Rev Esp Med Nucl Imagen Mol. 2015;xxx(xx):xxx–xxx

Clinical note

Incidental pathologic extracardiac uptake of ^{99m}Tc-tetrofosmin in myocardial perfusion imaging: Importance of patient background evaluation

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ARTICLE INFO

Article history:
Received 6 February 2015
Accepted 13 March 2015
Available online xxx

Keywords:
Myocardial perfusion SPECT
Extracardiac findings
Non-cardiac chest pain
^{99m}Tc-tetrofosmin

ABSTRACT

^{99m}Tc-tetrofosmin single photon emission computed tomography (^{99m}Tc-tetrofosmin SPECT) has an important role in the assessment of coronary artery disease. Despite being its main indication, this study does not only evaluate myocardial perfusion, but much more. Moreover, during the SPECT acquisition, the field area covered includes many important organs of the thorax and abdomen, so extracardiac abnormalities can be observed. The correct etiologic diagnosis of them is only possible if we understand how ^{99m}Tc-tetrofosmin works and make a comprehensive investigation of the clinical history of the patient.

Captación extracardíaca patológica de ^{99m}Tc-tetrofosmin, detectada incidentalmente en un estudio de perfusión miocárdica: importancia de la evaluación de los antecedentes clínicos del paciente

Palabras clave:
SPECT de perfusión miocárdica
Captación extracardíaca
Dolor torácico no cardiológico
^{99m}Tc-tetrofosmin

RESUMEN

La tomografía con ^{99m}Tc-tetrofosmin (^{99m}Tc-tetrofosmin SPECT) desempeña un papel fundamental en la evaluación de la enfermedad coronaria. A pesar de que esta es su principal indicación, debemos recordar que estos estudios no evalúan únicamente la perfusión miocárdica, sino mucho más. Además, durante la adquisición de la SPECT, el campo incluye gran parte del tórax y abdomen, por lo que podemos observar enfermedad extracardíaca en las regiones incluidas. Llegar a un correcto diagnóstico etiológico de esas alteraciones solo es posible si entendemos cómo funciona el ^{99m}Tc-tetrofosmin y realizamos una exhaustiva investigación de los antecedentes e historia clínica del paciente.

Introduction

^{99m}Tc-tetrofosmin single photon emission computed tomography (^{99m}Tc-tetrofosmin SPECT) is a well-established, non-invasive imaging technique in the management of angina and myocardial infarction, and has become widely used for diagnosis and assessment of prognosis in patients with known or suspected coronary artery disease. Furthermore it is important to note that ^{99m}Tc-tetrofosmin is an agent that has been used as oncotropic radiotracer, and is highly concentrated within neoplastic processes of several varieties because of its uptake in mitochondria, being excreted by hepatobiliary system.[1]

In ^{99m}Tc-tetrofosmin SPECT, although most of the information is obtained from the tomographic slices, the raw projection images should be examined in order to evaluate incidental cardiac or extracardiac findings, and to assess the quality of the study.[2]

We present a case in which myocardial perfusion imaging (MPI) revealed an unexpected extracardiac activity in posteriomedial region of the right hemithorax. Exhaustive clinical history revision was paramount to a correct evaluation of the finding.

Case report

A 71-year-old man, with a history of alcoholism until 5 years ago, without diabetes or hypertension, was referred for a ^{99m}Tc-tetrofosmin SPECT/CT because of chest pain. Patient was diagnosed of one year ago of squamous cell esophageal carcinoma stage pT2N0M0 and underwent esophagectomy. No chemotherapy or radiotherapy was required.

The day of the MPI, the patient underwent adenosine stress, and subsequently 740 MBq ^{99m}Tc-tetrofosmin was injected intravenously. Thirty minutes after radiotracer injection, a SPECT/CT

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http://dx.doi.org/10.1016/j.remn.2015.03.005
2253-654X/

Please cite this article in press as: González García B, et al. Incidental pathologic extracardiac uptake of ^{99m}Tc-tetrofosmin in myocardial perfusion imaging: Importance of patient background evaluation. Rev Esp Med Nucl Imagen Mol. 2015. http://dx.doi.org/10.1016/j.remn.2015.03.005

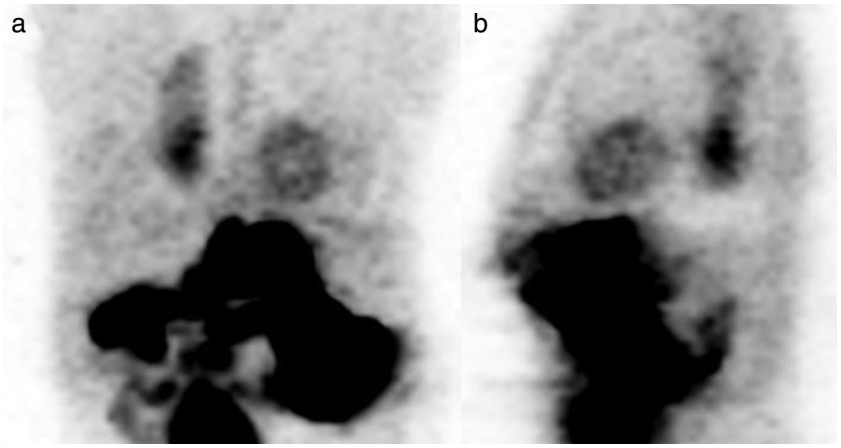

Fig. 1. Anterior and lateral raw data of ^{99m}Tc-tetrofosmin SPECT images at stress show vertical extracardiac linear activity, located in right posterior thorax, near the midline.

imaging with a dual head gamma-camera (Infinia Hawkeye, GE) was acquired. The cardiac images showed normal myocardial perfusion but, on the raw projection image, an extracardiac uptake, located in right posterior thorax, near the midline, was noted (Fig. 1). Reconstructed SPECT/CT slices confirmed the activity in the right-posterior mediastinum, with a linear morphology, in correspondence with an elongated mass on CT obtained for attenuation correction purpose (Fig. 2). Additionally, this CT showed massive left pleural effusion, without increased activity of the radiotracer.

This finding led us to consider on a dilemma: Was related to esophageal cancer recurrence or was a complication due to the received treatment? To clarify the finding interpretation, a revision of clinical and surgical patient background was performed. ^{18}F-FDG PET/CT at diagnosis, revealed the primary tumor in upper thoracic esophagus, without lymphadenopathy or distant metastasis (Fig. 3). Patient underwent surgery (esophagectomy, gastric tube reconstruction and esophagogastric anastomosis), and one month before the MPI request, another ^{18}F-FDG PET/CT was performed due to suspicion of relapse. The metabolic imaging confirmed locoregional and distant recurrence (Fig. 4), showing relapse in proximal esophagus, while no significant increase in glucose metabolism was evident in the lower 2/3 of the gastroplasty (which showed increased activity in ^{99m}Tc-tetrofosmin SPECT).

The comparison between SPECT/CT and PET/CT images (Fig. 5) showed that gastroplasty was dilated with liquid content, especially in distal region. Careful re-inspection of SPECT/CT determined that the increased activity corresponded to the content of the gastroplasty, so the findings were due to duodeno-gastro-esophageal reflux.

Discussion

^{99m}Tc-tetrofosmin is cleared from the blood and trapped into mitochondria, reflecting viable myocytes. Furthermore it has shown potential usefulness as tumor-imaging agent. Uptake in tumoral cells depends on the regional blood flow and cell membrane integrity, as well as mitochondrial density, which are increased in these cells. For that reason, many authors have explored the utility of ^{99m}Tc-tetrofosmin in the diagnosis of

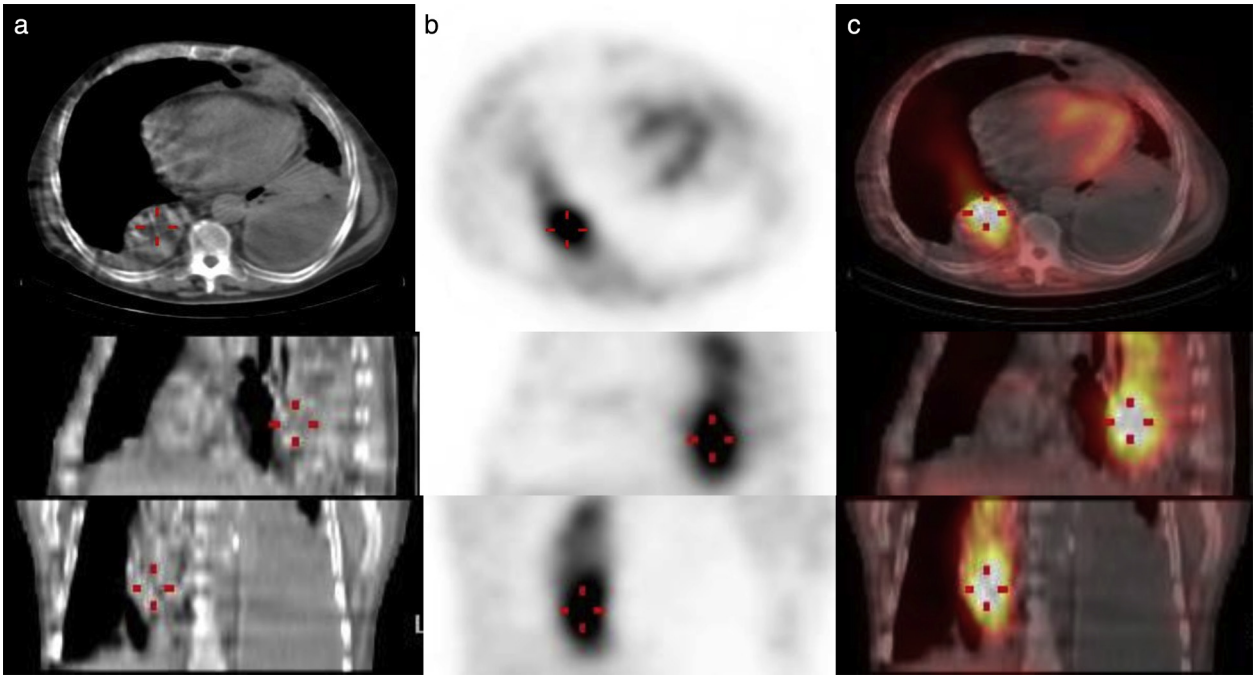

Fig. 2. ^{99m}Tc-tetrofosmin SPECT (b) and fused SPECT/CT (c) slices reveal an elongated mass with increased activity in right-posterior mediastinum.

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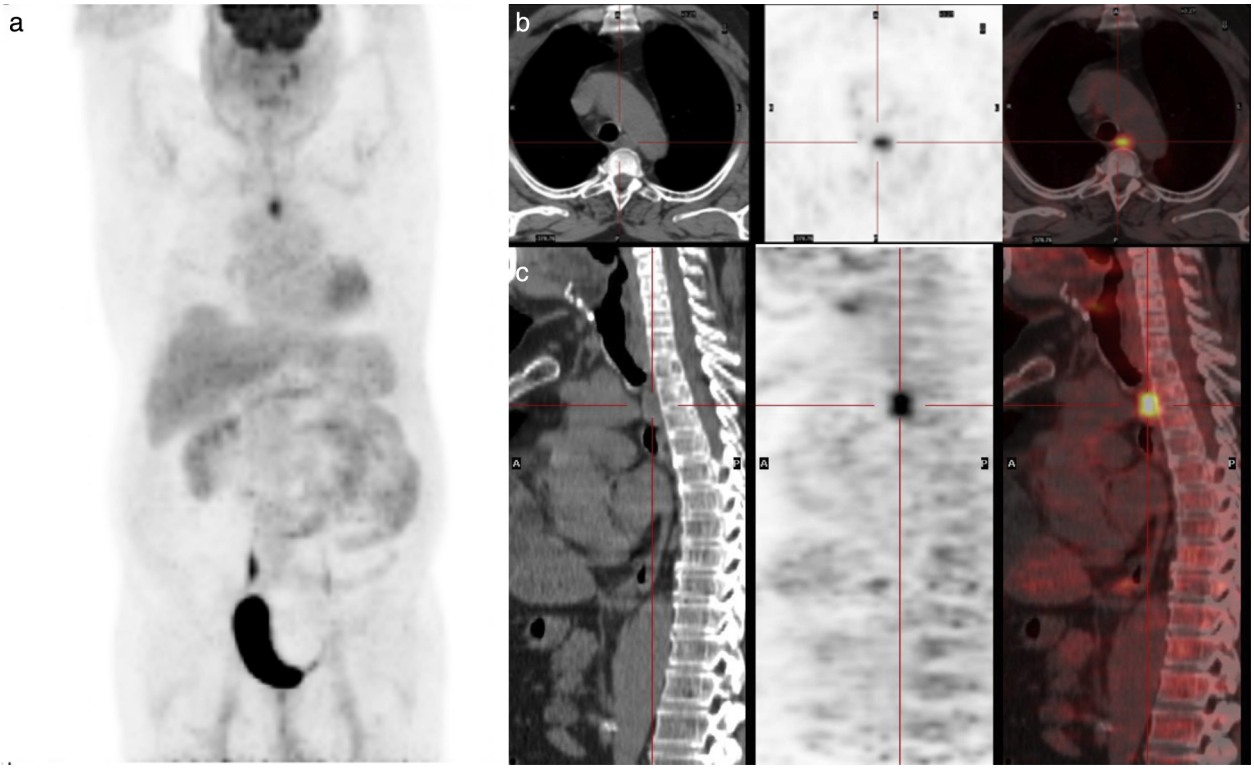

Fig. 3. ^{18}F-FDG PET/TC at diagnosis. Maximum-intensity-projection (a), axial (b) and sagital (c) PET/CT images show increased uptake in proximal esophagus due to esophageal carcinoma, without lymphadenopathy or distant metastasis.

various tumors, with a sensitivity and specificity of 82.5% and 100% respectively for esophageal cancer.[3]

In MPI, during SPECT acquisition, the detector of a gammacamera covers most of the thorax and the abdomen. The evaluation of three-dimensional displays on rotating raw data images has the ability to check for possible artifacts during acquisition and discern abnormalities of the organs or tissues above and below the diaphragm (heart, lungs, mediastinum, liver, spleen and kidneys). These abnormalities may occur between 0.69 and 41.3% of cases.[4,5] Table 1 shows a classification of these findings.

On the other hand, ^{99m}Tc-tetrofosmin is excreted by the hepatobiliary system, which allows the evaluation of the biliary tract, as well as detection of entero-gastric reflux.[6] It has been reported a prevalence of reflux of 8.3% in MPI, being the second most frequent intra-abdominal abnormality.[6]

To properly interpret the extracardiac uptake in our study, it was necessary to remember the pharmacokinetics of ^{99m}Tc-tetrofosmin, and to know the patient's clinical background, in which two relevant events were reported: first, he was diagnosed of esophageal cancer, with confirmed relapse one month

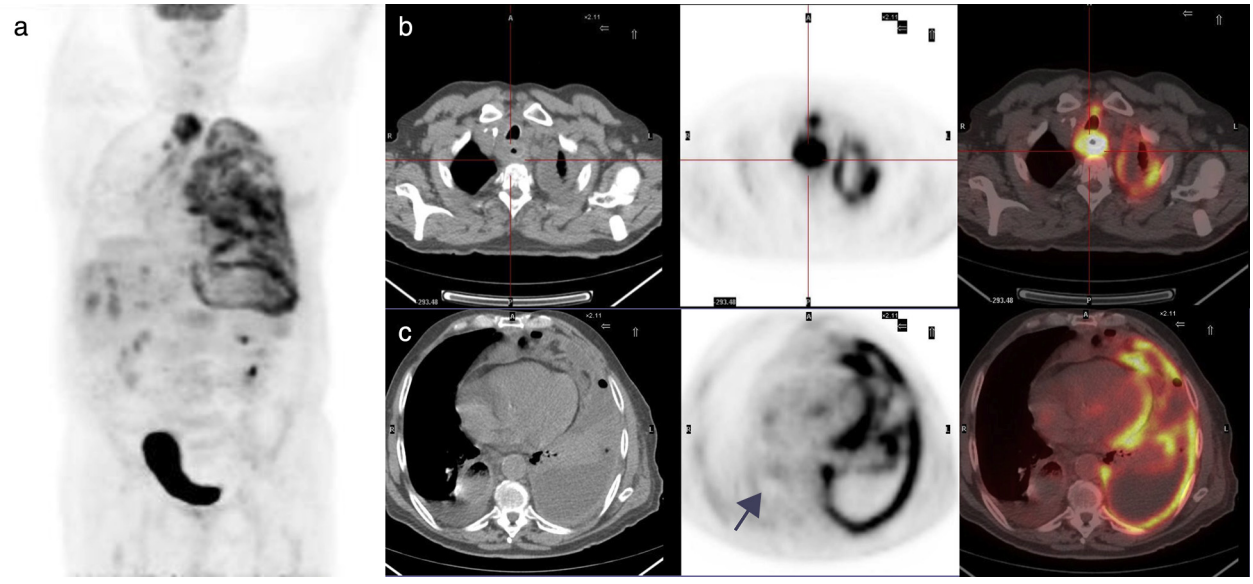

Fig. 4. ^{18}F-FDG PET/CT 1 month before myocardial perfusion study. Maximum-intensity-projection (a) and axial PET/CT images (b,c), show relapse in proximal esophagus while there is no increased activity in gastric tube (arrow).

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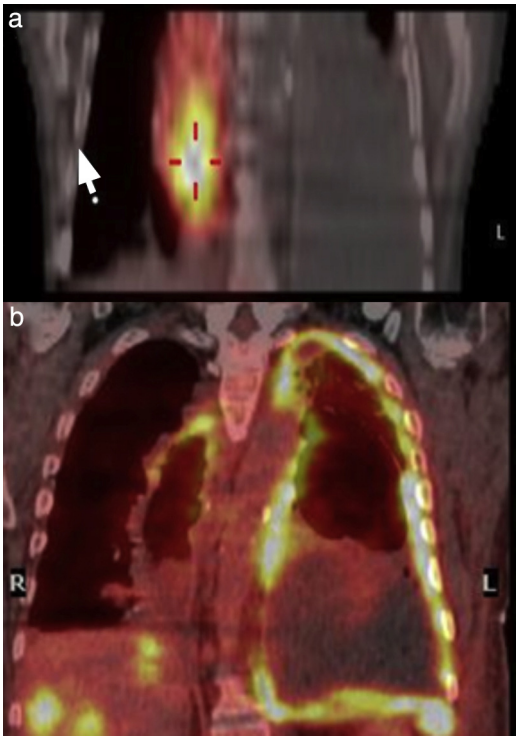

Fig. 5. ^{99m}Tc-tetrofosmin coronal SPECT/CT (a) and ^{18}F-FDG coronal PET/CT (b). The images show increased activity of ^{99m}Tc-tetrofosmin in SPECT/CT (a) corresponded to the content of the gastroplasty due to reflux. In PET/CT study we can see the dilated gastroplasty, with liquid content, and without hypermetabolism.

Table 1
Abnormalities in myocardial perfusion SPECT/CT studies.

Abnormalities above the diaphragm.	• Malignant or benign lesions in thyroid. • Parathyroid lesions (adenoma, hyperplasia, carcinoma). • Malignant (primary/metastatic) or benign lesions in the lungs. • Diffuse and bilateral uptake in the lungs. • Pleural or pericardial effusion. • Mediastinal tumor. • Sarcoidosis. • Duodenogastroesophageal reflux. • Hiatus hernia. • Lyphoma. • Breast cancer. • Sternal uptake in anemia and/or hypoxemia.
Abnormalities of the diaphragm.	• Elevation or displacement of the diaphragm.
Abnormalities below the diaphragm.	• Hepatomegaly, splenomegaly. • Cirrhosis with ascites. • Gastric empting abnormalities. • Duodenogastric biliary reflux. • Non-visualization of the gallbladder (cholelithiasis, acute cholecystitis, or cholecystectomy). • Focal benign (photopenic) or malignant (primary/metastatic) lesions in abdominal organs. • Vertebral uptake in anemia and/or hypoxemia.

before the MPI. Second, patient underwent esophagectomy, gastroplasty and esophagogastric anastomosis as treatment of his tumor. This surgical approach carries significant morbidity, including late complications such as stricture (up to 52% of patients), dumping syndrome, delayed gastric emptying, and esophagitis due to acid/bile regurgitation (up to 80% of cases). In order to perform the differential diagnosis of neoplastic recurrence vs bile reflux, it could be reasonable to recommend additional tests, such as a hepatobiliary scintigraphy to confirm reflux, or an endoscopy or any imaging test to confirm recurrence. Our patient underwent ^{18}F-FDG PET/CT one month before MPI, without evidence of recurrence in the lower 2/3 of the gastroplasty. CT slices showed that gastroplasty was dilated, and had liquid content. A re-inspection of SPECT/CT determined that the increased activity corresponded to the content of the gastroplasty, so we concluded that the findings were due to entero-gastric reflux. Other authors have previously reported bile reflux episodes in ^{99m}Tc-tetrofosmin SPECT studies performed on patients who had undergone gastroesophageal surgery.[7,8] In the present case report, we used additional information from ^{18}F-FDG PET/CT to reach the final diagnosis. This combined assessment has been previously described, but only in the evaluation of tumors.[9]

Finally, we must remember the reason why the myocardial perfusion imaging was requested: chest pain. The SPECT showed normal myocardial perfusion, so that coronary heart disease was excluded.

As many as 20% of patients with chest pain underwent catheterization have normal coronary arteries. Of them, up to 50% have pain secondary to digestive disorders.[10] When bile reflux presents several typical symptoms associated to chest pain, as heartburn, flatulence and/or nausea, is easily identifiable. However, when it only manifests as chest pain is difficult to establish its etiology, being necessary to rule out coronary disease. Our patient had bile reflux evidenced by ^{99m}Tc-tetrofosmin SPECT/CT, which had probably led to an irritation of the plasty wall and esophageal remnant, being a potentially treatable cause of chest pain.

Others might be the causes of the patient's pain: pleuropulmonary disease, with a massive pleural effusion requiring pleurodesis, or psychogenic etiology. The latter was considered the more likely cause by his Oncologist; however, given the MPI findings, it seems obvious that the massive esophagogastric reflux play a role as cause of pain (single or associated with others).

In conclusion, many benign or malignant abnormalities in the thorax and/or abdomen may be evidenced in a ^{99m}Tc-tetrofosmin SPECT/CT. Therefore, it is mandatory to review raw data images, report extracardiac findings and investigate the patient's background, in order to alert clinicians about causes on non-cardiologic chest pain (such bile reflux) or abnormalities that require further investigation.

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