Intensive FDG-PET/CT Uptake Suggestive of Malignancy Misleading the Diagnosis of Sclerosing Pneumocytoma

Sarra Zairi[1], Antoine Legras[1], Laure Gibault[2], Nadia Ghazzar Pierquet[3], Ciprian Pricopi[1] and Françoise Le Pimpec Barthes[1,*]

Departments of [1]General Thoracic Surgery; [2]Pathology; [3]Nuclear Medicine, Georges Pompidou European Hospital, Paris Descartes University, Paris, France

Abstract: *Introduction*: Combined Positron Emission Tomography-Computed Tomography with 18-fluoro-desoxy-glucose (FDG-PET/CT) is highly sensitive in differentiating malignant from benign pulmonary lesions and is part of the current recommended practices for non-invasive lung nodule assessment. However, many solid pulmonary nodules may show misleading miscellaneous features and can be mistakenly diagnosed as malignant lesions.

Case Report: Herein we report the case of a passive smoking female patient with multiple comorbidities, who was referred for a solitary pulmonary nodule randomly discovered. Chest imaging showed a middle lobe 16-mm nodule with an intensive uptake (SUVmax 7.6) highly suggestive of malignant origin. The patient underwent middle lobectomy with radical lymphadenectomy because the malignancy was not excluded on frozen section. Definitive pathological examination showed a sclerosing pneumocytoma.

Conclusion: FDG-PET/CT is an accurate imaging tool for assessment of solid pulmonary nodules. However, false positive results of some benign lesions have to be kept in mind. Therefore, FDG-PET/CT features have to be interpreted according to the patient's background and clinical data, in order to provide the best appropriate management.

Keywords: FDG-PET/CT, sclerosing pneumocytoma, SUVmax, pulmonary solitary nodule, diagnosis.

INTRODUCTION

Combined Positron Emission Tomography-Computed Tomography with 18-fluoro-desoxy-glucose (FDG-PET/CT) is highly sensitive in differentiating malignant from benign pulmonary lesions and is part of the current guidelines for solitary pulmonary nodule assessment [1,2]. However, many solitary pulmonary nodules may show misleading miscellaneous features and may be mistakenly diagnosed as malignant lesions. Sclerosing pneumocytomas are benign tumors, in which FDG-PET/CT characteristics are not well established and some authors reported unusual features for a lesion of benign origin [3]. We herein report a case of pneumocytoma (formerly called "sclerosing hemangioma"), which showed metabolic features of a malignant lesion and was managed accordingly.

CASE REPORT

A 70-year-old passive smoking female patient, with dyslipidemia, corneal guttata and hypertension was referred to our thoracic surgery department for a suspicious solitary middle lobe nodule randomly discovered.

Two months earlier, she presented an acute coronary syndrome, for which investigations revealed a Takotsubo cardiomyopathy. The patient had no respiratory signs. Chest X-ray and CT showed a middle lobe 16-mm solitary homogeneous nodule, not well marginated, seated in the lateral segment (Figure **1**). Fiberoptic-bronchoscopy was normal. Cerebral magnetic resonance imaging was normal. As recommended, FDG-PET/CT was performed (PET Discovery General Electric 690) and attenuation corrections were done with CT. An intravenous injection of 18-FDG (249 MBq) was performed at the beginning of the procedure, followed by PET/CT scanning from the vertex to mid-thigh, 60 minutes after.

The nodule was hypermetabolic, with a maximum standardized uptake value (SUVmax) of 7.6, highly suggestive of malignant origin (Figure **2**). Therefore, the patient underwent middle lobectomy with radical lymphadenectomy because the malignancy was not ruled out on frozen section. Pathological examination in macroscopy showed a solid nodule, which was yellow on cut section (Figure **3a**). Histologic examination showed a well-circumscribed un-encapsulated nodule, with a mixture of papillary, solid and sclerotic patterns, showing a population of cuboidal epithelial surface cells overlying a core of round cells (Figure **3b**). The epithelial surface cells showed a positive Cytokeratin (AE1/AE3) staining, whereas staining of the round cells was negative (Figure **3c**). Both cell types evidenced a diffuse membranous staining with epithelial membrane

*Address correspondence to these authors at the Department of General Thoracic Surgery, Georges Pompidou European Hospital, 20 rue Leblanc, 75015 Paris, France; Tel: +33 1 56 09 34 81; Fax: +33 1 56 09 33 80;
E-mail: francoise.lepimpec-barthes@aphp.fr

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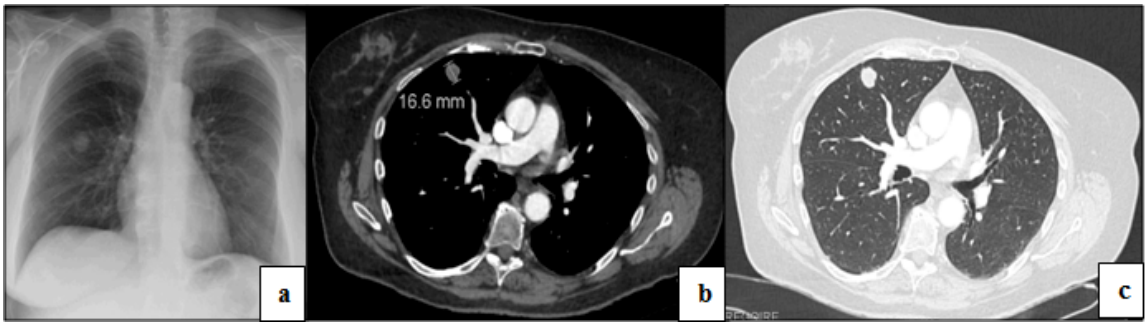

Figure 1: Chest x-ray showing the middle lobe solitary nodule (**a**) Axial enhanced CT in mediastinal (**b**) and parenchymal windows (**c**) showing the solitary lobulated nodule.

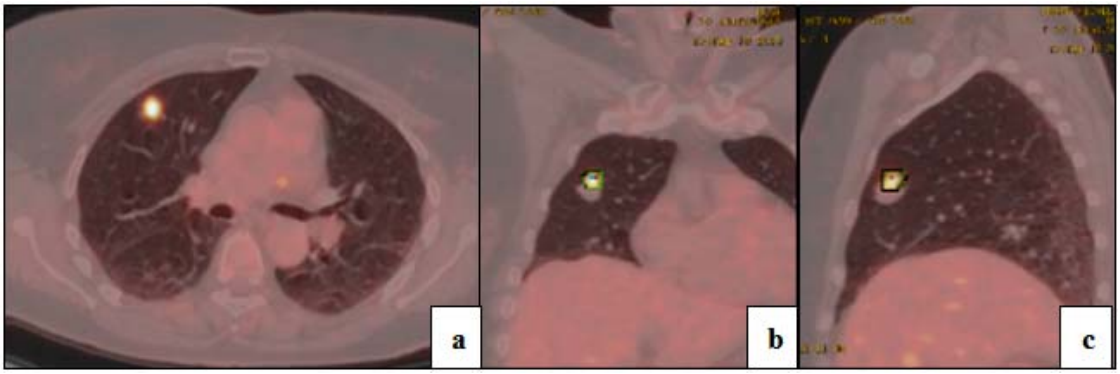

Figure 2: Axial (**a**), coronal (**b**) and sagittal (**c**) PET/CT sections, showing the nodule with significant FDG uptake.

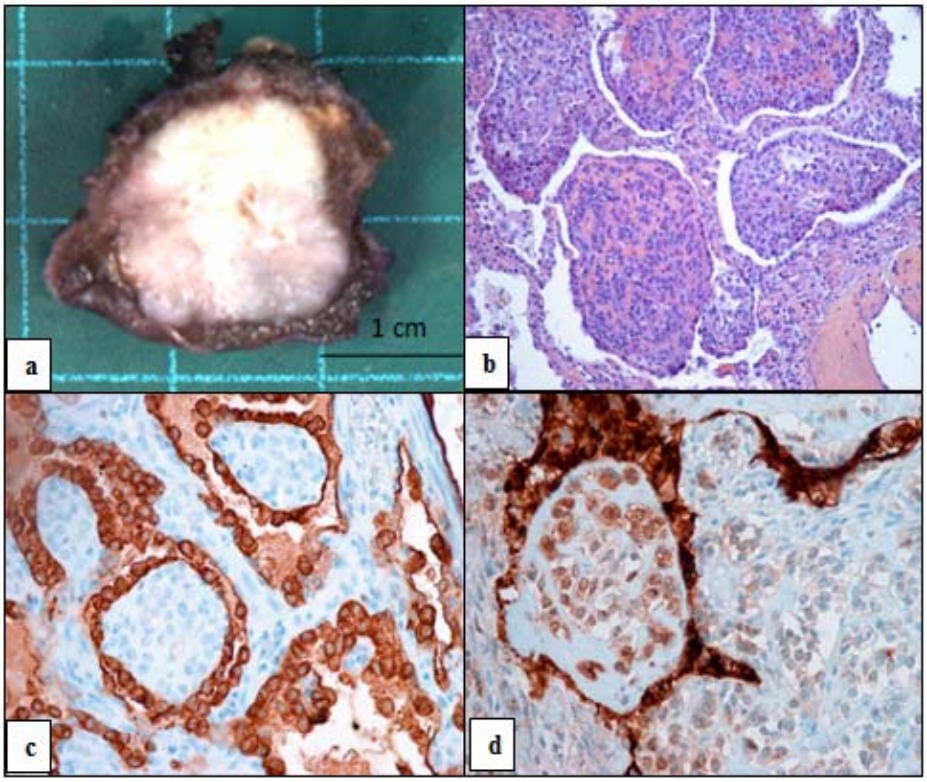

Figure 3: The nodule at macroscopy on cut section (**a**); HES (x20): A well-circumscribed unencapsulated nodule, with a mixture of papillary, solid and sclerotic patterns, here in a papillary area (**b**); the double cell-pattern with cuboidal epithelial surface cells, which show positive staining with cytokeratine AE1/AE3, overlying a contingent of round cells with negative staining (**c**); both cell patterns showing positive staining with epithelial membrane antigen (EMA) (**d**).

antigen (Figure **3d**). The features of these two cell types present within the lesion were characteristics of pulmonary sclerosing pneumocytoma and the diagnosis of malignancy was definitely ruled out. The postoperative course was uneventful and the patient was discharged on the 6th postoperative day.

DISCUSSION

Pulmonary sclerosing pneumocytoma formerly called "sclerosing hemangioma" is a benign tumor, which originates from type II pneumocyte epithelial cells [4] and presents in pathology four types of arrangements: papillary, sclerotic, solid and hemorrhagic [5,6]. It is often a random discovery in middle-aged asymptomatic women, as it is the case in our patient. However, respiratory signs such as chest pain, cough or hemoptysis have also been reported [7]. Chest CT shows non-specific morphological features of a solitary round, well-circumscribed enhancing nodule or mass peripherally seated [6-7]. Therefore, further investigation is necessary and FDG-PET/CT, being the most accurate imaging tool, is performed when available.

FDG-PET/CT is known to be more discriminating than clinical and morphological characteristics, in the study of solitary pulmonary nodules, with a sensitivity of 97% and a specificity of 85%. According to the American College of Chest Physicians' (ACCP) recent guidelines, it is the most sensitive and specific imaging tool [1, 2]. The accuracy of PET/CT in the diagnosis of malignant lesions is well established for nodules larger than 1 cm. It is correlated with cell dedifferentiation, disease aggressiveness, and tumor grade, which result in hypermetabolism and higher 18-FDG uptake, with a SUVmax of 2.5 being the commonly used threshold [8, 9]. However, following international guidelines, parenchymal lesions should be considered as positive in case of activity whatever the SUV max without any clear cutoff value, but instead a continuum between benign and malignancy [10]. Nevertheless, a solitary pulmonary nodule with SUVmax higher than 2.5 (hypermetabolic) is always suspicious and considered as potentially malignant if false positives are ruled out [9]. That was the case in our patient, who had a solitary pulmonary nodule with high FDG-uptake on PET-CT, with no evidence of infectious or granulomatous inflammatory diseases. However, the sensitivity of spatial resolution being too low, the SUVmax is no longer contributory for diagnosis if the lesion is smaller than 1cm and in ground glass opacities or subsolid nodules, [1, 2, 11-13].

The reported cases of sclerosing pneumocytoma, in which FDG-PET/CT was performed, showed various patterns of FDG uptake, ranging from hypometabolism to hypermetabolism [3, 7]. For cases with hypermetabolism, the diagnosis of malignancy was evoked, and therefore sclerosing pneumocytoma was considered as a potential false positive diagnosis [3]. The SUVmax of sclerosing pneumocytoma correlates significantly with the tumor size [3]. Hypermetabolism was found mainly in nodules of more than 2 cm, as in our case, due to growth potentials, and some authors interpreted the higher FDG uptake as evidence of low-grade malignancy [3]. Higher SUVmax was suggested to result from increased blood perfusion in the tumor due to the presence of papillary or hemangiomatous components [6, 14].

In our case, CT showed features of a solitary pulmonary nodule, not well marginated and peripherally seated. The patient's age, history of passive smoking and the imaging features were highly suspicious. Therefore, further investigation with FDG-PET/CT was indicated, according to the recommendations of the ACCP [2]. Clinical probability of malignancy is important to assess and plays a major role in the management strategy. Predictive risk factors for a malignant nodule related to the patient are: age, current or past smoking habit, and previous history of malignancies. For imaging features, large nodule diameter and volume, spiculated margins, and upper lobe location are predictors of potential malignant origin [2].

False-positive results, with high 18-FDG uptake are a real concern as they may result in unnecessary surgical procedures. Therefore, FDG-PET/CT images should be interpreted according to clinical features and patient's background. False-positive results have to be kept in mind [15].

CONCLUSION

FDG-PET/CT is actually the gold standard for accurate assessment of solitary pulmonary nodules. However, the patient's background and clinical data have to be considered and false positive results of some benign lesions, such as pulmonary sclerosing pneumocytoma, have to be kept in mind. Therefore, FDG-PET/CT features, although highly contributive for the diagnosis of pulmonary nodules, have to be interpreted according to the probability of cancer, in order to provide the best appropriate management.

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