The role of ^{18}F-FDG PET/CT imaging in paediatric Langerhans disease: Case report

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Abstract
Langerhans cell histiocytosis (LCH) is a haematological disorder, affecting single or multiple organs, characterized by abnormal proliferation of Langerhans cells in children. Accurate tumour delineation (number of lesions, organs involved) is crucial for staging/re-staging, and follow-up (response to therapy). Conventional imaging techniques (computed tomography (CT), magnetic resonance imaging(MRI)) have been employed for initial diagnosis, staging and assessment of response to therapy focusing on the healing effect therapeutic protocols have on the disease. In this case report, whole-body positron emission tomography/computed tomography (PET/CT) was shown either to provide information on the metabolic activity of histiocytes, or identify lesions otherwise asymptomatic. It is clear that PET/CT, combining anatomic and metabolic information, provides data for accurate staging, therapeutic protocol selection and assessment of response to therapy.

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Introduction

Langerhans cell histiocytosis (LCH) is a disorder characterized by abnormal proliferation of immune system cells called Langerhans cells, whose role is involved in the regulation of the immune system. They are normally found in the skin, lymph nodes, spleen, lungs, liver and the bone marrow [1, 2].

In LCH, there is proliferation of Langerhans cells which through blood circulation infiltrate different parts of the body. In LCH, Langerhans cells typically accumulate in bones but also in skin, lymph nodes, liver and spleen. Langerhans cell histiocytosis may occur at any age but is more commonly seen in children below the age of 10yrs, with bone involvement reported in 90% of the pediatric LCH cases [3-5].

Diagnostic tests include X-rays, magnetic resonance imaging (MRI), positron emission tomography/computed tomography (PET/CT) imaging, and biopsy. X-rays imaging is the first diagnostic step which determines whether further testing is required. MRI and CT imaging have been employed to detect bone lesions (skull, vertebrae, pelvis). The issue with MRI and CT is that they detect healing as opposed to disease remission which can deter the study of the response to a specific therapeutic protocol [6-9].

Treatment protocols include surgery (surgical removal of lesions followed by histopathology) chemotherapy and targeted therapy [10, 11].

Flurorine-18-fluorodeoxyglucose (^{18}F-FDG) PET/CT has been employed to identify metabolically active histiocytes and detect histiocytic lesions otherwise not identified in CT and MRI modalities. Positron emission tomography/CT has been proven sensitive and specific in both initial staging (whole-body imaging for the identification of osseous and extraosseous lesions) and evaluation of treatment response (therapy follow-up)[12-15].

In this work, a case report is presented reiterating the importance of whole body PET/CT in the staging and follow-up of Langerhans disease.

Materials and Methods

PET/CT imaging protocol

The PET/CT scans were acquired on a GE Discovery 710 SLS system equipped with an

AWZ800 workstation where the reconstruction and subsequent image analysis was carried out. Computed tomography scans without contrast enhancement were acquired in a Bright Speed 16 RT multidetector scanner (General Electric Healthcare, Chicago, IL, USA). Automated tube current modulation was used (beam current ranging between 29 and 210). Acquisition settings included gantry rotation time of 500ms, slice collimation 0.62mm, pitch 1.375 and temporal resolution of 741ms.

Patient preparation included a fasting period of at least 4-6hrs. To avoid dehydration only water was allowed during the fasting period. No workout was allowed. The patients were also instructed to wear 'warm' clothing prior imaging to avoid the 'brown fat' effect.

Prior scanning, the patients were informed about the imaging process and its duration. In cases where patient co-operation was difficult (e.g. young children) children were sedated to ensure immobilization throughout imaging.

Before the injection of the radiopharmaceutical, blood glucose level was confirmed, weight and height measurements were obtained and the required amount of radioactivity (MBq) was computed. Following the injection of the ^{18}F-FDG labelled pharmaceutical ($T_{1/2}$= 110min), the patient lie supine without any exercise or movement, in a low-lit warm room to avoid the brown fat activation effect.

A whole-body PET/CT scan was then acquired from the skull vertex to toes. Initially, a CT scan, employing a low-dose protocol, was acquired for the attenuation correction data to be obtained. Following PET acquisition, scatter correction, decay correction and CT-based attenuation correction were applied to the acquired data. Then, image reconstruction of the acquired data using an iterative algorithm (Ordered-Subset Expectation Maximisation-OSEM: 8 iterations, 21 subsets) was carried out. The resulting 3D image dataset comprised of voxels with dimensions 3.75mm [16, 17].

Data analysis

The results were assessed by visual interpretation and quantitative measurements of standardized uptake values (SUV) by one experienced nuclear medicine physician and one paediatric radiologist based on the ^{18}F-FDG metabolism. Regions of interest (ROI) were manually delineated on the PET data. The SUV_{max} of the ROI on PET images was measured and the radioactivity background of normal liver parenchyma was established in each case.

Clinical case report

A 6 years old boy was diagnosed with LCH (a single lesion at 11th thoracic vertebra/TH11). The boy presented to the pediatric department with severe pain at the lower thoracic spine region. After an MRI scan, biopsy was carried out which confirmed LCH and the boy underwent chemotherapy treatment according to LCH-IV protocol. An ^{18}FDG PET/CT scan was performed at the end of the chemotherapy scheme which was negative for metabolically active LCH lesions.

Four months following the completion of the protocol, the boy complained for pain at the upper thoracic spine. A thoracic spinal MRI scan showed a new lesion at 3rd thoracic vertebra, which was confirmed by biopsy as LCH. A second operation was performed to remove this lesion and the post-biopsy MRI showed the entire TH3 vertebra being affected by the disease. The MRI scan was acquired on the specific pathologic areas, as a follow up imaging procedure. A whole-body ^{18}F-FDG PET/CT was carried out showing the already known osteolytic lesion at 3th thoracic vertebra (Figure1), with increased metabolic rate (SUV_{max}: 3.4) and a new lesion at 5th lumbar vertebra (SUV_{max}: 2.46) (Figure 2). During chemotherapy the patient was evaluated with MRI. At the end of chemotherapy, a whole-body ^{18}F-FDG PET/CT scan confirmed decrease in the metabolic rate of the affected vertebrae. No pain was reported at the time of the PET/CT scan.

In conclusion, Langerhans cell histiocytosis is a systematic haematologicdisease, today considered as a myeloid malignancy, involving single or multiple organs. The accurate lesion delineation, the number of lesions as well as the involvement of one or multiple organs play an important role for disease

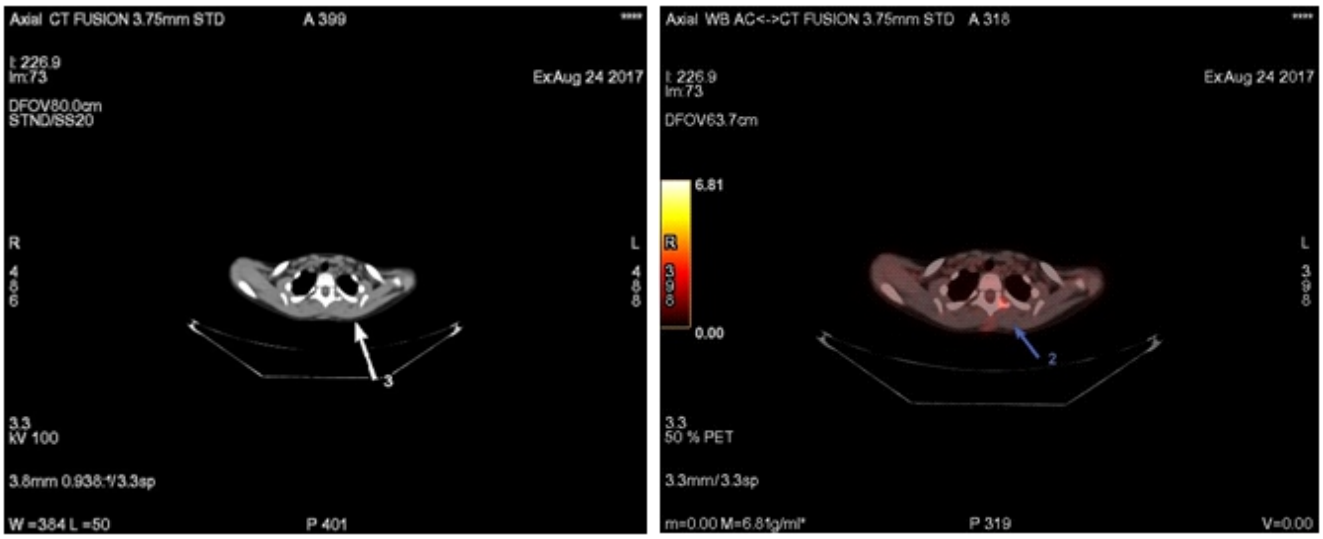

Figure 1. a) Axial CT slice, and b) axial PET/CT fused slice at level of TH3. Osteolytic hypermetabolic lesion at the TH3 left pedicle.

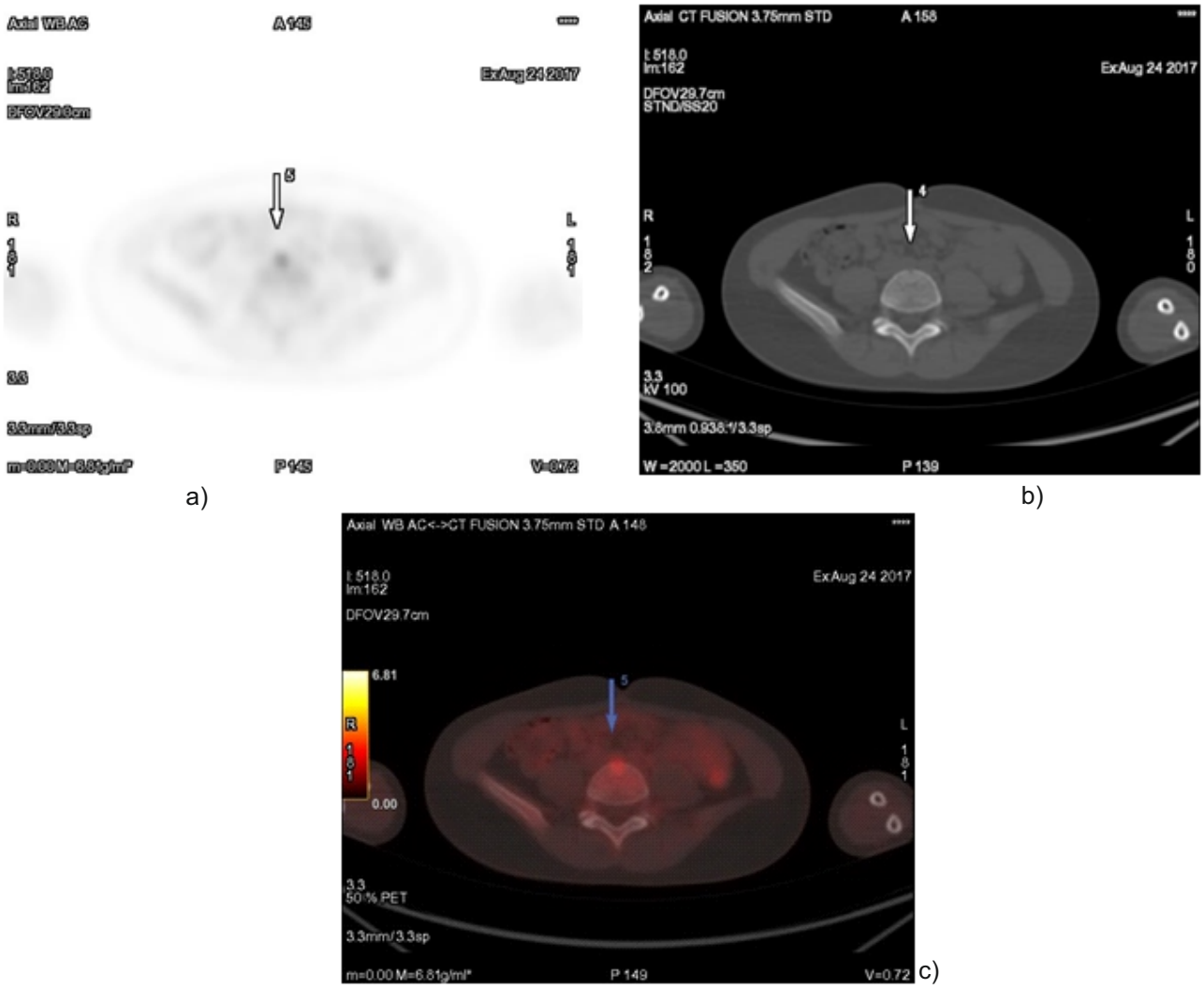

Figure 2. a) Axial PET slice, b) axial PET-CT fused slice, and c) axial CT slice at L5 level. Hypermetabolic osteolytic lesion at the anterior surface of the L5 vertebral body.

staging and decision on the appropriate therapeutic protocol. Staging is based on imaging and confirmed by biopsy. The role of ^{18}F-FDG PET/CT as imaging modality has not yet been completely determined [18].

This case report shows the important role of the ^{18}F-FDG PET/CT scan in diagnosis, therapy follow-up and re-staging of children suffering from LCH. The main advantage of this imaging technique compared to MRI which is considered the gold-standard in image-based diagnosis, is the combination of whole body anatomical and metabolic information to detect LCH lesions not detectable on conventional imaging modalities. This fact enables to distinguish metabolically active from inactive disease and the identification of otherwise a symptomatic lesions [19].

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