Incidental detection and monitoring of spontaneous recovery of sarcoidosis via fluorine-18-fluoroethyl-choline positron emission tomography/computed tomography

Abstract

We report a case of sarcoidosis detected incidentally by using fluorine-18-fluoroethylcholine-positron emission tomography/computed tomography ($^{18}$F-FECH-PET/CT) in a 72 years old patient with prostate cancer, who had been referred for restaging after relapse indicated prostate specific antigen (PSA). The $^{18}$F-FECH-PET/CT examination showed a focal increased uptake in the prostate bed suggestive for local recurrence, in addition to multifocal uptake in the mediastinum matching with enlarged hilar and paratracheal lymph nodes. Histopathology revealed sarcoidosis. No treatment was recommended. Two years later the patient was referred again to us because of another recurrent PSA elevation. The second $^{18}$F-FECH-PET/CT showed again the previously described local recurrence, but did not show the previously described mediastinal findings nor the enlarged hilar and paratracheal lymph nodes, thus, illustrating spontaneous healing of sarcoidosis. In conclusion, this case suggests that $^{18}$F-FECH PET/CT study can show positive findings in sarcoidosis that were no longer detectable after two years, suggestive of spontaneous recovery.

Introduction

Sarcoidosis is a granulomatous disease of unknown etiology, with potential to involve any organ. Its importance is emphasized through capability to mimic cancer, by its radiological appearance and its metabolic activity. Thus, it may constitute a diagnostic challenge for both radiologists and nuclear medicine physicians. The primary involvement includes lungs as well as lymph nodes predominantly in the hilar and paratracheal regions, mainly through granulomatous invasion, which may explain the high glucose metabolism using $^{18}$FDG-PET/CT. The latter exhibits an ability to detect sarcoidosis, however its main limitation is to recognize sarcoidosis among many other disorders causing intrathoracic lymphadenopathies.

The fluorine-18-fluoroethylcholine-positron emission tomography/computed tomography ($^{18}$F-FECH-PET/CT) scan is an established tool for the diagnosis of prostate cancer (PCA) and follow-up after treatment. Nevertheless, the use of $^{18}$F-FECH-PET/CT can be also extended in many malignant as well as non-malignant disorders.

Although the diagnostic value of choline-PET in sarcoidosis had been already described by others [1], who have used [carbon-11 ($^{11}$C)] labeled choline, this report is according to our knowledge the first report about sarcoidosis, using $^{18}$F-labeled choline.

The purpose of this study is to demonstrate a possible application of $^{18}$F-FECH-PET/CT in the diagnosis and treatment monitoring of sarcoidosis, and its use as a source of false positive results.

Case report

A 72 years old patient with confirmed PCA Gleason score 6, treated initially with brachytherapy had been referred to our department in August 2009, eleven years after the first diagnosis for a $^{18}$F-FECH-PET/CT study due to biochemical recurrence (prostate-specific antigen (PSA) 12.66ng/mL). The patient was asymptomatic.

A focal increased uptake in the prostate bed was showed in $^{18}$F-FECH-PET/CT, thereby, a local recurrence was suspected. Further intensive multifocal uptake areas were found in the mediastinum. In the associated CT, these findings were assigned to numerous pathological enlarged lymph nodes (hilar and paratracheal) (Fig. 1). However, these findings do not necessarily associate to PCA. Therefore, we considered lymphoma as a possible dif-
Case Report

Differential diagnosis for the mediastinal findings in $^{18}$F-FECH-PET/CT. Final diagnosis of the mediastinal findings was confirmed by a mediastinoscopy based biopsy. The subsequent histopathological analysis revealed a sarcoidosis. The patient received hormonal treatment for local recurrence of PCA. No treatment was recommended for sarcoidosis and in clinical follow-up that followed he developed no symptoms.

Two years later, in October 2011, the patient was referred again to our department due to recurrent PSA elevation (7.4ng/mL). The follow-up $^{18}$F-FECH-PET/CT examination exhibited again the previous local recurrence without evidence of metastatic disease. Additionally, the new examination demonstrated absence of the previously described mediastinal lymph nodes. The associated CT showed a normalization of the lymph nodes size, illustrating a spontaneous healing of biopsy-confirmed sarcoidosis (Fig. 1).

There is no report in the literature about the potential effect of hormonal treatment used in PCA patients with synchronous sarcoidosis, which may explain the loss of choline uptake and the decrease in size of the involved lymph nodes as an effective antihormonic treatment.

Figure 1. The $^{18}$F-FECH-PET/CT scan-baseline: A: Maximum intensity projection (MIP) shows a pathologic uptake in prostatic loggia, suggestive for local recurrent (arrow) in addition to multifocal increased uptake in the middle mediastinum. A1, a1: Native CT-thorax coronal and axial planes show pathological enlarged hilar and paratracheal lymph nodes (red curved arrow). A2, a2: Fused image coronal and transaxial views show that the mediastinal findings are corresponding with the described enlarged hilar and paratracheal lymph nodes (yellow curved arrow). After biopsy, the described mediastinal findings were confirmed to be due to sarcoidosis. The $^{18}$F-FECH-PET/CT follow-up (2 years later). B: Maximum intensity projection shows again the known local recurrence (arrow) and an absence of the previously described mediastinal findings. B1, b1: Pure CT-thorax coronal and axial planes show a normalization of the size of the prior described lymph node. B2, b2: Fused images, coronal and transaxial views confirm that the previously described multifocal uptake is no longer delineated.

Discussion

Sarcoidosis may cause a bilateral intrathoracic lymphadenopathy among many other disorders and there is a long list of inflammatory/malignant diseases in differential diagnosis, most of them share a high affinity for $^{18}$F-FDG. For this reason, $^{18}$F-FDG-PET/CT cannot be recommended to distinguish sarcoidosis from other causes of a lymphadenopathy. Granulomas of sarcoidosis are characterized by accumulation of many types of inflammatory cells including monocytes, macrophages and activated T-lymphocytes, with overproduction of inflammatory mediators. That may explain the high affinity to $^{18}$F-FDG, which leads to an enhanced $^{18}$F-FDG accumulation. Therefore, the $^{18}$F-FDG uptake as measured by SUV cannot be used for differentiation between lymphadenopathy secondary to malignancies and sarcoidosis [2, 3].

Others demonstrated the inefficiency of $^{18}$F-FDG-PET/CT in differentiating sarcoidosis from malignant tumors and suggested the use of multitracer studies [2].

It is known that $^{18}$F-FECH-PET/CT can be used for the diagnosis of PCA, due to the alteration of lipid metabolism including overexpression of fatty acid synthesis and choline kinase [4-5]. Two mechanisms have been suggested to explain the increased choline uptake in PCA cells [6-15]. The first is due to increased cell proliferation, since choline is a precursor for biosynthesis of phosphatidylcholine and other phospholipids, the major components of cell membrane. In the light of this mechanism choline uptake is supposed to reflect cell proliferation [6]. The second explanation is overproduction of choline kinase in cancer cells, which was confirmed in human-derived PCA [7]. Choline kinase, phosphorylates free choline to phosphocholine, which is the initial step of choline metabolism, and after a series of chemical reactions phosphatidylcholine is formed, which is the major constituent of cell membrane [4-5].

Although $^{18}$F-FECH-PET/CT is mainly used in prostate diagnostics, a positive choline uptake had been described in multiple disorders not related with PCA. Others reported in 15 of 80 patients (18.7%) abnormal findings, not suggestive for PCA localizations [8]. Furthermore, in primary lung cancer, others compared $^{11}$C choline with $^{18}$F-FDG-PET, and found that $^{11}$C-choline PET had a clinical diagnostic value comparable to that of $^{18}$F-FDG for tumors of more than 1.5cm in diameter [9]. Others described positive FECH uptake in lymphomas, meningiomas and gliomas [8]. Others reported a case of thymus cancer detected incidentally with $^{18}$F-FECH-PET/CT [10]. In the same context, others discussed the usefulness of $^{11}$C-choline in mediastinal tumors and reported an accuracy of 63% [1].

A possible explanation for the enhanced choline uptake in sarcoidosis may be the enhanced accumulation of many types of inflammatory cells including activated T-lymphocytes. Basically, lymphocytes express most components of the cholinergic system including acetylcholine, muscarinic and nicotinic receptors, choline acetyltransferase, high affinity choline transporter and acetylcholinesterase [11-12].
This may explain choline accumulation in sarcoidosis and in lymphoproliferative disorders such as lymphomas. The second possible hypothesis is the increased proliferation of T lymphocytes, which in turn raises the need of choline since it is the precursor of the structural components of cell membranes [13].

In spite of the described positive choline uptake in sarcoidosis, 18F-FECH-PET/CT studies face comparable limitations similar to 18F-FDG-PET in the lack of specificity. An advantage of 18F-FECH-PET/CT may be that the spectrum of differential diagnosis of mediastinal positive findings is less extended than in 18F-FDG-PET. For example, in tuberculosis, which can cause a similar lymphadenopathy, the 18F-FDG-PET showed high uptake, while there was no real choline uptake [9-14].

However, 18F-FECH-PET/CT may be of value in the follow-up of sarcoidosis even better than 18F-FDG-PET/CT due to its superior tumor to background signal. In this regard, it is worth mentioning that spontaneous recovery rate in sarcoidosis is very high, about 70% [16].

In conclusion, this case suggests that 18F-FECH-PET/CT study can show positive findings in sarcoidosis that were no longer detectable after two years, suggestive of spontaneous recovery.

The authors declare that they have no conflicts of interest.

Bibliography

4. Teirstein, A.S., J. Machac, O. Almeida et al. Results of 18F-FECH-PET. For example, in tuberculosis, which can cause a similar lymphadenopathy, the 18F-FDG-PET showed high uptake, while there was no real choline uptake [9-14].