Clinical note

Pitfalls with 18F-choline PET/CT in patients with prostate cancer


Servicio de Medicina Nuclear, Hospital General Universitario de Ciudad Real, Ciudad Real, Spain

A R T I C L E   I N F O

Article history:
Received 5 December 2011
Accepted 20 January 2012

Keywords:
18F-choline
PET-CT
Prostate cancer
Pitfalls

A B S T R A C T

The 18F-choline PET-CT (FCH) has better performance in the assessment of patients with prostate cancer than 18F-FDG could do. However, similarly, it is also not a tumor specific radiotracer.

We present four 18F-FCH PET-CT scans in which false positive findings were correctly assessed after evaluation with CT, clinical parameters and/or histological analysis.

© 2011 Elsevier España, S.L. and SEMNIM. All rights reserved.

Falsos positivos en PET-TC con 18F-Colina en pacientes con cáncer de próstata

R E S U M E N

La PET-TC con 18F-Colina (FCH) posee un mayor rendimiento en la valoración de pacientes con cáncer de próstata que la 18F-FDG; no obstante, al igual que esta, tampoco es un radiotrazador específico tumoral.

Presentamos cuatro estudios PET-TC realizados con 18F-FCH donde obtuvimos hallazgos falsos positivos catalogados correctamente tras la valoración con la TC, parámetros clínicos y/o análisis histológico.

© 2011 Elsevier España, S.L. y SEMNIM. Todos los derechos reservados.

Introduction

In clinical practice positron emission tomography (PET) has traditionally been associated with the radiotracer analog of glucose 2-(18F) fluoro-2-desoxy-d-glucose (FDG), presenting a high sensitivity for the detection of the most prevalent malignant tumors with respect to staging, evaluation of response to treatment and follow-up. On the other hand, other neoplasms such as carcinoma of the prostate, neuroendocrine tumors and hepatocarcinomas, among others, do not generally demonstrate significant avidity for FDG.1

Thus, in patients with prostate cancer PET with FDG has a reduced sensitivity in both the determination of the primary tumor and in the detection of abdominopelvic adenopathies, with the additional limitation of excretion of the radiotracer through the ureters, bladder and intestine.2 However, FDG may have greater diagnostic profitability in patients with aggressive, undifferentiated prostate cancers with or without metastatic involvement.3

Due to the diagnostic limitations of PET with FDG in the study of prostate cancer, new radiotracers such as 18F-fluoro-5 alpha-dehydrotestosterone,11C-acetate,11C-methionine,11C-choline and 18F-fluorocholine (18F-FCH) have been developed. Among these, the choline analogs are the most frequently used.1,3

The short half life of 11C limits its availability in centers which do not have a cyclotron. On the other hand, 18F-FCH is more accessible, although its greater urinary excretion may lead to artifacts in the pelvic zone complicating interpretation.1

The radiotracer 18F-FCH has physiological distribution in the liver, pancreas, salivary and lacrimal glands, the spleen, kidneys and bone marrow.4 In addition, the uptake is not specific of neoplastic cells since prostatic and extraprostatic inflammatory processes may present avidity by 18F-FCH and present false positives.4

Considering the increasing use of this radiotracer it is important to know its biodistribution pattern and variants. We present 4 cases in which PET-CT with 18F-FCH showed false positive results of extraprostatic localization in which joint evaluation with CT and the clinical parameters or the histological results were crucial to establish the correct diagnosis.

Case 1

This patient was diagnosed with Gleason 7 prostate cancer and treated with local radiotherapy and antiandrogen therapy. During the follow-up an elevation was observed in serum PSA levels (January 2010: 066 ng/ml; June 2010: 2.49 ng/ml; July 2010: 4.03 ng/ml). PET-CT study showed adenopathies in the pelvis with uptake by 18F-FCH suggestive of malignancy and a hypermetabolic focal uptake in the 4th left costal arch in correspondence with a fracture callus (Fig. 1).
Delayed or dynamic images may therefore be recommended in cases of persistence of metabolic activity. Other possible indications are use in patients with biochemical relapse of prostate carcinoma as a second tumor treated by radiotherapy. During the follow-up repeated elevations were observed in serum PSA levels (May 2010: 1.54 ng/ml, November 2010: 3.78 ng/ml) compatible with biochemical relapse.

The PET-CT study with 18F-FCH demonstrated malignant involvement of retroperitoneal and pelvic adenopathies without alterations in the prostate. As incidental finding a nodule with increased uptake was detected in the right thyroid lobe for which a study was recommended to determine cellularity. This study was negative for malignancy and was compatible with nodular hyperplasia (Fig. 2).

Case 2

A patient diagnosed with renal carcinoma treated by right nephrectomy without adjuvant treatment also had a Gleason 7 prostate carcinoma as a second tumor treated by radiotherapy. During the follow-up repeated elevations were observed in serum PSA levels (May 2010: 1.54 ng/ml, November 2010: 3.78 ng/ml) compatible with biochemical relapse.

The PET-CT study with 18F-FCH demonstrated malignant involvement of retroperitoneal and pelvic adenopathies without alterations in the prostate. As incidental finding a nodule with increased uptake was detected in the right thyroid lobe for which a study was recommended to determine cellularity. This study was negative for malignancy and was compatible with nodular hyperplasia (Fig. 2).

Case 3

A patient diagnosed with Gleason 5 prostate carcinoma was treated only with androgen blockade. During the follow-up an elevation in serum PSA levels was detected compatible with biochemical progression, despite the hormone treatment (PSA February/10: 0.44 ng/ml, May/10: 0.55 ng/ml). In the PET-CT with 18F-FCH prostatic hypermetabolism was observed probably related to residual disease. Subcentimetric adenopathies were observed in the mediastinum with moderate uptake by 18F-FCH suggestive of a reactive process which was confirmed during follow-up (Fig. 3).

Case 4

This patient was diagnosed with Gleason 7 prostate cancer in the right prostatic lobe and was treated by neoadjuvant androgenic blockade combined with radiotherapy. A progressive elevation in serum PSA levels was observed posteriorly achieving a maximum of 14.3 ng/ml. The PET-CT study with 18F-FCH was positive, detecting bone and retroperitoneal lymph node metastases. In addition, a slight increase of the radiotracer activity was observed in a right subcutaneous periscapular nodule related to an infected sebaceous cyst (Fig. 4).

Figure 1. Case 1: patient with biochemical relapse. Axial PET-CT images of the thorax show an increase in 18F-FCH activity in the posterior zone of the 4th left costal arch next to the costal-vertebral union. This finding correlated with the CT image with an increase in focal density related to a fracture callus.

Figure 2. Case 2: patient with biochemical relapse. Axial PET-CT images show a slight increase in 18F-FCH uptake in the right thyroid lobe related to a nodular formation shown in the CT image. FNAP was negative for malignancy.

Discussion

Choline is a small molecule which rapidly integrates into the cellular membrane as phosphatidylcholine on intravenous injection, becoming a metabolic marker of the membrane. Prostate cancer cells, even those of low grade tumors, have increased choline-kinase activity and have affinity for choline. However, this radiotracer is not useful in the differentiation between benign or malignant diseases of the prostate.

The indications for the radiotracer choline analogs are early diagnosis of recurrence of prostate carcinoma treated with surgery and/or radiotherapy with repeated elevations in serum PSA levels and negative imaging tests and tumoral staging on suspicion of disseminated disease. Other possible indications are use in radiotherapy planning, treatment monitoring (hormone and/or radiotherapy) and definition of the anatomical region to undergo biopsy in cases of persistent PSA elevation with repeated negative biopsies.

Precise knowledge of the normal biodistribution of 18F-FCH is fundamental for correct interpretation of the study in patients with prostate cancer. Physiologically 18F-FCH presents more intense uptake in the liver and pancreas, with moderate/high uptake in the spleen and salivary and lacrimal glands and less intense uptake in bone marrow and the intestine, and greater variations among patients. 18F-FCH is eliminated by the kidney, bladder and ureters. Cerebral uptake is exceptional except in the choroid plexus and pituitary gland. Uptake may also be seen in the route of administration (upper limb veins) and axillary lymph nodes due to extravasation of the radiotracer.

Some benign conditions such as inflammatory lymph nodes show a transitory increase in 18F-FCH with the "phenomenon of lymphatic lavage" reported in both inguinal and cervical lymph nodes showing a reduction in uptake at 20 min post-administration of the radiotracer. Delayed or dynamic images may therefore be necessary to resolve the transitory increases in uptake in benign tissue. Among the benign pathologies demonstrating uptake by 18F-FCH osteoarthritis is of note in both advanced and early phases, especially in the presence of osteophytes. Case 1 shows how other processes with an increase in osteogenic activity such as a fracture callus may demonstrate uptake by the radiotracer.
Moreover, increases in the uptake of 18F-FCH have been described in other benign processes in relation to lymphadenopathies, pulmonary nodules, pleuritis, thyroiditis, esophagitis and otomastoiditis. Increases have even been reported with 11C-choline in cases of post-hepatectomy hepatic regeneration, proliferative synovitis and inflammatory pulmonary nodules.8,9 Uptake of 18F-FCH has also been reported in thyroiditis.4 In Case 2 the patient had a thyroid nodule which was diagnosed as benign by FNAP.

In short, inflammatory phenomena are the most frequent cause of false positive results with 18F-FCH and may affect up to 15% of the patients.4 In a recent study uptake of 18F-FCH was observed in systemic adenopathies in 5% of the patients with prostate cancer, defining these findings as not suspicious of malignancy. Lymph node involvement only of the mediastinum was also detected in another 5% of the cases, in association or not with inflammatory pulmonary disease.4 The patient of Case 3 had a history of chronic lung disease which could justify the uptake of 18F-FCH in the mediastinal lymph nodes. Other authors have also described avidity for 11C-choline in processes such as sarcoidosis, noncaseating granulomas and tuberculosis.10 One of our cases corresponded to an infected sebaceous cyst with positive uptake (Case 4).

Apart from unusual localizations of metastasis, the capacity of 18F-FCH should always be considered in the detection of inflammatory lesions in clinical practice. Thus, the integrated interpretation of PET findings within the clinical context of the patients is fundamental for correct elaboration of the diagnostic report.11,12 Knowledge of the limitations induced by infectious/inflammatory or proliferative processes of benign origin in studies with 18F-FCH-PET allows false interpretations which reduce the specificity of this technique to be avoided.

References