Respiratory Medicine Case Reports 29 (2020) 100999

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: http://www.elsevier.com/locate/rmcr

A case of lymphangioleiomyomatosis with diffuse large B-cell lymphoma: Usefulness of FDG-PET

Mami Orimo [a], Mitsuko Kondo [a,*], Kiyoshi Takeyama [a], Kenta Masui [b,c], Junji Tanaka [d], Etsuko Tagaya [a]

[a] Department of Respiratory Medicine, Tokyo Women's Medical University, Japan
[b] Department of Pathology, Tokyo Women's Medical University, Japan
[c] Department of Surgical Pathology, Tokyo Women's Medical University, Japan
[d] Department of Hematology, Tokyo Women's Medical University, Japan

ARTICLE INFO

Keywords:
Diffuse large B-cell lymphoma (DLBCL)
FDG-PET
Lymphangioleiomyomatosis (LAM)

ABSTRACT

Lymphangioleiomyomatosis (LAM) is characterized by cystic lung disease, abdominal tumor and involvement of the axial lymph nodes. We report a very rare case of LAM with malignant lymphoma. A 51-year-old female had medical history of recurrent pneumothorax and nephrectomy for a left renal angiomyolipoma and was diagnosed with LAM by video-assisted thoracoscopic surgery at the age of 30. She presented with left neck mass. Computed tomography and magnetic response imaging showed multiple enlarged cervical lymph nodes. ^{18}F-fluorodeoxyglucose-positron emission tomography (FDG-PET) showed abnormal uptake in the mass. We suspected a malignant tumor or extrapulmonary lesion of LAM, and performed surgical biopsy. Pathologically, diffuse large B-cell lymphoma was diagnosed, but LAM was not detected. After she received six cycles of R–CHOP chemotherapy, FDG-PET turned negative and complete metabolic response was achieved. As LAM is reported to be silent for FDG-PET, unusual uptake of FDG is useful for identifying other neoplasms. For this case, FDG-PET was useful for the differential diagnosis and therapeutic evaluation.

1. Introduction

Lymphangioleiomyomatosis (LAM) is a rare progressive multisystem disorder, occurs predominantly in women during childbearing years, and is characterized by proliferation of abnormal smooth-muscle-like cell (LAM cell) in the lung, kidney and axial lymph nodes. If the patient has extrapulmonary lesions, it would be difficult to distinguish LAM from other lymphoid disease including malignant lymphoma. As far as we know, there are only two reports of LAM complicated with malignant lymphoma [1,2]. Here, we report a rare case of LAM complicated with diffuse large B-cell lymphoma (DLBCL), in which ^{18}F-fluorodeoxyglucose-positron emission tomography (FDG-PET) was very helpful for the differential diagnosis and therapeutic evaluation.

2. Case report

A 51-year-old non-smoker Japanese female presented with a solitary subcutaneous mass on the left side of her neck over the last three months. She had a medical history of recurrent pneumothorax since the age of 21 and nephrectomy for a left renal angiomyolipoma at the age of 23. She was diagnosed as LAM by video-assisted thoracoscopic surgery at the age of 30. She had no other clinical features and family history of tuberous sclerosis (TSC) and was followed without treatment. On admission, she was afebrile, blood pressure 116/80 mmHg, pulse rate 111/min, respiratory rate of 15 times/min with O_2 saturation of 96% with room air. The cervical mass measured 4.5 × 4.5 cm and was mobile with a slight tenderness. A respiratory examination revealed rhonchi on both lungs. Initial investigation revealed a white cell count of 13,950/L, a C-reactive protein level of 8.57 mg/dL, LDH of 444 U/L and soluble IL-2 receptor of 755 U/mL. A chest computed tomography (CT) showed multiple, thin-walled cysts on both lungs (Fig. 1A). A neck CT showed multiple enlarged cervical and axillary lymph nodes. Magnetic resonance imaging (MRI) revealed well-defined mass, the content of which was hypointense in T1-weighted sequences (Fig. 1Ba) and hyperintense in T2-weighted sequences (Fig. 1Bb). ^{18}F-fluorodeoxyglucose-positron emission tomography (FDG-PET) showed uptake in the mass with a maximal standardized uptake value of 28.9 (Fig. 1C). We suspected malignant tumor or lymphatic involvements of LAM.

* Corresponding author. 8-1 Kawada-cho, Shinjuku-ku, Tokyo, 162-8666, Japan.
E-mail address: kondo.mitsuko@twmu.ac.jp (M. Kondo).

https://doi.org/10.1016/j.rmcr.2020.100999
Received 12 December 2019; Accepted 14 January 2020
Available online 16 January 2020

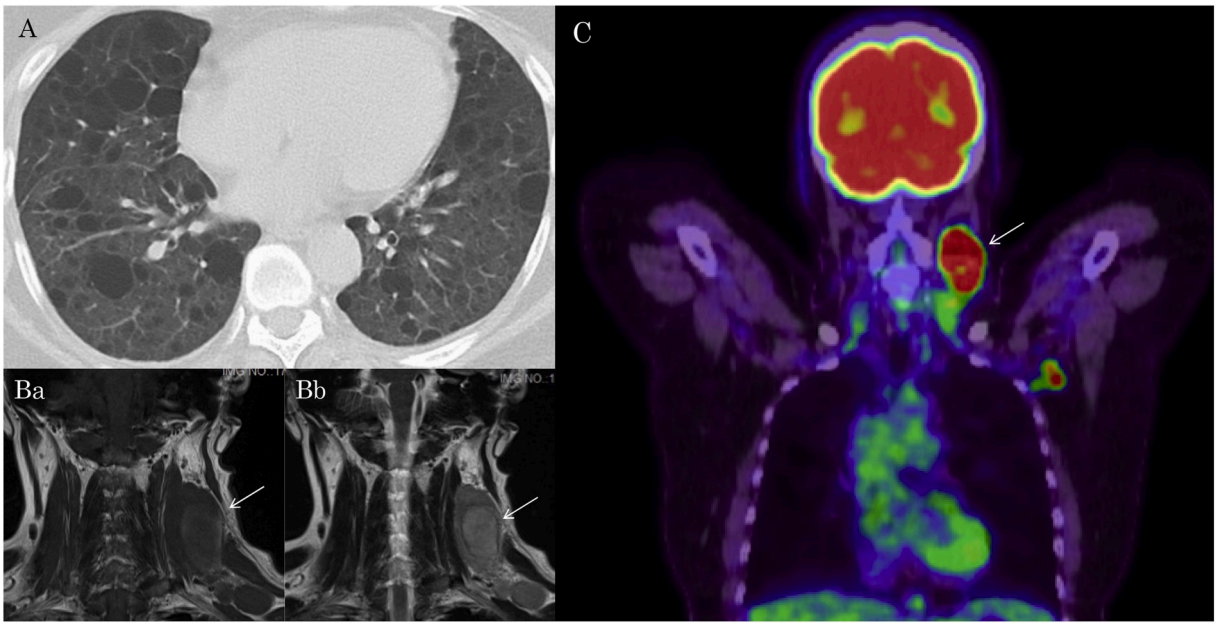

Fig. 1. Radiographic images of this case. (A) Chest CT finding. Diffuse thin-walled cysts are typical features of LAM. (B) Magnetic response images of the neck mass. The well defined mass (arrow) was hypointense in T1-weighted sequences (a) and hyperintense in T2-weighted sequences (b). (C) ^{18}F-fluorodeoxyglucose-positron emission tomography. Abnormal uptake was observed at the mass (arrow).

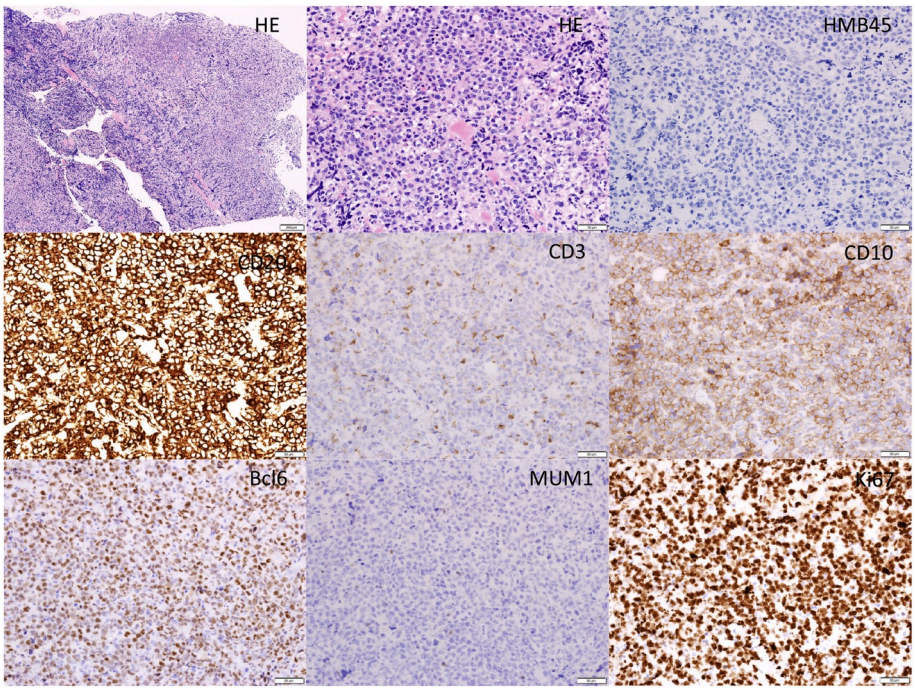

Fig. 2. Histological findings of the resected cervical mass. Atypical cells with high N/C ratio, large nuclei and clear cytoplasm proliferated diffusely. Tumor cells were immunopositive for leukocyte common antigen, CD20, CD10 and Bcl-6, but negative for HMB-45 and MUM-1. CD-3-positive small T lymphocytes were scattered. Around 70–80% of the tumor was classified as DLBCL, germinal center type.

We performed surgical biopsy. Histologically, the obtained specimen showed diffusely proliferating neoplastic lymphoid cells with high nucleocytoplasmic ratio, large nuclei and clear cytoplasm. These cells were immunohistochemically positive for CD45 (leukocyte common antigen), CD20, CD79a, CD10 and Bcl-6, but negative for pan-cytokeratin (clone AE1/AE3), epithelial membrane antigen (EMA), S-100 protein, melanosome-associated antigen (clone HMB-45), c-kit, podoplanin (clone D2-40), CD30, latent membrane protein-1 (LMP-1) and MUM-1. CD3-positive small T lymphocytes were scattered. Ki-67 (clone MIB-1) labeling index was 70–80% (Fig. 2). Based on these histological findings, we diagnosed the lesion as diffuse large B cell lymphoma (DLBCL). Thereafter, six cycles of R–CHOP chemotherapy were performed. Although rhonchi worsened during the chemotherapy, the additional systemic corticosteroid and inhalation of bronchodilators were effective. FDG-PET uptake turned negative, and we then decided that her lymphoma reached to complete metabolic response (CMR). She had remained in CMR for six months, and her LAM lesion in the lungs had been stable.

3. Discussion

LAM is a rare, neoplastic disease characterized by cystic destruction of the lung, abdominal tumors and lymphatic abnormalities. We sometimes need to distinguish extrapulmonary LAM lesion, such as a lymph nodes from other malignant disease. The sonographic and CT characteristics of LAM are not specific and are similar to other malignant disease. An increase in size during the day [3] is reported as one of the characteristic phenomena in LAM, although it is limited in the abdominal and pelvic lesions, and is difficult to detect small-sized lesions. Delayed enhancement MRI may also be helpful to distinguish LAM from necrotic lymphadenopathy [4], but this has not been established. Regarding FDG-PET, previous report suggested that no abnormal uptake was identified in LAM lesions. LAM is classified as either sporadic or TSC-associated cases. Pathogenesis of both forms of LAM involves either *TSC1* or *TSC2* gene abnormality. *TSC1* and *TSC2* genes encode proteins, named as hamartin and tuberin, respectively. These molecules form a complex to negatively regulate the mammalian target of rapamycin complex 1 (mTOR1) mediating the mTOR pathway signal. Therefore, LAM is considered to be caused by excessive activation of mTOR pathway with increased glucose uptake. However, mTORC1 activity by itself is insufficient for increasing glycolysis in LAM cells, and constitutive mTOR activity negatively regulates glucose transporter trafficking [5]. Thus, LAM lesions lead to decreased glucose uptake and cannot exhibit increased uptake of FDG on PET. In contrast, many malignant tumors use glucose as energy and have a high rate of glycolysis. Therefore, FDG-PET is helpful to distinguish LAM from other malignant disease. In this case, FDG-PET was useful for identifying DLBCL. Therefore, we suggested that FDG-PET would be useful as an indicator of disease progression for DLBCL in LAM patients. There are only two reports of LAM complicated with lymphoma [1,2]. Although it is sometimes difficult to distinguish lymphoma from extrapulmonary LAM lesions by several modalities, we conclude that FDG-PET may be useful to detect the development of other malignant neoplasm.

Declaration of competing interest

The authors state that they have no Conflict of Interest.

References

[1] Y.L. Wan, L.Y. Shih, S.F. Ko, et al., Imaging findings of retroperitoneal lymphangiomyomatosis in a patient with lymphoma, Clin. Imaging 30 (3) (2006) 218–220, https://doi.org/10.1016/j.clinimag.2005.10.010.

[2] L.R. Young, D.N. Franz, P. Nagarkatte, et al., Utility of [18F]2-fluoro-2-deoxyglucose-PET in sporadic and tuberous sclerosis-associated lymphangioleiomyomatosis, Chest 136 (3) (2009) 926–933, https://doi.org/10.1378/chest.09-0336.

[3] N.A. Avila, A.J. Dwyer, D.V. Murphy-Johnson, et al., Sonography of lymphangioleiomyoma in lymphangioleiomyomatosis: demonstration of diurnal variation in lesion size, AJR Am. J. Roentgenol. 184 (2) (2005) 459–464, https://doi.org/10.2214/ajr.184.2.01840459.

[4] E. Maeda, M. Akahane, Y. Inoue, et al., Delayed enhancement of pelvic lymphangiomyoma associated with lymphangioleiomyomatosis on MR imaging, Eur. Radiol. 15 (12) (2005) 2528–2531, https://doi.org/10.1007/s00330-005-2860-4 (2005: 9b).

[5] X. Jiang, H. Kenerson, L. Aicher, et al., The tuberous sclerosis complex regulates trafficking of glucose transporters and glucose uptake, Am. J. Pathol. 172 (6) (2008) 1748–1756, https://doi.org/10.2353/ajpath.2008.070958.