pulmonary and bone marrow lesions in a patient with chronic adult T-cell leukemia and description of this rare disease

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Abstract
A 69 years old woman with adult T-cell leukemia (ATL) (chronic type) was referred for a fluorine-18 fluorodeoxyglucose positron emission and computed tomography (^{18}F-FDG PET/CT). Multiple hypermetabolic pulmonary and bone lesions were evident. The patient underwent chemotherapy, but did not respond, and she died approximately 8 months from the onset of symptoms. Autopsy showed ATL cells infiltrating the lung parenchyma and the pulmonary hilum. *In conclusion*, we present a case of hypermetabolic pulmonary lesions associated with thoracic CT findings on a ^{18}F-FDG PET/CT scan in a patient with a chronic adult T-cell leukemia.

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Introduction

Fluorine-18 fluorodeoxyglucose positron emission tomography computed tomography (^{18}F-FDG PET/CT) has proven useful in staging, recurrence and therapeutic effect of blood disorders such as malignant lymphoma and multiple myeloma [1, 2]. Adult T cell leukemia (ATL) is an extremely rare hematological disease, associated with infection by the human T lymphotrophic virus type I (HTLV-1), which is endemic in southwestern Japan, Caribbean countries and South Africa; Unites States and Europe are considered low-risk areas [3]. There are limited literature data regarding ^{18}F-FDG PET/CT in relation to the aforementioned disease. We describe herein the case of pulmonary and bone involvement on the ^{18}F-FDG PET/CT scan in a patient with ATL.

Case presentation

A 69 years old woman with a recent diagnosis of ATL was referred to the department of hematology in our institution for further investigation and follow-up. As a bilateral reticular shadow appeared on the chest radiography, a pulmonary ATL involvement was suspected. Laboratory data showed an increased level of WBC [17100/mm3 (normal: 4000-9000)] and lymphocytosis (45%) on peripheral blood analysis. Levels of lactate dehydrohydroxygenase (LDH), soluble interleukin 2 receptor (IL2R) and C-reactive protein (CRP) were increased [LDH 465U/L, (normal: 119-229), IL2R 12385U/mL (normal: 220-530), CRP 2.56mg/dL (normal< 0.3)]. Serum albumin, blood urea nitrogen (BUN) were 3.81g/dL (normal: 4.0-5.0) and 12.0mg/dL (normal: 8-22), respectively. As for the rest of the laboratory analysis, (hemoglobin, red blood cells, platelets, liver and creatinine and electrolytes) there was within normal range and no abnormal findings were found on the clinical examination. Transbronchial lung biopsy (TBLB) and bronchoalveolar lavage (BAL) were negative for ATL cells. However, the level of CD4 cells was increased (CD4: 86.5%, CD8: 50.6%, CD4/8: 1.71). Fluorine-18-FDG-PET/CT was performed to determine initial staging for ATL before chemotherapy. An integrated full-ring PET/CT scanner (Gemini-GXL 16; Philips Medical Systems, Inc., Cleveland, OH, USA) was used for data acquisition. The patient fasted for 4h to maintain serum glucose concentrations below 120mg/dL (blood glucose level was 98mg/dL at the moment of injection). She was i.v. injected by 260MBq (4.4MBq/kg) of ^{18}F-FDG via the antecubital vein. Whole-body imaging was performed at approximately 60min after ^{18}F-FDG injection in the supine position, from the level of the auditory meatus to the mid-thigh. Computed tomography was used for attenuation correction of the PET. Images were reconstructed using the 3D line of response-row-action maximum likelihood algorithm (3D-LOR-RAMLA; Philips, Eindhoven,

The Netherlands). The total PET examination time for the whole-body images was approximately 30min. Multiple hypermetabolic foci of ^{18}F-FDG uptake were localized in bilateral lung fields, the hilar region and the skeleton (Fig. 1). The maximum standardized uptake values (SUV max) for both lung fields ranged from 2.06 to 5.46. On the CT image, ground glass attenuation (GGA), non-segmental consolidation, bronchovascular bundle thicking, and centrilobular nodules were bilaterally observed (Fig. 2). Bone marrow aspiration biopsy was performed at the iliac bone, and bone marrow was infiltrated by ATL cells. Therefore, ATL diagnosis with lung and bone involvement was established. LSG15 protocol [7] cycles of VCAP (vincristine, cyclophosphamide, doxorubicin and prednisone), AMP (doxorubicin, ranimustine and prednisone) and VECP (vindesine, etoposide, carboplatin and prednisone)] was considered, because LSG15 protocol improves the clinical outcome of ATL patients [4]. However, this patient hoped to receive chemotherapy in outpatients department after 1 cycle anticancer drug by hospitalization, and the patient underwent T-COP protocol (anthracycline, cyclophosphamide, vincristine, and prednisone) as first line chemotherapy. Unfortunately, her general condition and the conventional CT findings after 1 cycle TCOP chemotherapy were not improved. The disease response after 1 cycle T-COP therapy according to the Japan Clinical Oncology Group (JCOG) response criteria was: stable disease (SD) [5]. The patient was discharged from our hospital temporarily, and followed up in outpatients department. The values of IL2R, calcium, and LDH were increased after two cycles of T-COP treatment in outpatient department. The disease response after cycle 2 of T-COP treatment according to JCOG response criteria was: progressive disease (PD), because systemic bone destruction was progressed on CT image after cycle 2 of T-COP treatment [5]. The patient underwent second line chemotherapy with the LSG15 protocol. Unfortunately, a clinical progression under the second line chemotherapy was also observed and the patient died approximately 8 months after the onset of symptoms, due to septic shock and a dramatic deterioration of the respiratory function. Autopsy revealed many ATL cells infiltrating the lung parenchyma and the pulmonary hilum, confirming initial diagnosis (Fig. 3).

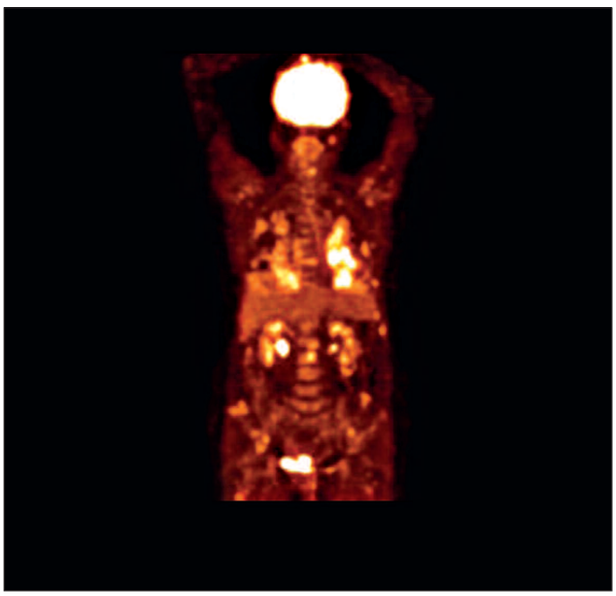

Figure 1. The MIP image of ^{18}F-FDG PET/CT evidencing multiple hypermetabolic foci of ^{18}F-FDG uptake on the lung parenchyma and the hilar region bilaterally, as well as the axial skeleton and the femoral bones.

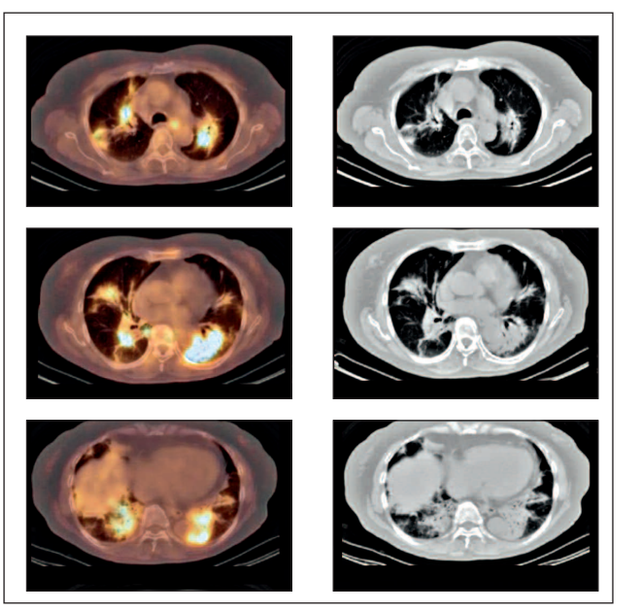

Figure 2. The CT images of PET/CT show ground glass attenuation (GGA), non-segmental consolidation, bronchiectasis, thickening of the bronchovascular bundle, and the centrilobular nodule in bilateral lung fields. Multiple hypermetabolic lesions are consistent with these CT findings.

Discussion

Adult T cell leukemia is classified into four subtypes: lymphoma type, acute type, chronic type, and smoldering type, and the frequencies of the four subtypes are as follows: acute type, 55%; lymphoma type, 20%; chronic type, 20%; and smoldering type, 5% [6]. A previous study, in which Japanese patients with ATL were followed for a maximum duration of 7 years, reported that the 4-year survival rates for acute, lymphoma, chronic, and smolding type were 5.0%, 5.7%, 26.9%, and 62.8% respectively, with the median survival time (MST) of 6.2 months, 10.2 months, 24.3 months and 5 years, respectively [6]. The chronic and smolding subtypes of ATL are considered indolent, and are usually managed with watchful waiting until disease progression to acute crisis. However, recently, Takasaki et al (2010) have suggested that the prognosis of indolent ATL was poor with the MST of 4.1 years, and the estimated 15 year overall survival rates were 14.1% [7]. Also, the survival rate and MST of smoldering subtype tend to be shorter than chronic subtype and transformation rate for acute crisis of smoldering ATL and chronic ATL were 60% and 40%, respectively [7]. Potential poor prognostic factors for chronic ATL were defined as those with at least one of the following 3 factors; low serum albumin, high LDH, and high BUN according to previous reports [8]. Thus, the patients with indolent type should be carefully observed in clinical practice. This patent had poor prognostic factors of chronic ATL because of low albumin

levels and high LDL levels, and his status was transformed to acute crisis. Upper GI tract endoscopy, with biopsy should be considered, because GI involvement is frequent in aggressive ATL [9]. The upper GI endoscopy was not done, however, the finding of ATL infiltration was not detected on both ^{18}F-FDG-PET/CT and autopsy.

To our knowledge, data concerning ^{18}F-FDG PET or PET/CT findings in patients with ATL are scarce, and the usefulness of ^{18}F-FDG PET/CT is not well established, although recommended and, if possible, even prior to treatment.

In a case report by Watanabe et al (2008), hypermetabolic lesions of ^{18}F-FDG were evidenced in the lymph nodes of the neck and the mediastinum, on the liver and subcutaneously (buttocks) [10]. Kako et al (2007) reported ^{18}F-FDG avid lesions in ATL patients, however, none of them had bone marrow involvement [11]. Feemey el al (2010) have evaluated nine ATL patients with hypermetabolic lesions, either at the time of initial staging or at relapse [12]. Three patients had ^{18}F-FDG avid cutaneous and subcutaneous lesions, eight had ^{18}F-FDG avid lymphadenopathy, and six patients had hypermetabolic extranodal diseases involving the spleen (n =3), bone (n = 2), and liver, nasopharynx, nose, lung, parotid glands (n =1) [6]. The mean SUV max values of these lesions were 15.5 (range: 2.3-14.8) [12]. Other researchers reported rare cases of cardiac and bone marrow involvement in ATL [13, 14]. We present a case with multiple hypermetabolic lesions (in the lung, the mediastinal hilar lymph node and the bone marrow). The ^{18}F-FDG PET/CT image of the combination of pulmonary and bone marrow involvement is quite rare. The SUV max for both lung fields of this case ranged from 2.06 to 5.46, which was lower than levels with Feemy et al (2010), because the mean value and the range of Feemy et al. was calculated from SUV max values of various lesions including pulmonary lesions [12].

Fluorine-18-FDG PET/CT was performed to determine the staging of ATL before T-COP chemotherapy. However, we could not perform ^{18}F-FDG PET/CT to evaluate the therapeutic effect of ATL, because ^{18}F-FDG PET/CT for evaluating the therapeutic effect of malignant tumor was out of insurance coverage in those days in Japan. Therefore, conventional CT was performed to evaluate the therapeutic effect of ATL.

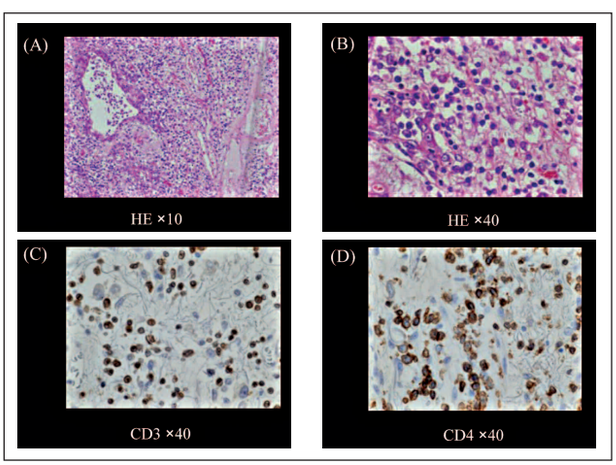

Figure 3. Hematoxlin-eosin staining shows high increased abnormal lymphocytes with cerebriform or flower-like nuclei in bilateral lung fields (A, B). Immunohistochemical staining was positive for both CD3 (C) and CD4 (D) and negative for CD 20 and CD8.

In the presented case, the morphological imaging findings on the pulmonary parenchyma were similar with those reported by Okada et al (2004) [15]. Differential diagnosis of pulmonary ATL involvement includes collagen-related lung disease, drug-induced lung injury and cryptogenic organizing pneumonia (COP). This patient had no history of either collagen disease or drug administration before symptom onset. Other differential diagnoses are hemorrhage and cytomegalovirus infection [15], however, findings suggestive of hemorrhage or cytomegalovirus infection were not observed.

In conclusion, the combination of bone marrow and pulmonary involvement on ^{18}F-FDG PET/CT image is quite rare case. Hypermetabolic pulmonary lesions associated with thoracic CT finding such as GGA, non-segmental consolidation, bronchovascular bundle thicking, and centrilobular nodules were considered to be pulmonary involvement in a patient with ATL.

The authors declare that they have no conflicts of interest.

Bibliography

1. Juweid ME, Stroobants S, Hoekstra OS et al. Imaging Subcommittee of International Harmonization Project in Lymphoma Use of positron emission tomography for response assessment of lymphoma; consensus of the imaging subcommittee of international harmonization project in lymphoma. *J Clin Oncol* 2007; 25: 571-8.
2. Aqurwal A, Chrindel A, Subramaniam RM. Evolving role of FDG PET/CT in multiple myeloma imaging and management. *Am J Roentgenol* 2013; 200: 884-90.
3. Gibbs WN, Lofters WS, Campbell M et al. Non–Hodgkin lymphoma in Jamaica and its relation to adult T-cell leukemia-lymphoma. *Ann Intern Med* 1987; 106: 361-8.
4. Tsurusaki K, Hermine O, Bazabachi A et al. Definition, prognostic factors, treatment, and response criteria of adult T-cell leukemia-lymphoma; A proposal from an international consensus meeting. *J Clin Oncol* 2009; 27: 453-9.
5. Tsurusaki K, Utsunomya A, Fukuda H et al. VCAP-AMP-VECP com pared with biweekly CHOP for adult T-cell leukemia-lymphoma; Japan Clinical Oncology Group Study JCOG 9801; *J Clin Oncol* 2007; 25: 5458-64.
6. Shimoyama M. Diagnostic criteria and classification of clinical subtype of adult T-cell leukemia-lymphoma; a report from the Lymphoma Study Group (1984-87). *Br J Haematol* 1991; 79: 428-37.
7. Takasaki Y, Iwanaga M, Imaizumi Y et al. Long term study of indolent adult T-cell leukemia-lymphoma. *Blood* 2010; 115: 4337-43.
8. Shimoyama M. Chemotherapy of ATL. In: Takatsuki K, Ed. *Adult T-cell Leukemia*. Oxford, United Kingdom: Oxford University Press; 1994: 221-37.
9. Utsunomiya A, Hanada S, Terada A et al. Adult T-cell leukemia with leukemia cell infiltration into the gastrointestinal tract. *Cancer* 1990; 65: 327-32.
10. Watanabe N, Murakami J, Kameda K et al. F-18 FDG-PET imaging in adult T cell leukemia lymphoma. *Clin Nucl Med* 2008; 33: 423-55.
11. Kako S, Izutsu K, Ota Y et al. FDG-PET in T-cell and NK-cell neo plasms. *Ann Oncol* 2007; 18: 1685-90.
12. Feemey J, Horwitz S, Gonen M et al. Characterization of T-cell lymphomas by FDG-PET/CT. *Am J Ronetogenol* 2010; 195: 333-40.
13. Nagayama H, Sueyoshi E, Hayashida T et al. Cardiac involvement of Adult T-cell leulemia/lymphoma. *Can J Cardiol* 2012; 28: 516.
14. Takahashi T, Tsukuda H, Ito H et al. Primary and isolated adult T-cell leukemia/lymphoma of the bone marrow. *Intern Med* 2011; 50: 2393-6.
15. Okada F, Ando Y, Kondo Y et al. Thoracic CT findings of adult T cell leukemia or lymphoma. *Am J Ronetogenol* 2004; 182: 761-7.