Early detection of intravascular large B-cell lymphoma by 18F-FDG-PET/CT with diffuse FDG uptake in the lung without respiratory symptoms or chest CT abnormalities

Masato Shiiba¹*, Koji Izutsu², Makiko Ishihara¹

¹ Department of Diagnostic Imaging Center, Toranomon Hospital, Tokyo, Japan
² Department of Hematology, Toranomon Hospital, Tokyo, Japan

ARTICLE INFO

Article type:
Case Report

Article history:
Received: 18 Dec 2013
Revised: 7 Feb 2014
Accepted: 10 Feb 2014

Keywords:
IVLBCL
Intravascular large B-cell lymphoma
FDG-PET
Diffuse lung uptake

ABSTRACT

Intravascular large B-cell lymphoma (IVLBCL) is a rare and aggressive subtype of systemic extranodal non-Hodgkin diffuse large B-cell lymphoma (DLBCL). We report a rare case of IVLBCL who showed diffuse 18F-fluorodeoxyglucose (FDG) uptake in the lung in FDG positron emission tomography/computed tomography (PET/CT) without respiratory symptoms or chest CT abnormalities. Serum biochemical studies showed a raised level of lactate dehydrogenase (LDH) and serum soluble interleukin-2 receptor (sIL-2R), which suggested the presence of malignant lymphoma strongly. A non-contrast CT showed no abnormalities in the lung fields, no lymphadenopathy was found. FDG-PET/CT revealed diffuse FDG uptake in the both lungs and in spleen as well as multiple hot spots in the liver. Under the suspicion of IVLBCL especially by the diffuse FDG uptake in the lung, a random skin biopsy was performed from three regions, the left forearm, right abdomen and left thigh in which there had been no evidence of FDG uptake. The definite diagnosis of IVLBCL was made based on the pathological analysis of the specimen from the left thigh. She achieved complete remission (CR) after combined chemoimmunotherapy. FDG-PET/CT was useful for the early detection of IVLBCL even without respiratory symptoms or any abnormal findings by chest CT.

Introduction

Intravascular large B-cell lymphoma (IVLBCL) is a rare subtype of systemic extranodal non-Hodgkin diffuse large B-cell lymphoma (DLBCL), occurring less than 1% of all lymphomas (1). IVLBCL is characterized by the proliferation of tumor cells restricted to the lumina of vessels, capillaries in particular as defined by World Health Organization published in 2008 whereas lymph nodes are typically spared (1).

This disease is aggressive and the clinical course is deleterious when the diagnosis and treatment are delayed although the definite diagnosis is difficult to make, often made antemortem period and autopsy (1). This is due in a large part to a variety of common symptoms resulting from occlusion of small vessels by tumor cells in various tissues. Because appropriate chemotherapy in the early stage of this disease is potentially effective, comparable to conventional DLBCLs (2), the early diagnosis is important.

Please cite this paper as:
Shiiba M, Izutsu K, Ishihara M. Early detection of intravascular large B-cell lymphoma by 18F-FDG-PET/CT with diffuse FDG uptake in the lung without respiratory symptoms or chest CT abnormalities. Asia Oceania J Nucl Med Biol. 2014; 2(1):65-68.
powerful functional imaging tool in the assessment of non-Hodgkin lymphoma (3). However there is paucity of reports on FDG-PET in IVLBCL.

We present here a case of IVLBCL who had no respiratory symptoms which could occur in the near future nor chest computed tomography (CT) abnormalities. Diffuse FDG uptake in the lung on FDG-PET/CT was helpful in the early diagnosis of IVLBCL.

Case Report

A 53-year-old woman was suspected a hematologic disease in a medical checking. She presented with nocturnal sweating 1 week before consulting. Her past and family history was unremarkable. Clinical examination was also unremarkable, lymphadenopathy was absent. Her hematological profile was as follows: hemoglobin: 10.4 g/dl, hematocrit: 30.9%, white blood cell count: 3.0 × 10³ per μl (neutrophils 57%, lymphocytes 26%, monocytes 9.5%, eosinophils 0.0% and basophils 0.0%), platelet count: 10.0 × 10⁴ per μl. Serum biochemical studies showed a raised level of lactate dehydrogenase (LDH): 849 U/L (normal range: 119-229 U/L) and serum soluble interleukin-2 receptor (sIL-2R): 2380 U/ml (145-519 U/ml), which suggested the presence of malignant lymphoma strongly.

A non-contrast enhanced CT of chest, abdomen and pelvis was performed, some low density areas in the liver and splenomegaly were detected and no lymphadenopathy was found. No abnormalities were detected in the lung fields, although high-resolution CT was not applied. FDG-PET/CT was undertaken within two weeks after CT, revealed diffuse FDG uptake in the both lungs and in spleen as well as multiple hot spots in the liver (Figure 1). She had fever up to 38°C the next day. Three days after PET/CT a random skin biopsy was performed from three regions, the left forearm, right abdomen and left thigh in which there had been no evidence of FDG uptake. The pathological analysis of the specimen from the left thigh showed the proliferation of large lymphoma cells in the lumina of small vessels and the tumor cells were positive for CD20, demonstrating origin from B-cell lineage (Figure 2). The definite diagnosis of IVLBCL was made based on the pathological result.

An R-CHOP chemotherapy regimen (Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone) was started immediately. She received two courses of high dose-methotrexate (HD-HTX) and Rituximab as prophylaxis for central nervous system relapse after total of six cycles of R-CHOP. FDG-PET/CT after these therapies demonstrated complete disappearance of all abnormal uptakes including the diffuse uptake in the lungs. She achieved complete remission (CR) (Figure 3).
IVLBCl FDG-PET  Shiiba M et al
Asia Oceania J Nucl Med Biol. 2014; 2(1):65-68.

Figure 3. Maximum intensity projection (MIP) image of FDG-PET after the completion of combined chemoimmuno-therapy. Abnormal FDG uptakes completely disappeared

Discussion
We reported a case of IVLBCl in whom abnormal FDG uptake was shown in the lung, spleen and liver. The diffuse lung uptake of FDG was especially suggestive of IVLBCl and she could be sent to random skin biopsy for definite diagnosis and prompt immunotherapy before emerging of respiratory or systemic symptoms.

To the extent of our search 15 case reports have been reported to date (4-18). Miura Y et al reported four patients with IVLBCl and another article reported four patients (19). In total, FDG-PET findings has been reported in 23 patients with IVLBCl and 11 cases (11/23, 47.8%) demonstrated diffuse FDG uptake in the lung (4-10). Among them, 6 cases were evaluated with chest CT too. Five of these patients (5/6, 83.3%) showed no apparent abnormalities in the lung fields similar to our case report. The other reported abnormal foci of FDG uptake were in the bone marrow (13/23, 57.0%), spleen (7/23, 30.0%), renal cortex (5/23, 22.0%), uterus/vagina (4/23, 17.4%), adrenals (3/23, 13.0%), lymph nodes (2/23, 8.7%) and stomach (1/23, 4.0%). This case report showed diffuse FDG uptake in the spleen and multiple FDG-avid lesions in the liver. Foci of FDG uptake in the reticuloendothelial systems may lead us to the possibility of IVLBCl.

In this case report no abnormal FDG uptake was detected in the cutaneous lesions, but it is reasonable to apply a random skin biopsy for the definite diagnosis of IVLBCl suggested by FDG-PET. The usefulness of random skin biopsy from unaffected skin for the definite diagnosis of IVLBCl has been proposed (20). Furthermore, Shimada et al reported that FDG-PET was able to detect only two of seven pathologically confirmed lesions (19). This suggests that the density of tumor cells might be lower than the detectability of PET imaging, but malignant cells could spread various organs without apparent signs of involvement.

In conclusion we reported a case of IVLBCl with diffuse FDG uptake in the lung without respiratory symptoms or chest CT abnormalities, which could be diagnosed early by a random skin biopsy and achieved CR with combined chemoimmunotherapy. FDG-PET provided an important information for recalling IVLBCl and could indicate random skin biopsy which could diagnose early, and lead to prompt chemotherapy, contributing to CR and long-term survival.

Acknowledgement
The authors have declared no conflicts of interest.

References
1. Orwat DE, Batalis NL. Intravascular large B-cell lymphoma. Arch Pathol Lab Med. 2012; 136(3): 333-8.
2. Masaki Y, Dong L, Nakajima A, Iwao H, Miki M, Kurose N, et al. Intravascular large B cell lymphoma: proposed of the strategy for early diagnosis and treatment of patients with rapid deteriorating condition. Int J Hematol. 2009; 89(5):600-10.
3. Shimada K, Kinoshita T, Naoe T, Nakamura S. Presentation and management of intravascular large B-cell lymphoma. Lancet Oncol. 2009;10(9):895-902.
4. Joshi PV, Lele VR, Shaikh I. Mortui vivos docent--the dead teach the living: 18-fluorodeoxyglucose positron emission tomography-computed tomography findings in a case of intravascular B cell lymphoma. J Cancer Res Ther. 2013;9(1):141-4.
5. Kitanaka A, Kubota Y, Imatoki O, Ohnishi H, Fukumoto T, Kurokohchi K, et al. Intravascular large B-cell lymphoma with FDG accumulation in the lung lacking CT/(67)gallium scintigraphy abnormality. Hematol Oncol. 2009;27(1):46-9.
6. Kohan AA, Paganimi L, Biedak P, Arma JI, Dalurzo MC, Garcia-Monaco RD. Pulmonary intravascular lymphoma detected by FDG PET-CT: a case report. Rev Esp Med Nucl Imagen Mol. 2013; 32(5):318-20.
7. Kotake T, Kosugi S, Takimoto T, Nakata S, Shiga J, Nagate Y, et al. Intravascular large B-cell lymphoma presenting pulmonary arterial
hypertension as an initial manifestation. Intern Med. 2010; 49(1):51-4.
8. Miura Y, Tsudo M. Fluorodeoxyglucose-PET/CT for diagnosis of intravascular large B-cell lymphoma. Mayo Clin Proc. 2010; 85(8):e56-7.
9. Wagner T, Brechemier D, Dugert E, Le Guellec S, Julian A, Hitzel A, et al. Diffuse pulmonary uptake on FDG-PET with normal CT diagnosed as intravascular large B-cell lymphoma: a case report and a discussion of the causes of diffuse FDG uptake in the lungs. Cancer Imaging. 2012; 12:7-12.
10. Yamashita H, Suzuki A, Takahashi Y, Kubota K, Kano T, Mimori A. Intravascular large B-cell lymphoma with diffuse FDG uptake in the lung by 18FDG-PET/CT without chest CT findings. Ann Nucl Med. 2012; 26(6):515-21.
11. Boslooper K, Dijkhuizen D, van der Velden AW, Dal M, Meilof JF, Hoogenberg K. Intravascular lymphoma as an unusual cause of multifocal cerebral infarctions discovered on FDG-PET/CT. Neth J Med. 2010; 68(6):261-4.
12. Hemmaway CJ, Danga A, Igbolowe U, Radunovic A. FDG-PET guided diagnosis of vaginal intravascular diffuse large B-cell lymphoma. Br J Haematol. 2012; 158(6):678.
13. Hoshino A, Kawada E, Urita T, Itoh K, Sakamoto H, Fujita K, et al. Usefulness of FDG-PET to diagnose intravascular lymphomatosis presenting as fever of unknown origin. Am J Hematol. 2004; 76(3):236-9.
14. Lannoo L, Smets S, Steenkiste E, Delforge M, Moerman P, Stroobants S, et al. Intravascular large B-cell lymphoma of the uterus presenting as fever of unknown origin (FUO) and revealed by FDG-PET. Acta Clin Belg. 2007; 62(3):187-90.
15. Nakazato T, Sanada Y, Mihiara A, Ito C, Aisa Y, Nakamura N. PET-negative pulmonary intravascular large B cell lymphoma diagnosed by a random transbronchial lung biopsy. Ann Hematol. 2012; 91(5):811-2.
16. Sanli Y, Turkmen C, Saka B, Kilicaslan I, Dogan O, Ertten N, et al. 18F-FDG PET/CT in a case of intravascular large B-cell lymphoma. Eur J Nucl Med Mol Imaging. 2010; 37(9):1801.
17. Takahashi T, Minato M, Tsukuda H, Yoshimoto M, Tsujisaki M. Successful treatment of intravascular large B-cell lymphoma diagnosed by bone marrow biopsy and FDG-PET scan. Intern Med. 2008; 47(10):975-9.
18. Takeoka Y, Inaba A, Fujitani Y, Kosaka S, Yamamura R, Senzaki H, et al. Intravascular large B-cell lymphoma diagnosed by FDG-PET/CT and endometrial biopsy. Rinsho Ketsueki. 2011; 52(11):1777-81.
19. Shimada K, Kosugi H, Shimada S, Narimatsu H, Koyama Y, Suzuki N, et al. Evaluation of organ involvement in intravascular large B-cell lymphoma by 18F-fluorodeoxyglucose positron emission tomography. Int J Hematol. 2008; 88(2):149-53.
20. Asada N, Odawara J, Kimura S, Aoki T, Yamakura M, Takeuchi M, et al. Use of random skin biopsy for diagnosis of intravascular large B-cell lymphoma. Mayo Clin Proc. 2007; 82(12):1525-7.