CASE REPORT

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

T. Wagnera,e, D. Brechemierb, E. Dugertc, S. Le Guellecd, A. Juliana, A. Hitzela and O. Beyne-Rauzyb

aNuclear Medicine Department, bInternal Medicine Department, cNeuroradiology Department, dPathology Department, Toulouse Purpan University Hospital, Place du Docteur Baylac, Toulouse, France; eNuclear Medicine Department, Royal Free Hospital, London, UK

Corresponding address: Dr Wagner Thomas, Nuclear Medicine Department, Purpan University Hospital, Place du Docteur Baylac, TSA 40031, 31059 Toulouse cedex 9, France.
Email: Thomwagner@hotmail.com

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Abstract

A 71-year-old woman was admitted to our hospital with asthenia, weight loss, fever, cognitive impairment and shortness of breath. Physical examination showed hemiparesis and cerebellar ataxia. There was no superficial lymphadenopathy. Blood tests showed raised levels of C-reactive protein and lactate dehydrogenase. Bone marrow aspiration and biopsy were negative. [18F]fluorodeoxyglucose (FDG)-positron emission tomography (PET)/computed tomography (CT) showed intense uptake within a right apical nodule and intense and diffuse uptake of FDG in the lungs without corresponding structural CT abnormality. Lung biopsy showed intravascular large B-cell lymphoma (IVLBCL). FDG-PET findings in IVLBCL and causes of diffuse FDG lung uptake with and without CT abnormalities are discussed.

Keywords: Lymphoma; FDG-PET/CT; lung uptake.

Introduction

Intravascular large B-cell lymphoma (IVLBCL) is a rare subtype of extranodal diffuse large B-cell lymphoma in which the lymphoma cells proliferate exclusively in the lumina of small vessels[1]. It was first described by Pfleger and Tappeiner in 1959[2]. It usually occurs in elderly patients, with a gender ratio close to 1 and a small preponderance in males. The most frequent presenting symptoms are fever and general fatigue, neurological symptoms and skin eruptions. Other common clinical findings at initial diagnosis are very heterogeneous and include gastrointestinal symptoms, dyspnea and oedema[1]. Subclinical respiratory involvement is found in 60% of patients at autopsy[3,4]. Lymphoma cells are usually not found in the lymph nodes and in the reticuloendothelial system[5]. Diagnosis is often delayed due to the non-specific symptoms and diagnosis of IVLBCL at autopsy is not uncommon. Therapy usually consists of chemotherapy and rituximab[1].

Case report

A 71-year-old woman was admitted to the internal medicine department of our hospital because of a 3-month history of deterioration of general condition. She had been hospitalized twice before in the previous 3 months before because of fever and raised inflammatory markers that persisted despite antibiotic therapy. A first thoraco-abdomino-pelvic computed tomography (CT) scan had not shown any abnormality and a second scan 2 months later demonstrated hepatosplenomegaly...
without lymphadenopathy. Brain CT scan with contrast showed focal enhancement in the right frontal lobe, the right occipital lobe and the cerebellum. Other investigations such as echocardiography, CT scan of the sinuses, colonoscopy, temporal artery biopsy and bone marrow aspiration did not show significant abnormalities. She was then admitted to our department for further investigation.

She presented with marked deterioration of general condition, asthenia, 5 kg weight loss, high-grade fever with shivering, shortness of breath and cognitive impairment. Physical examination showed hemiparesis and cerebellar ataxia of the right side. No superficial lymphadenopathy was found. Blood tests showed normocytic anaemia, normal white blood cell count and raised inflammatory markers.

\[^{18}F\]Fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT scan showed bilateral high-grade diffuse homogeneous FDG uptake in the posterior and inferior aspect of the lungs, without corresponding CT abnormality (Fig. 1). There was also focal intense FDG uptake within a right apical nodule. Brain magnetic resonance imaging (MRI) demonstrated disseminated ischemic lesions of different age.

The FDG-PET/CT findings led to pulmonary endoscopy with biopsy. No macroscopic endobronchial abnormality was visualized. Pathologic examination of the biopsies showed large atypical lymphoid cells entirely located in the lumina of the septal capillary bed in the lung. These lymphoid cells had irregular nuclear contours, coarse chromatin, prominent nucleoli, and relatively abundant basophilic cytoplasm. The neoplastic cells in the lung were strongly and diffusely positive for CD20 and demonstrated a high proliferation index as revealed by MIB-1 (Ki-67). Diagnosis was IVLBCL.

R-CHOP therapy was started and FDG-PET/CT evaluation after 2 cycles of chemotherapy showed resolution of the right apical nodule and marked decrease in lung uptake bilaterally with a persistent low-grade homogeneous uptake, consistent with partial metabolic response (Figs. 2–4). It was therefore assumed that IVLBCL involvement in the lung presented as diffuse lung uptake in areas without CT abnormality and as focal uptake in a nodule.

**Discussion**

This case report illustrates the added value of FDG-PET/CT in managing patients with general symptoms and no obvious diagnosis, leading here to the diagnosis of IVLCL. In particular, the most striking aspect of the PET/CT scan in this patient was the intense and diffuse bilateral FDG lung uptake without pulmonary parenchymal abnormality on CT. This pattern has been described
Figure 2  FDG-PET/CT evaluation after 2 cycles of chemotherapy demonstrated a marked decrease in bilateral lung uptake with a persistent low-grade homogeneous uptake and resolution of the right apical nodule. Top row is a fused image transverse section of the lungs and MIP, status post-chemotherapy. Bottom row is a fused image transverse section of the lungs and MIP, status pre-chemotherapy.

Figure 3  (a) The large atypical lymphoid cells are entirely located in the lumina of the septal capillary bed in the lung (hematoxylin–eosin, original magnification × 400). These lymphoid cells have irregular nuclear contours, coarse chromatin, prominent nucleoli, and relatively abundant basophilic cytoplasm. (b) Immunohistochemical features of the IVLBCL. The neoplastic cells in the lung are strongly and diffusely positive for CD20 (original magnifications × 200). (c) The neoplastic cells demonstrate a high proliferation index as revealed by MIB-1 (Ki-67) (original magnification × 200).
before in patients with IVLCBL. Miura et al. [6] described diffuse bilateral FDG uptake in the lungs, in the bilateral renal cortex and in the bones in 4 consecutive patients. No lung CT abnormality was reported in at least one of the patients but no information on the lung CT is provided for the 3 remaining patients. No follow-up imaging was mentioned. Kotake et al. [7] described bilateral and diffuse FDG accumulation in the lungs without CT abnormality and in the spleen in a patient with pulmonary hypertension. Follow-up with PET/CT showed resolution of the lung and spleen uptake after 2 cycles of chemotherapy. Kitanaka et al. [8] reported bilateral lung uptake on FDG-PET in a patient with fever and splenomegaly who had negative $^{67}$Ga scintigraphy and high-resolution chest CT scan. Follow-up PET showed resolution of the lung uptake after 6 cycles of chemotherapy. Our case report was different from the cases described above as it had an association of focal FDG accumulation within a lung nodule and diffuse accumulation in areas of normally ventilated lung on CT.

Various FDG-PET findings have been depicted in patients with IVLCBL (Table 1). Rare involved organs include the stomach [9], lymph node [10] and meninges [11]. Two published articles mention negative FDG-PET findings in IVLBCL [12,13]. Shimada et al. [1] found only 2 FDG-positive lesions out of 7 pathologically confirmed lesions.

There have been a number of reports of diffuse lung uptake (Table 2). Yamane et al. [15] have described bilateral diffuse FDG lung uptake in a case of drug-induced

Table 1 Sites of IVLBCL involvement with positive FDG-PET findings in the literature

| Site                  | Bone | Kidney | Lung | Spleen | Adrenal glands | Brain | Uterus |
|-----------------------|------|--------|------|--------|----------------|-------|--------|
| Article(s)            | [6,9,10,21–23] | [6,10,14,25] | [6–8] | [7–9,21,25] | [10,22,26] | [27]  | [10,28] |
| Number of patients    | 11   | 7      | 6    | 6      | 3              | 2     | 2      |
pneumonitis in a patient treated with chemotherapy, where high-resolution CT (HRCT) performed on the same day did not show any abnormality. Three days later, a repeat HRCT showed disseminated patchy ground-glass opacities and interlobular septum thickening, in keeping with pneumonitis. Von Rohr et al.\textsuperscript{[16]} reported a case of bleomycin-induced pneumonitis. FDG-PET showed unilateral diffuse FDG lung uptake corresponding with HRCT abnormality in keeping with bleomycin-induced pneumonitis. Rodrigues et al.\textsuperscript{[17]} studied 8 patients at risk of acute respiratory distress syndrome (ARDS) following blunt thoracic trauma and pulmonary contusion. All patients had FDG-PET 24–72 h after admission and did not meet the criteria for ARDS. Four patients went on to develop ARDS; 3 of these 4 patients had diffuse bilateral FDG lung uptake with increased FDG uptake in areas of normally aerated lung on CT scan. Yu et al.\textsuperscript{[18]} reported a case of bilateral diffuse intense FDG uptake in posterior lower lungs in a patient with aspiration pneumonia. CT scan demonstrated a patchy area of consolidation in both posterior lower lungs. Prakash et al.\textsuperscript{[19]} have described bilateral diffuse lung uptake in lymphangitic carcinomatosis. Groves et al.\textsuperscript{[20]} have described diffuse bilateral lung FDG uptake in 2/36 patients with idiopathic pulmonary fibrosis and diffuse parenchymal lung disease. FDG uptake corresponded to abnormality on HRCT with the most intense areas of uptake corresponding most often to regions of honeycombing.

From our search of the literature, it seems that bilateral diffuse FDG lung uptake with negative CT can be caused by chemotherapy-induced pneumonitis, ARDS or IVLCL; and the only aetiology where CT remains negative after a few days is IVLCL.

### Conclusion

Diffuse bilateral FDG lung uptake with persistent normal lung CT scan must raise suspicion of IVLCL. In the absence of other targets for tissue sampling, random lung biopsies may lead to a diagnosis.

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