

Lung Scintigraphy With Technetium 99m Depreotide in the Assessment of Solitary Pulmonary Nodules

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A solitary pulmonary nodule (SPN) is defined as a parenchymal lesion measuring less than 3 cm in diameter that is not associated with other lesions. Ninety percent of SPNs are discovered incidentally and most are benign. The management of radiographically indeterminate SPNs has not been established and invasive procedures must be undertaken in order to understand the nature of the nodule. We review our experience with the use of somatostatin receptor scintigraphy with technetium Tc^{99m} depreotide in 10 patients with suspected malignant SPN. We discuss the limitations and applications of this technique in the evaluation of whether SPNs are benign or malignant for the purpose of identifying patients for biopsy. For this application, this technique can be considered an alternative to positron emission tomography using fluorine-18 fluorodeoxyglucose.

Key words: Solitary pulmonary nodule (SPN). Technetium Tc^{99m} depreotide. Lung scintigraphy.

La gammagrafía con ^{99m}Tc -depreótida en la valoración del nódulo pulmonar solitario

El nódulo pulmonar solitario (NPS) se define como una lesión parenquimatosa única, con un tamaño inferior a 3 cm de diámetro y no asociada a otras lesiones. El 90% se descubre de forma casual y la mayoría es de naturaleza benigna. El tratamiento de los NPS radiológicamente indeterminados no está del todo establecido, y es necesaria la realización de técnicas invasivas con el fin de conocer la naturaleza de la lesión.

Presentamos nuestra experiencia en la gammagrafía de receptores de somatostatina con ^{99m}Tc -depreótida en 10 pacientes con NPS sospechosos de malignidad. Discutimos las limitaciones y aplicaciones de esta técnica en la diferenciación de la naturaleza benigna o maligna de las lesiones para seleccionar a los pacientes candidatos a biopsia, terreno donde puede considerarse una alternativa a la tomografía por emisión de positrones con ^{18}F fluorodesoxiglucosa.

Palabras clave: Nódulo pulmonar solitario. ^{99m}Tc -depreótida. Gammagrafía pulmonar.

Introduction

A solitary pulmonary nodule (SPN) is defined as a single, well-defined parenchymal lesion that is round or oval, measuring less than 3 cm in diameter, surrounded by normal lung tissue, and not associated with other lesions or atelectases. Ninety percent of SPNs are discovered incidentally in a simple chest x-ray or computed tomography (CT) scan. Although the majority are benign, 30% to 40% of cases are malignant and correspond to stage I lung cancer.^{1,2} Therefore, until malignancy is ruled out, all SPNs should be considered malignant in high-risk patients.³

The use of radiographic assessment continues to be controversial, and it is often necessary to use invasive techniques to determine the nature of the SPN.^{4,5}

We review our experience with the use of somatostatin receptor scintigraphy with technetium Tc^{99m} depreotide in 10 patients with suspected malignant SPN and we discuss the limitations and applications of this technique in the evaluation of SPNs.

Case Description

We performed somatostatin receptor scintigraphy with technetium Tc^{99m} depreotide in 10 men aged 47 to 75 years old with chest x-rays and/or CT scans showing SPNs suspected to be malignant. Each patient was administered an intravenous dose of approximately 47 μ g of depreotide radiolabeled with 740 MBq of Tc^{99m} (NeoSpect; Amersham Health, Piscataway, NJ, USA). The scan was performed between 90 and 120 minutes after the radiopharmaceutical was administered. The patient was placed in a supine position with arms extended over the head while the following scans

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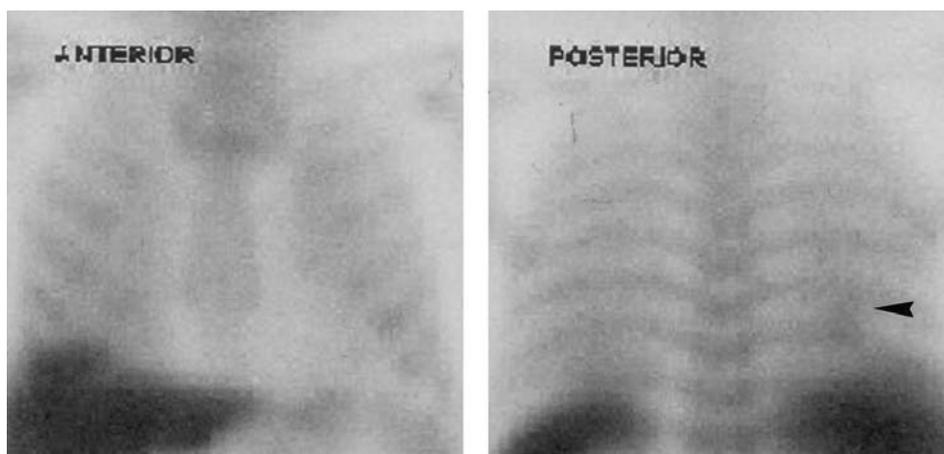


Figure 1. A round nodule 2 cm in diameter located in the right upper lobe in a 70-year-old patient. Anterior and posterior planar scintigraphy scans of the chest where slight uptake of technetium Tc^{99m} depreotide can be observed (arrow).

were carried out: anterior and posterior planar images of the chest (low energy general purpose collimator, 256×256 matrix, 10-minute scan time, energy window of 140%±10% KeV); scintigraphy; and single photon emission CT (SPECT) (low energy general purpose collimator, 128×128 matrix, circular orbit, step-by-step acquisition, 360° rotation, 120 scans, 30-second scan time, energy window of 140%±10% KeV) using a dual-head gamma camera (General Electric, Millennium MG, Buckinghamshire, UK).

The planar and SPECT images were manually interpreted. A positive study was indicated by abnormal and increased uptake when compared to adjacent lung tissue and when a corresponding pulmonary lesion was identified in the chest x-ray, CT scan, or both. The SPECT was qualitatively assessed by comparing the uptake by lesions in comparison with the uptake at reference points in chest and upper abdomen (vertebrae, sternum, ribs, and liver) using the following scale: *a*) less than the reference point; *b*) equal to the reference point; and *c*) greater than the reference point. The lesion-to-background ratio was calculated comparing the activity of the region surrounding the lesion with the activity of the equivalent region in the healthy lung.

The SPECT images were positive in 9 patients, but the planar scans were positive in only 4 cases. Seven patients with positive results underwent surgery; 5 had adenocarcinoma, one had actinomycosis, and one had tuberculosis. Two patients refused invasive treatment and SPN growth was observed in subsequent CT scans in both. The patients with negative results opted for conservative treatment and remained asymptomatic 18 months following scintigraphy. In addition, the findings in 2 patients who underwent positron emission tomography with F-18 fluorodeoxyglucose coincided with the findings from

scintigraphy with technetium Tc^{99m} depreotide: positive for adenocarcinoma in one and negative in the other. In the qualitative analysis, 4 malignant lesions had greater uptake than the vertebral column and 5 had uptake scores greater than 7. The benign lesions had less uptake than the vertebrae and had scores less than 7. In the semiquantitative analysis, the lesion-to-background ratios ranged from 1.7 to 2.7 (mean 2.0) for the malignant lesions and 1.6 to 1.8 for the benign lesions.

Discussion

Depreotide is a synthetic decapeptide with a cyclical sequence of 6 amino acids and a molecular weight of 1358 that bonds easily with subtypes 2, 3, and 5 of somatostatin receptors.⁶ Although somatostatin receptors are expressed in normal tissue, they are expressed to a greater extent in many malignant tumors and in some inflammatory processes. The somatostatin receptors are overexpressed in the majority of neuroendocrine tumors, including small cell lung cancer, and subtype 3 is expressed in non-small cell lung cancer.⁷ This overexpression of somatostatin receptors allows for the differentiation of these types of neoplasms from other tissues through scintigraphy with technetium Tc^{99m} depreotide.

In order to interpret technetium Tc^{99m} depreotide scintigraphy, it is necessary to obtain SPECT images, which provide greater contrast between lesions and surrounding tissue than do planar scans and which can be directly compared with CT scans, as in Figures 1 and

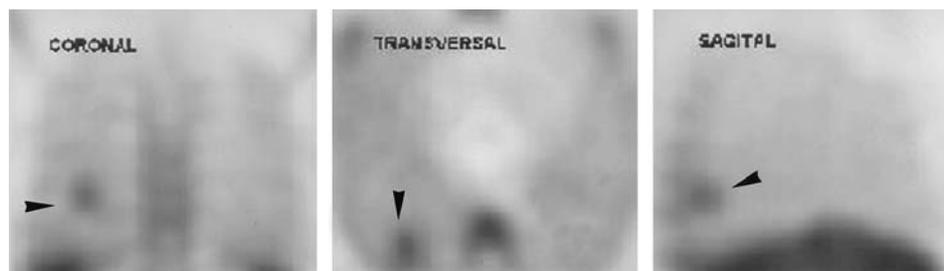


Figure 2. Coronal, transversal, and sagittal slices using single photon emission computed tomography with technetium Tc^{99m} depreotide. Intense focal uptake can be observed in the right inferior lobe (arrows) corresponding to a well-defined adenocarcinoma.

2. In a multicenter study on the assessment of SPNs and lung masses, scintigraphy with technetium Tc^{99m} depreotide had a sensitivity of 96.6% and a specificity of 73.1%.⁸ For 88 of the 114 patients in that study, histology was consistent with malignancy. An earlier study of 30 patients with indeterminate SPNs greater than 1 cm in diameter demonstrated that this method had a sensitivity of 93% and a specificity of 88% with positive and negative predictive values of 87% and 93%, respectively.⁹ Grewal et al¹⁰ compared the effectiveness of scintigraphy with the effectiveness of CT in the evaluation of 39 patients with SPNs and found that the two techniques have a sensitivity of 100% and 90%, a specificity of 43% and 19%, a positive predictive value of 64% and 53%, and a negative predictive value of 100% and 67%, respectively. They concluded that scintigraphy with Tc^{99m} depreotide is a sensitive imaging technique with greater specificity and negative predictive value than CT in the evaluation of the SPNs.

The main cause of false negatives using technetium Tc^{99m} depreotide scintigraphy is the activation of lymphocytes in infectious granulomas, such as coccidioidomycosis and tuberculosis.^{8,9} False positives have also been associated with hamartomas⁸ and round atelectases.¹¹ To improve the specificity of the technique, various options have been suggested. Lesions with equal or greater activity than the vertebral column^{12,13} or lesions with a lesion-to-background uptake ratio greater than 2.0 can be considered malignant.^{14,15} In our group of patients, false positives resulted from actinomycosis and tuberculosis. Only 4 malignant lesions had more uptake than the vertebrae. In the semiquantitative analysis, the mean value of the lesion-to-background ratio was 2.0 (range: 1.7 to 2.7) for the malignant lesions and 1.6 and 1.8 for the benign lesions.

Gambhir et al¹⁶ analyzed the cost-effectiveness of 4 procedures in SPN management: radiographic treatment, CT alone, CT and scintigraphy with Tc^{99m} depreotide, and thoracotomy. The combination of indeterminate CT and scintigraphy with Tc^{99m} depreotide was found to be the most cost-effective option for a population with a high probability for malignancy (14%-71%). The combination of scintigraphy and CT-guided biopsy was more accurate than any other single technique in the selection of patients who were candidates for thoracotomy.⁷

Another useful technique in the diagnosis and treatment of SPNs is video-assisted thoracoscopic surgery, which provides a highly accurate diagnosis and which avoids delays in the treatment of potentially curable lung cancers.¹⁷

Scintigraphy with Tc^{99m} depreotide can aid in the differential diagnosis of SPNs and in the selection of patients who are candidates for biopsies and/or thoracotomy.^{7,16,18,19} This technique can be considered an alternative to positron emission tomography with fluorine-18 fluorodeoxyglucose in the assessment of

SPNs due to its lower cost and wider availability,^{7,16,18,19} even though it provides different functional information about the lesion.²⁰

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