Nucl Med Mol Imaging (2013) 47:205–207
DOI 10.1007/s13139-013-0203-y

CASE REPORT

Unsuspected Active Sarcoidosis Diagnosed by 18F-FDG PET/CT During the Search for a Primary Tumour in a Patient with Bone Lesions

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Received: 27 August 2012 / Revised: 21 March 2013 / Accepted: 1 April 2013 / Published online: 24 April 2013

Abstract Sarcoidosis is a systemic chronic inflammatory disease of unknown aetiology, characterised by granulomatous lesions with heterogeneous clinical manifestations affecting multiple organs and tissues. Although the respiratory system is most commonly affected, the disease may also present with bone lesions. We report the case of a 31-year-old woman who presented with low back pain and no history of cancer and who was found to have suspicious lesions involving the entire spine on magnetic resonance imaging (MRI). The patient underwent 18F-fluorodeoxyglucose (FDG) PET/CT to search for a primary tumour and for staging purposes. 18F-FDG PET/CT revealed a pattern of hypermetabolic activity in widespread skeletal lesions and in a single left cervical lymph node. The primary tumour was not found, thus suggesting a haematologic disorder. Subsequent biopsies of a cervical lymph node and of bone tissue from L4 revealed active sarcoidosis with no evidence of cancer. This underlines the importance of considering all alternatives when hypermetabolic lesions are found on 18F-FDG PET/CT. Furthermore, 18F-FDG PET can be very useful to indicate accessible sites for guiding fine-needle aspiration cytology (FNAC).

Keywords Sarcoidosis · 18F-FDG PET/CT · Metastatic bone lesion · MRI · Uncertain primary

Federico Caobelli and Sara Vincenzina Gabanelli contributed equally to this work.

The authors state that they are responsible for the research they have designed and carried out and that they have participated in drafting and revising the manuscript submitted, which they approve in its content. They also state that the research reported in the article was undertaken in compliance with the Helsinki Declaration and the international principles governing research on animals.

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Introduction

Sarcoidosis is a systemic chronic inflammatory disease of unknown aetiology, most commonly affecting young adults, characterised by non-caseating epithelial granulomatous lesions with heterogeneous clinical manifestations affecting multiple organs and tissues.

The respiratory system is most commonly affected, but other organs may be involved, including eyes, skin, lymph nodes, liver, spleen, kidneys, heart and bone marrow [1].

Isolated extrapulmonary disease is rare; in particular, vertebral sarcoidosis is a very rare condition in which sclerotic changes in the vertebrae often mimic metastatic disease [2–4].

18F-FDG PET/CT has been widely validated for the detection of primary tumours in patients with metastatic disease. Likewise, 18F-FDG PET/CT has also been widely used in the diagnosis and follow-up of chronic inflammatory disease, such as granulomatous ones [5].

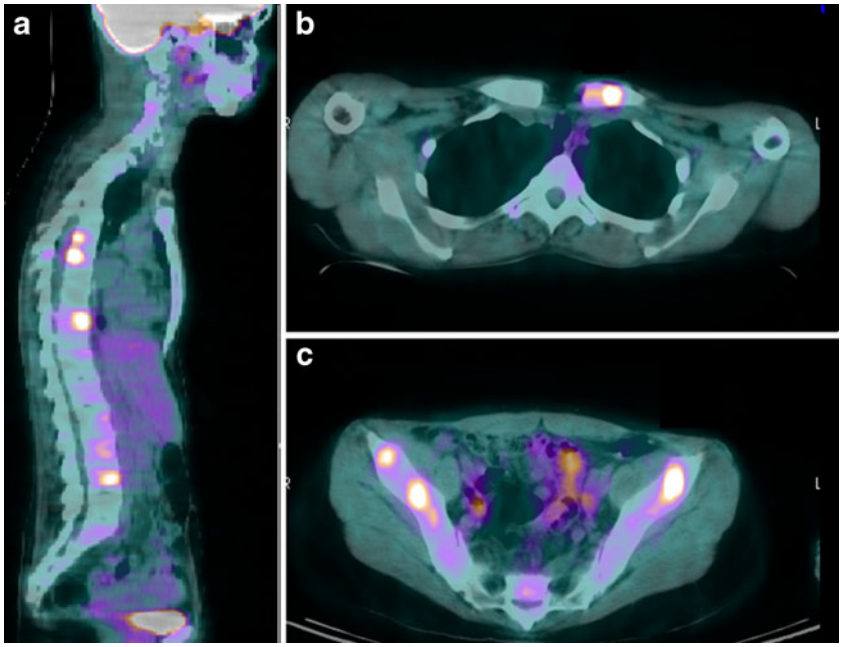

Fig. 1 18F-fluorodeoxyglucose PET/CT sagittal scan (**a**) showing extended spine involvement (especially T5-T7, T10, L1-L4 vertebrae); transaxial scans (**b**, **c**) of a 31-year-old woman showed multiple areas of hypermetabolic fluorodeoxyglucose uptake in the sternum and hip bone

We here present the case of a 31-year-old woman with suspected spine metastasis who underwent 18F-FDG PET/CT to find the primary tumour.

Case Description

A 31-year-old woman with a long-lasting history of back pain was referred to our hospital for suspected metastatic bone lesions from an uncertain primary because of radiological evidence on MRI of multiple osteolytic lesions that were widespread on the axial skeleton.

The patient had no history of either cancer or any other disease, but a history of possible bilateral sacroilitis, which was later excluded by second-stage tests.

Whole-body PET/CT was performed 60 min after the administration of 270 MBq of 18F-FDG using a 3D PET/CT scanner (Biograph HR, Siemens AG).

18F-FDG PET/CT images showed multiple areas of pathological FDG uptake in the spine (especially T5-T7, T10, L1-L4), sternum, ribs, hip bone and right femoral shaft (Fig. 1). PET images also showed hypermetabolic activity in a left cervical lymph node on level IV (Fig. 2).

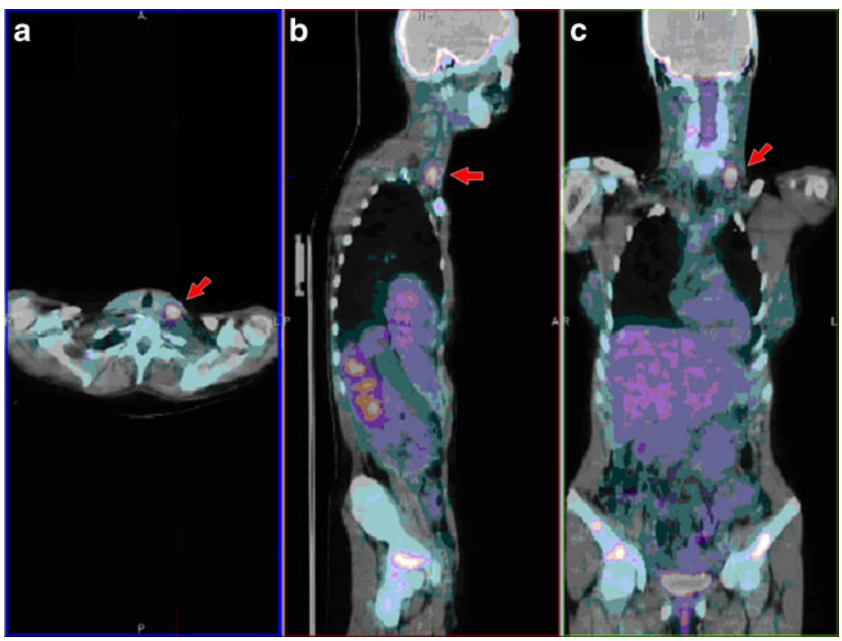

Fig. 2 18F-PET PET/CT transaxial (**a**), sagittal (**b**) and coronal scans (**c**) of the same patient showed focal FDG uptake in a left cervical lymph node (12×19×22 mm, see *arrows*) where fine-needle aspiration revealed a non-caseating epithelial granulomatous lesion

These images were highly suggestive of widespread skeletal metastases, but a clear primary could not be demonstrated, thus suggesting a possible haematologic disease.

US-guided fine-needle aspiration cytology (FNAC) of the lymph node, shown by PET/CT, was performed and revealed a non-caseating epithelial granulomatous lesion, negative on Ziehl-Neelsen staining. Surgical biopsy of the cervical lymph node and of bone tissue from L4 and L5 confirmed the diagnosis of sarcoidosis, although the patient did not present the typical involvement of hilar lymph nodes and pulmonary infiltration.

The patient was advised to undergo therapy with prednisone (25 mg/day) in order to reduce the risk of progression in skeletal sites.

Discussion

Bone involvement in sarcoidosis is rare and can lead to the false-positive appearance of metastatic disease on PET/CT. In fact, accumulation of FDG at the sites of infection or inflammation can cause false-positive results when this imaging technique is used in the setting of suspected or known malignancy, as happens in inflammatory disorders such as osteomyelitis, tuberculosis, Mycobacterium avium intracellular infection and sarcoidosis [6].

When 18F-FDG PET images show hypermetabolic activity in skeletal lesions, sarcoidosis and other inflammatory lesions such as granulomatous processes should be considered for a differential diagnosis among lymphoproliferative diseases and metastatic involvement from a primary tumour.

In particular, the extended bone involvement, the absence of pulmonary uptake and the intense hypermetabolism in a left cervical lymph node would most probably have led to the diagnosis of a lymphoproliferative disease, but, as a matter of fact, both sarcoidosis and lymphomas may affect lymphoid systems and bone and appear with high metabolic activity on 18F-FDG PET images.

The prognostic significance of bone involvement in sarcoidosis patients, as well as a possible increased risk of fracture at these sites, is debatable, even if it has been associated with a chronic course of the disease; therefore, establishing its presence is valuable in the clinical assessment of these patients [7, 8]. 18F-FDG PET/CT could also be useful to identify extrapulmonary involvement, performing a single imaging procedure, and to guide biopsy sampling in cases needing pathological confirmation [9].

Recently, some authors have proposed new PET tracers to detect malignancy; these in combination with 18F-FDG PET may be an effective method to distinguish sarcoidosis from malignancy. Kaira et al. proposed fluorine-18-alpha-methyltyrosine (18F-FMT), an amino acid tracer for PET, in combination with 18F-FDG PET for the diagnosis of sarcoidosis in patients with suspected malignancy: all patients showed an increased uptake of 18F-FDG and no increase in the accumulation of 18F-FMT in their lymphadenopathy and in all extranodal lesions [10].

Only a few reports on 18F-FDG findings in extrapulmonary sarcoidosis can be found in the literature [9, 11], but, unlike other reports, our case perfectly mimicks a lymphoma pattern because of the absence of pulmonary involvement as well as hilar lymph nodes, although the biopsy of the cervical lymph node clarified the diagnosis, showing a non-caseating epithelial granulomatous lesion.

This underlines once more the importance of considering all alternatives when hypermetabolic lesions are found on 18F-FDG PET/CT. Furthermore, 18F-FDG PET can be very useful to indicate accessible sites for guiding FNAC, which in many cases is indispensable for obtaining a diagnosis.

Conflict of interest The authors declare no conflict of interest.

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