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 adenocarcinoma 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 metabolic behaviour of two lesions, leading to misdiagnosis and erroneous disease staging in an oncology patient. 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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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 glycolytic 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. The presence of false positive [18F]FDG-PET/CT results in an oncologic patient can lead to misdiagnosis and in our case, the patient presented several confounding findings which lead to initial disease upstaging. Our aim is both, to offer explanations for these findings, and evaluate possible solutions in order to optimise patient management.

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 hiperdensity 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 heterogenous 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 a $^{18}$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 18F FDG-PET/CT lesion in the upper lobe of the right lung corresponding to tuberculosis. B) Transaxial 18F 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 tuberculostatic treatment.

Discussion

The role of [18]F-FDG-PET in characterising solitary lung nodules has been extensively studied1-3. Increased [18]F-FDG uptake has been reported in almost all tumor types4 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 studies5, 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, neo-adjuvant 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 site6. 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 tuberculosis lesion 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 granuloma7. Tuberculomas are a late complication of tuberculosis (TB) and appear radiologically as well-defined nodules mainly localised in the upper lobes, radiologically as well-defined nodules mainly localised in the upper lobes, showing calcification in only 20-30% of the cases8, with an average size no bigger than 3 cm in diameter9. There are several studies on TB lesions showing [18]F-FDG uptake mimicking malignancy, such as disseminated systemic TB, lymphadenitis or pneumonitis10,11 and some studying the effects on cancer diagnosis in highly prevalent TB Asian countries12, but there are less studies making reference to quantitative uptake values of these lesions13,14. 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 more uptake occurs in hypoxic conditions that is why, as the tumor grows in size and more central hypoxic areas appear, more uptake occurs15. Tuberculomas, in a chronic phase are hardly surrounded by blood vessels, and are composed of cellular infiltrates, mainly macrophages. These cells also increase their glycolytic activity in hypoxic conditions thus increasing [18]F-FDG uptake16. Granulation tissue and macrophages are also present in tumors, as several authors reported17,18. 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 tumor19. 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 al20, propose a solution for discriminating these lesions in their study comparing [18]F-FDG vs [18]CCholine 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 treatment21. 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 TB22.

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 model23, 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%24. 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 uptake25. Others propose sampling of every mediastinal node seen on PET during mediastinoscopy in order to improve accuracy26. 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 attenuation27. PET images have been previously described28,29 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