PET/CT findings in a multicentric form of Castleman's disease

Abstract

We report a case of a multicentric form of Castleman's disease (CD). A thoracic computerized tomography (CT) scan showed multiple mediastinal and bilateral axillary lymph nodes. Fluoro-18 fluoro deoxyglucose (^{18}F-FDG) positron emission tomography-PET/CT scan demonstrated increased ^{18}F-FDG accumulation in multiple lymphatic regions and in bilateral pleural areas. The histopathological sampling of an excised left axillary lymph node revealed a multicentric form of CD, of an intermediate (mixed) cell type. The disease, its differential diagnosis and the diagnostic contribution of nuclear medicine imaging, are described.

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Introduction

Castleman's disease (CD) or angiofollicular lymph node hyperplasia is a rare benign lymphoproliferative disorder, which was first described in 1954 [1]. The etiology of this disorder is unknown. CD is most often found in the mediastinum (67%), but can be identified wherever lymphoid tissue is normally present [2]. Histologically, CD is classified into tree subtypes: the hyaline vascular type, the plasma cell type and the intermediate (mixed) cell type [3]. The hyaline vascular cell variant, accounts for more than 80%-90% of the cases and is usually asymptomatic. Patients with systemic illness may have fever, sweats, weight loss and fatigue. The majority of these cases are unicentric, usually appear as a slow-growing mass and are successfully treated by surgery. The plasma cell type makes up 10%-20% of CD cases and is usually multicentric. Multicentric form is characterized by systemic symptoms and laboratory findings of inflammatory activity and is associated with relatively higher morbidity and mortality compared to the unicentric form. The patients with the multicentric form do not benefit from surgery and are often referred to multimodality treatment [4]. Multicentric CD may degenerate into malignant lymphoma or vascular neoplasms such as Kaposi's sarcoma, follicular dendritic cell tumor and plasmacytoma [5]. In these patients radiotherapy, chemotherapy, corticosteroids treatment and anti-cytokine treatment have all been used, with variable responses [6].

We report a case of a multicentic form of CD and evaluate the importance of fluoro-18 fluoro deoxy glycose (^{18}F-FDG) positron emission tomography/computerized tomography (PET/CT) imaging in the diagnosis of multicentric form of CD.

Case report

A 59 year old woman presented with a 6 months of weakness, normochromic microcytic anemia, intermittent low-grade fever, night sweating, elevated erythrocyte sedimentation rate and a 7 kg weight loss, within the last 3 months. She had no history of any local pain or discomfort. A chest CT demonstrated multiple enlarged mediastinal and bilateral axillary lymph nodes (Fig. 1). Needle biopsy obtained from the right supraclavicular lymph node, was not diagnostic.

The patient was referred to our department for a PET/CT scan to assess the metabolic status of the known lymphadenomegalies. After six hours fast and having serum glucose 78 mg/dl, the patient was injected with 488.4 MBq of ^{18}F-FDG intravenously (iv). After one hour waiting in a semireclined relaxed chair, the patient was imaged using an integrated PET/CT scanner which consisted of a full-ring HI-REZ LSO PET and a 6-slice CT (Siemens Biograph 6, Knoxville, Tennessee, USA). The CT portion of the study was done without an iv contrast medium, just for defining anatomical landmarks and making attenuation correc-

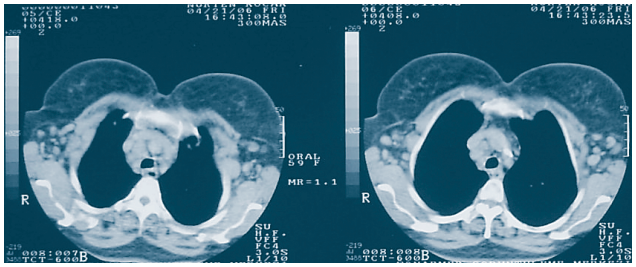

Figure 1. Chest CT images show enlarged mediastinal and bilateral axillar lymph nodes.

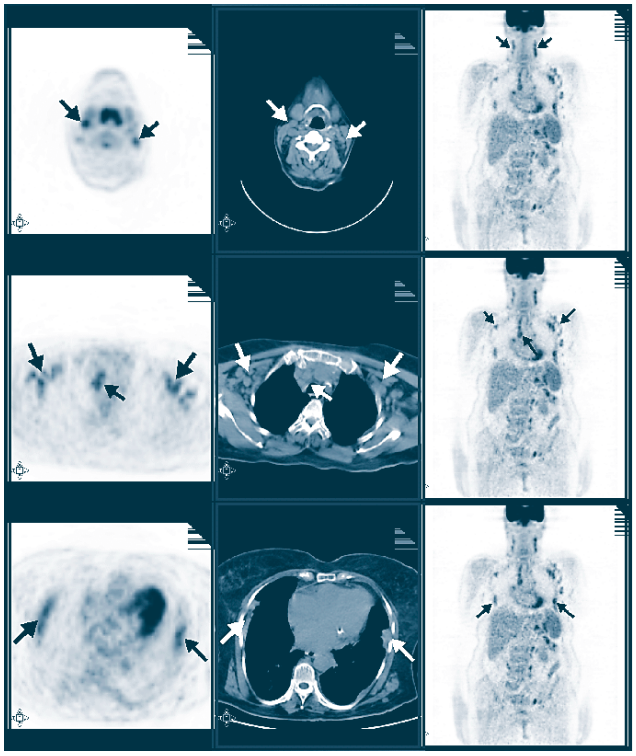

Figure 2. Some selected slices of PET/CT scan are shown, which demonstrate bilateral cervical lymph nodes involvement (upper row), mediastinal and axillary lymph nodes (middle row) and pleural ^{18}F-FDG accumulation (lower row).

tion on PET images. Slightly increased ^{18}F-FDG accumulation in the bilateral cervical axillary and multiple bilateral mediastinal lymph nodes was observed on both PET and the correlative CT images (Fig. 2). The maximum standard uptake values (SUVmax) for the cervical, axillary and mediastinal lymph nodes were 6.3, 6.4 and 6.1, respectively. Increased ^{18}F-FDG accumulation was also observed in the lymph nodes of the splenic hilus and the bilateral pleural surfaces, with SUV max values of 5.4 and 5.7, respectively. Histopathological examination of an excised left axillary lymph node performed after the PET/CT imaging, showed intermediate (mixed) cell type of CD (Fig. 3).

The patient was informed about the expected benefits and complications of treatment options available, i.e., steroids, chemotherapy and/or radiotherapy. She preferred to be followed-up without any treatment. During a year of follow-up, she remained in a steady clinical condition but loosing some weight.

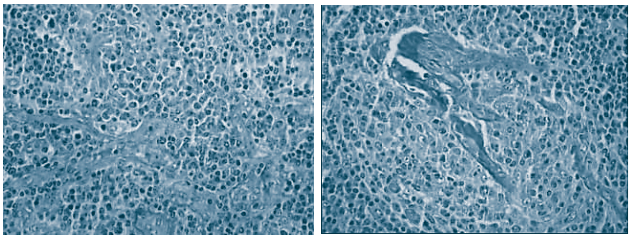

Figure 3. Histopathological section shows hyalinized blood vessels in germinal centre (left side) and sheets of plasma cells in the interfollicular area (right side). This findings are consistent with the diagnosis of intermediate (mixed) cell type of Castleman's disease (H+E.40X).

Discussion

CD has many synonyms, including angiofollicular mediastinal lymph node hyperplasia, angiomatous lymphoid hamartoma, lymph nodal hamartoma, follicular lymphoreticuloma and benign giant lymphoma [7, 8].

Diagnosis of disseminated CD should be considered in any patient with multicentric lymphadenopathy. Lymphadenopathy of POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, multiple myeloma and skin changes) frequently resembles histologically CD [9, 10]. CD has been linked to interleukin 6 (IL-6) overproduction. IL-6 is a major contributor to the systemic manifestations of CD [11]. The radiology appearance of CD is non-specific; the differential diagnosis includes granulomatous disorders, inflammatory lymphadenopathy and malignant lesions such as lymphoma and metastatic tumor [12, 13]. Although studies using gallium-67 citrate (^{67}Ga-C) for the evaluation of CD are limited, ^{67}Ga-C can be used to differentiate CD from lymphoma, because it is accumulated in the CD lesions to a lesser degree than to lymphoma lesions [14]. ^{18}F-FDG PET despite its high sensitivity for the diagnosis of neoplastic tissue is not specific for the differential diagnosis of CD from other benign or malignant lymphoproliferative diseases. Active granulomatous and inflammatory disorders may also show high accumulation of ^{18}F-FDG as in malignant diseases [15]. Similar to our case, it has been previously shown that CD, as a benign disorder also shows slight to moderate ^{18}F-FDG uptake over the lymph nodes involved [16]. Furthermore, low-and intermediate-grade lymphomas may sometimes show low grade ^{18}F-FDG uptake on the PET scans [17, 18]. Therefore, it can be concluded that ^{18}F-FDG PET findings add no more for the diagnosis of lymphomas than clinical or radiological findings. The accurate diagnosis is based on the histological evaluation of the surgical specimen. *In conclusion* in spite of its inefficiency in the differential diagnosis of CD from other lymphoproliferative diseases, the ^{18}F-FDG PET/CT scan and especially the PET findings, indicate a high SUV and can thus distinguish the localized from the multicentric types of CD, which has a significant impact on clinical management.

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