Nota Clínica

Carcinoma, tuberculosis and elastofibroma in one patient: is [18F]FDG-PET/CT helpful?

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ABSTRACT

We present the case of a woman with persistent dorsal pain and two solid lung lesions documented on multidetector CT which showed concomitant [18F]FDG uptake. One of the lesions proved to be adenocarci- noma at biopsy and presented a lower [18F]FDG uptake when compared to the second lesion, which was smaller in size, and was postsurgically diagnosed as tuberculoma. This case portrays the paradoxical meta- bolic behaviour of two lesions, leading to misdiagnosis and erroneous disease staging in an oncology pa- tient. Incidentally, the patient also had an elastofibroma dorsi, a rare benign tumour which can also be a possible source of false results in the PET exam. We provide explanations and possible solutions to these findings in order to familiarise the physician with them, and optimise patient management.

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Carcinoma, tuberculosis y elastofibroma en un paciente: ¿es una ayuda la 18F- FDG-PET/CT?

RESUMEN

Se presenta el caso de una mujer con dorsalgia persistente y 2 lesiones pulmonares de carácter sólido visualizadas en tomografía computarizada multidetector. Dichas lesiones mostraban concomitantemente captación de [18F]FDG. Una de las lesiones se diagnosticó de adenocarcinoma tras la biopsia, y presentaba una captación de [18F]FDG de menor intensidad que la mostrada por la segunda lesión, de menor tamaño, y que tras la cirugía se diagnosticó como tuberculoma. Este caso demuestra cómo el comportamiento metabólico paradójico de 2 lesiones puede suponer un diagnóstico y estadificación oncológico erróneo. Incidental- mente, la paciente también se vio afectada de un elastofibroma dorsi, un tumor benigno poco frecuente, que puede ser, a su vez, causa de falsos positivos en el examen PET (tomografía por emisión de positrones). Con este caso se pretende ofrecer razonamientos y posibles soluciones a estos hallazgos, así como familiarizar al médico con estas entidades para optimizar el tratamiento del paciente oncológico.

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Introduction

The role of 2-[18F]fluoro-2-deoxyglucose-Positron Emission Tomography/Computed Tomography ([18F]FDG-PET/CT) in the management of solitary lung nodules has been extensively studied1-3. [18F]FDG uptake reflects on the cell’s glycolitic activity, which is increased in the setting of malignant tumors and during inflammation4, becoming sometimes hard to distinguish between them. [18F]FDG uptake is also increased as the tumor mass becomes larger and the blood supply is limited because hypoxia stimulates metabolic activity in cancer cells5. The case presented appears to be paradoxical as the highest uptake was documented in the smaller benign lesion, whereas the cancerous lesion was less radioactive in spite of its larger size, and its potentially higher metabolic activity.

Incidentally, the patient presented another rare condition known as elastofibroma dorsi, a benign tumor of fairly unknown metabolic behaviour, which in the presence of concomitant cancer, deserves some attention6,7.

Case description

A 76 year old woman with mild dyspnea, right dorso-lumbar pain lasting 6 months and no other relevant clinical history presented with a hyperdensity in the right lung as revealed by a chest X-ray.

A contrast enhanced thorax helical multidetector Computed Tomography (CT) showed a solid parenchymal lesion (27 mm in transax-
ial diameter) in the dorsal segment of the right lung upper lobe with irregular margins and tracts connecting with the pleura. A second solid lesion was localised in the basal pyramid of the right inferior lobe (38 mm in transaxial diameter) of heterogeneous characteristics, irregular borders and contacting the scissure. The CT scan also revealed the presence of node involvement in the hilar region of the right lung. The abdomino-pelvic and brain CT were anodyne.

Given the two lung lesions described, the patient was sent to the nuclear medicine department for an $^{18}$F-FDG-PET/CT scan for further characterisation. This scan revealed the presence of $[^{18}F]$FDG uptake in the lesion of the right upper lobe with a maximal standardized uptake value corrected for body weight (SUVbw max) of 8.32 and a milder radiopharmaceutical uptake (SUVbw max 3.74) in the inferior right lobe. In the right hilar region, another area of light uptake was identified (SUVbw max 2.66). These findings were all interpreted as viable tumor tissue. Additionally, a $[^{18}F]$FDG extensive uptake was localised in the right infrascapular muscle; the presence of elastofibroma was suggested (fig. 1).

The patient underwent a CT guided biopsy of the right inferior lobe lesion due to better percutaneous access, with the result being a well-differentiated adenocarcinoma.

The tumor was classified as stage IV, given the presence of lung lesions in two different lobes (M1), and followed 4 cycles of chemotherapy (carboplatinum and gemcitabine protocol). The follow-up CT scans (2 and 4 months after the biopsy) showed a decrease in transaxial diameter of the upper right lobe lesion (from 27 to 21 and further on to 20 mm). The more caudal lesion in the right lower lobe, did not show changes in transaxial diameter, though the anterior-posterior diameter seemed to reduce from 32 to 28 mm. Adenopathies visualised in the right hilar region remained stable.

Due to the radiological response, the patient was scheduled for a right upper lobe wedge resection of the lesion and right inferior lobectomy with radical hilar-mediastinal lymphadenectomy. Additional resection of the right infra-scapular lesion observed in the imaging was performed. The histopathologic report showed:

- Adenocarcinoma of right inferior lobe with focal infiltration of the visceral pleura.
- Fragment from the right superior lobe containing multiple small nodules (maximum axial diameter 5 mm) corresponding to chronic giant-cellular necrotizing granulomatous inflammation, positive for alcohol-acid resistant bacilli.
- All lymphadenopathies resected showed histiocitosis, anthracosis and focal giant-cellular granulomatous inflammation.
- Posterior thoracic wall formation was positive for elastofibroma.

Figure 1. A) Transaxial $^{18}$FFDG-PET/CT lesion in the upper lobe of the right lung corresponding to tuberculosis. B) Transaxial $^{18}$F FDG-PET/CT image showing lesion of the right lower lobe in correspondence to adenocarcinoma and right hilar lymph-nodes reactive to TB infection. C) Transaxial $[^{18}F]$FDG-PET/CT visualising right sub-scapular elastofibroma. Image in the right lower corner shows $[^{18}F]$FDG-PET condensed coronal view identifying the findings above mentioned.
The patient recovered successfully and was restaged postsurgically ypT2ypN0. No further adjuvant therapy was indicated, and she was referred to a specialist for specific tuberculosis treatment.

Discussion

The role of \( ^{18}\)F-FDG-PET in characterising solitary lung nodules has been extensively studied\(^1\). Increased \( ^{18}\)F-FDG uptake has been reported in almost all tumor types\(^8\) with an accuracy of 96.8% and a specificity of 78%. However, \( ^{18}\)F-FDG is not a tumor specific agent and many benign lesions have demonstrated uptake in PET studies\(^9\), hence histologic confirmation is mandatory in the initial diagnosis of malignancy. Once malignancy is confirmed FDG-PET may also allow staging of disease pursuing radical surgery in the initial stages, neoadjuvant chemotherapy and surgery in locally advanced tumors, and palliative chemotherapy in patients with IIIb-IV disease. In the presence of several radiologically suspicious lesions, tissue sampling should always be performed whenever possible. In this sense, Borrego et al study the efficacy and clinical impact of FDG-PET in the staging of non-small cell lung carcinoma in 115 patients showing that the second most frequent site for false positive findings is the lung parenchyma, after the mediastinum. Bypass of equivocal lesions, is therefore specially relevant in this site\(^10\). In our case, the presence of two parenchymal lesions was confirmed through imaging, although pathologic confirmation was only achievable in one of them. The fact that the benign tuberculomas of the upper right lobe had a particularly difficult biopsy access and a surprisingly high FDG uptake, lead to disease upstaging. Through this case report, we therefore want to put emphasis on the relevance of pathologic confirmation of all equivocal lesions as well as the need for a deeper understanding of the biological behaviour of FDG positive lesions which will enable us a more accurate image interpretation.

Solitary lung nodules may sometimes be radiologically identical to tumors: of these, about one third appear to be granuloma\(^11\). Tuberculomas are a late complication of tuberculosis (TB) and appear radiologically as well-defined nodules mainly localised in the upper lobes, showing calcification in only 20–30% of the cases\(^12\), with an average size no bigger than 3 cm in diameter\(^11\). There are several studies on TB lesions showing \( ^{18}\)F-FDG uptake mimicking malignancy, such as disseminated systemic TB, lymphadenitis or pneumonitis\(^13\)–\(^15\), and some studying the effects on cancer diagnosis in highly prevalent TB Asian countries\(^16\), but there are less studies making reference to quantitative uptake values of these lesions\(^17,18\). In our case, tuberculoma showed a SUVbw max which three-folded the SUVbw max of the cancer lesion (8.32 vs 2.66) even though the TB lesion was smaller in size compared to the tumor (27 mm vs 38 mm). In cancer, tumor cells increase their glucose transporter activity under hypoxic conditions thus increasing \( ^{18}\)F-FDG uptake\(^19\). Granulation tissue and macrophages are also present in tumors, as several authors reported\(^20,21\). They suggested, that the presence of an increased \( ^{18}\)F-FDG uptake in aggressive tumors could be caused by the infiltration and higher metabolic activity of macrophages in the tumor\(^21\). Considering these findings and the fact that our patient presented with a well-differentiated adenocarcinoma, would account for the difference in \( ^{18}\)F-FDG uptake. Hara et al\(^22\), propose a solution for discriminating these lesions in their study comparing \( ^{18}\)F-FDG vs \( ^{18}\)F-Choline uptake in cancer and TB, concluding that whereas both lesions show elevated \( ^{18}\)F-FDG uptake, only cancer shows high uptake with choline, and TB lesions are hardly visualised. Another method suggested is the follow-up of suspicious lesions performing a dual time point \( ^{18}\)F-FDG-PET to show increased/decreased SUV after treatment\(^22\). Interferon-γ release assays could also be a powerful diagnostic tool and has been proposed as the test to be applied in low-incidence high income settings, proving to be more specific than skin test detecting latent TB\(^23\).

In our case, tuberculoma showed a decrease in volume following chemotherapy treatment, whereas the tumor lesion hardly responded. Sandrini et al in a recent work, demonstrated the bactericidal effect of gemcitabine and other nucleoside analogs on S. pyogenes infection in a mouse model\(^24\), so that a similar effect on TB infection cannot be discarded as a possible cause for our findings.

Although the end point of this case was to outline the misdiagnosis M1 disease and the causes of the false positive (FP) finding, the concomitant appearance of hilar nodes has its own relevance. The accuracy of PET has been proved to be consistently superior to CT in identifying N1–3 disease with an overall sensitivity of 79%–84% and a specificity of 89%–91%\(^25\). Even so, in mediastinal staging the presence of FP results, makes histologic confirmation necessary. In our study, hilar nodes showed increased tracer uptake in the PET/CT scan, and hence where initially assumed as tumoral. There are studies which identify the presence of hyperintense/calciﬁed nodes as benign in more than 90% of the cases regardless of the \( ^{18}\)F-FDG uptake\(^26\). Others propose sampling of every mediastinal node seen on PET during mediastinoscopy in order to improve accuracy\(^26\). Generally, increased awareness of the possibility of diverse pathological processes should be recommended, specially in TB endemic countries.

Incidentally, our patient presented with another lesion, an elastofibroma. This is a rare benign tumor of unclear pathophysiology, more prevalent in elderly women and usually localised at the tip of the scapula. It may be bilateral, and although it is usually clinically silent, it can cause swelling, snapping with arm movement, or pain, as was our patient’s case. It is mainly composed of fibrous collagenous strands, hence biopsy is frequently inconclusive due to its hypocellularity. If no symptoms appear, no treatment is required, thus differential image diagnosis is crucial. CT appearance is usually diagnostic, showing a mass with margins indistinguishable from the surrounding muscle, with internal striations or scattered areas of fat attenuation\(^27\). PET images have been previously described\(^28\) as showing light-moderate diffuse \( ^{18}\)F-FDG uptake with a SUV around 1.8. Physicians should become familiarised with this entity in order to avoid false positive results in cancer patients.

References


