Clinical note

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


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**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.

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**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 onocotracer, 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
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. 18F-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 18F-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 99mTc-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

99mTc-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 99mTc-tetrofosmin in the diagnosis of
various tumors, with a sensitivity and specificity of 82.5% and 100% respectively for esophageal cancer.1

In MPI, during SPECT acquisition, the detector of a gamma-camera 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.

Fig. 3. 18F-FDG PET/CT 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.

On the other hand, 99mTc-tetrofosmin is excreted by the hepatobiliary system, which allows the evaluation of the biliary tract, as well as detection of enterogastric 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 99mTc-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. 18F-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).
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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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: pulmonary 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.

References