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Original article

Effectivity and clinical impact of ^{18}F-FDG PET in the diagnosis of unsuspected second primary tumors☆

L. Caballero Gullón*, I. Borrego Dorado, R. Vázquez Albertino

Unidad de Diagnóstico por la Imagen, Servicio de Medicina Nuclear, Hospital Universitario Virgen del Rocío, Sevilla, Spain

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ABSTRACT

Objective: This study is aimed to determine the capacity and clinical impact of the ^{18}F-FDG-PET to detect previously unsuspected second primary tumors.
Materials and methods: This is a retrospective cross-sectional study of 1984 consecutive scans performed between March 2004 and March 2005, identifying those studies that had reported the presence of hypermetabolic lesions, that had not been previously suspected or detected and that could be suggestive of second primary tumors. Diagnosis was made histopathologically or by clinical and radiological follow-up for a period exceeding one year.
Results: 62 findings suggestive of second primary tumors were detected in 58 patients (3.1%). The reasons for the study for this group of patients were diverse, the most common being the differential diagnosis of solitary pulmonary nodules. A total of 43.5% of lesions were not followed-up. We confirmed the existence of 35 lesions, either by pathology study (21 lesions, 13 second primary tumors, the incidence in our population was 0.65%) or clinical and radiological follow-up (14 lesions, none of which corresponded to second primary tumors). The total clinical impact was the discovery of unexpected 14 lesions in 12 patients.
Conclusion: The presence of second primary tumors on ^{18}F-FDG-PET is relatively common. These lesions should be monitored clinically for accurate diagnosis. In a high percentage, they correspond to unexpected second primary tumors in an early stage and therefore amenable to curative treatment or for which tumor treatment planning may be modified.

Efectividad e impacto clínico de la PET-^{18}F-FDG en el diagnóstico de segundos tumores primarios insospechados

Palabras clave:
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RESUMEN

Objetivo: Evaluar la capacidad e impacto clínico de la PET-^{18}F-FDG en el diagnóstico de segundos tumores primarios malignos inesperados.
Material y métodos: Estudio retrospectivo transversal descriptivo de 1.984 exploraciones PET-^{18}F-FDG consecutivas realizadas entre marzo de 2004 y marzo de 2005, identificándose aquellos estudios en los que se había informado de la presencia de lesiones hipermetabólicas, no sospechadas ni detectadas previamente y que pudiesen ser sugestivas de segundos tumores primarios. Se obtuvo un diagnóstico histopatológico o mediante seguimiento clínico-radiológico durante un período de tiempo superior a un año.
Resultados: Se detectaron 62 hallazgos sugestivos de incidentalomas en 58 pacientes (3,1%). Los motivos de indicación en este grupo de pacientes fueron diversos siendo los más frecuentes el diagnóstico diferencial de benignidad vs malignidad de nódulos pulmonares solitarios. Un 43,5% de las lesiones no tuvieron seguimiento. Se confirmó la existencia de 35 lesiones, bien mediante estudio anatomopatológico (21 lesiones, 13 incidentalomas, la incidencia en nuestra población fue del 0,65%) o por seguimiento clínico-radiológico (14 lesiones, ninguna de ellas correspondió a segundos tumores primarios). El impacto clínico total fue el hallazgo de 14 lesiones no esperadas en 12 pacientes.
Conclusiones: La presencia de incidentalomas en la PET-^{18}F-FDG es relativamente frecuente. Estas lesiones deben ser objeto de seguimiento clínico para su diagnóstico exacto. En un alto porcentaje se corresponden con segundos tumores primarios inesperados en fase incipiente y, por lo tanto, susceptibles de tratamiento curativo o que pueden modificar la planificación del tratamiento del tumor ya conocido.

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* Corresponding author.
E-mail address: luiscaballerogullon.mnuclear@gmail.com (L. Caballero Gullón).

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Introduction

The possibility of a second primary tumor appearing in the same patient has been reported for decades and has been widely described in the scientific literature.[1,2] Studies performed by the U.S. *National Cancer Institute's Surveillance, Epidemiology, and End Results* (SEER) have shown that multiple primary neoplasms make up 13.1% of the cancers in males and 13.7% of those in women. There is evidence that a person who has survived one cancer has twice the probability of developing a new primary tumor than an individual with the same age and genre with no previous oncologic history. The development of these tumors is increasingly more frequent due to the increase in the use of chemotherapeutic agents and radiotherapy, which raise the probability of the appearance of a new malignant tumor, and is also related to the intrinsic risk of the oncologic patient to develop these tumors, as well as genetic factors and the frequent association of different types of cancers with the same etiology. The detection of these tumors is also on the rise because of the technological advances in the diagnostic tools currently available which allow the detection of malignant involvement in early stages.[1,2] In addition, these tools constitute an important prognostic factor in patients with cancer, being able to determine treatment failure and the increase in mortality of some specific types of oncologic disease.[1,3,4] These lesions are often tumors with a poor prognosis which are frequently located in already treated or unexpected areas in which early diagnosis is difficult to achieve.[3–5] Although the management of each patient is individual, the therapeutic options in these second or third primary tumors are generally compromised by the treatment of a tumor with a worse prognosis. Nonetheless, early diagnosis of these tumors may lead to successful treatment.[1,3]

Positron emission tomography with ^{18}F-fluordeoxyglucose (PET-^{18}F-FDG) is a diagnostic technique which is successfully and increasingly used in the diagnosis and follow-up of the treatment of a rising number of malignant neoplasms, including their initial staging, restaging of recurrence and the monitoring of response to chemo- and radiotherapy. It is also used in the characterization of undetermined lesions such as the solitary pulmonary nodule (SPN) and in the investigation of tumors of unknown origin.[6–10] Some reports have even described the capacity of this technique in the screening of some cancers and in the detection of new malignant tumors in a reduced fraction of asymptomatic patients. PET-^{18}F-FDG has demonstrated greater diagnostic precision than computerized tomography (CT) in the detection of metastatic lesions or unexpected tumoral recurrences of malignant tumors and has shown its capacity for the diagnosis of other primary tumors.[11,12]

The objective of this study was to evaluate the capacity and clinical impact of PET-^{18}F-FDG in the diagnosis of unexpected second malignant primary tumors in 1984 PET-^{18}F-FDG studies performed in our unit from March 2004 to March 2005.

Material and methods

Study population

We carried out a transversal descriptive study including a cohort of 1984 consecutive whole body PET-^{18}F-FDG studies in our unit from March 2004 to March 2005. The aim of these studies was to achieve the initial staging or restaging of already known tumors, the differential diagnosis of benign/malignant lesions of undetermined nature or the evaluation of the response to treatment of tumors, with retrospective analysis of the results of these studies.

Positron emission tomography

The PET-^{18}F-FDG studies were performed using an ECAT® EXACT^{TM} HR+ (Siemens) tomographic equipment after the intravenous administration of 370–444 MBq of ^{18}F-FDG. Previous preparation consisted of 6 h of fasting; fluids without sugar were accepted and physical exercise was limited in the previous 12 h. Normoglycemia (<120 mg/dl) was confirmed in all the patients. In addition, patient preparation included prior administration of a muscle relaxant (50 mg of oral tetrazepam) as well as hydration with intramuscular saline serum and a diuretic (0.25 furosemide/Kg of weight) 30 min after the administration of the radiotracer with the aim of improving the technical quality of the images and minimizing the dosimetry of the patient.[13] All the patients were studied from the temporal region to the proximal third of the femur, performing a whole body scan in the case of patients with melanomas, acquiring the study at 10 min/bed. Thus, 70% corresponded to the acquisition of emission images and the remainder to the time for the acquisition of transmission image. 2D emission images were acquired with and without attenuation correction by transmission and image reconstruction were carried out using iterative reconstruction (2 iterations/8 subsets) in coronal, transversal and sagittal planes.

Interpretation of the PET-^{18}F-FDG study

Each PET-^{18}F-FDG study was evaluated by 2 experts in nuclear medicine, including the emission images without correction of attenuation, assessing the pathological accumulation of the radiotracer by visual and semiquantitative analyses, and with the determination of the standardized uptake value (SUV). Pathological lesions suspected of malignancy were interpreted as those with tracer deposits not explained by known physiological or inflammatory processes according to the clinical history of the patient and the anamnesis prior to the study and which corresponded to the primary tumor studied or were suggestive of malignancy, compatible with local invasion, with lymph node involvement or hematogenous metastatic dissemination. Incidental accumulation of FDG was defined as focal, segmental or multifocal not related to the usual site of metastasis of a known tumor or which was not associated with a known benign disease or to physiological elimination of the tracer.

The PET-^{18}F-FDG studies were performed consecutively over the established time period with the inclusion criteria being the identification of studies reporting the presence of incidental accumulation of FDG suspicious of second primary tumors. All incidental accumulations compatible with benign involvement or physiological activity were excluded.

Lesion analysis and confirmation

The final diagnosis was obtained on review of the clinical record of the patients, with confirmation of these findings being made by the histopathological results or clinical–radiological follow-up over more than one year.

Results

Of the 1984 PET-^{18}F-FDG studies performed in 2004 and 2005, 58 studies carried out in 58 patients (19 women and 39 men) with a mean age of 62.1 ± 14.4 years (range: 22–85 years) detected 62 findings suggestive of incidental tumors compatible with second or third primary tumors (Fig. 1). This represents that the frequency of PET findings suggestive of the presence of second primary tumors or premalignant lesions in our population was of 3.1% (62 out of 1984). The reasons for indication in this group of patients were