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ORIGINAL ARTICLE

False positive PET scan deserves attention

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Summary

Purpose: *Pulmonary focal lesions are frequently identified incidentally. Furthermore, a final diagnosis is really a considerable problem for patients having risk factors for malignancy or particularly for a newly detected nodule during the postoperative period after any kind of lung surgery. For treatment decisions, the nature of the lesions needs to be clarified. Relatively recently positron emission tomography (PET) scan has been introduced as a non-invasive imaging method for the diagnosis of lesions on the basis of metabolic activity.*

Methods: *In this study 19 cases with false-positive nodules on PET scan are presented. Chest x-rays and thoracic computed tomographies (CT) were performed to all patients. Due to abnormal/suspicious lesions on radiologic imagies, PET scan was performed to these patients and high standard uptake values (SUV) above the cut-off value of 2.5 were suggestive of malignancy. Invasive procedures were performed to the patients with high suspicion of malignancy.*

Results: *Histology of the resected lesions showed that all of them were benign and therefore the PET results were false-positive. The final diagnoses were tuberculosis, aspergilloma, bronchiolitis obliterans organizing pneumonia (BOOP), sarcoidosis, sequestration, anthracosis and hamartoma.*

Conclusion: *Patients living especially in countries with a high incidence of granulomatous diseases like tuberculosis, or patients in postoperative periods with high SUV should be studied thoroughly for false-positive PET results.*

Key words: *cancer, false-positive, positron emission tomography, pulmonary nodule, tuberculosis*

Introduction

Non-small cell lung cancer (NSCLC) is one of the commonest causes of death due to malignancy. Pulmonary focal lesions are frequently diagnosed incidentally. It has been estimated that 30-50% of these pulmonary lesions are malignant; this rate increases even further in a patient with previous history of malignancy [1,2]. For treatment decisions, the nature of the lesions needs to be clarified before therapy. In benign lesions, operative procedures may be postponed or a less-invasive procedure may be applied. However, all non-invasive diagnostic methods lack specificity and sensitivity with regard to the potential malignancy of the lesion. Relatively recently 18F-flouro-2-deoxy-D-Glucose positron emission tomography (18F-FDG-PET) has been introduced as another non-invasive imaging modality based on metabolic activity.

In this retrospective study we report 19 patients with pulmonary nodules, all of which were detected during the evaluation of a lung lesion at chest x-ray. Three of the patients were operated because of lung pathologies: 2 for lung cancer and 1 for pneumothorax. Although the lesions of all patients were deemed as malignant based on FDG-PET scans, they were eventually histologically diagnosed as benign conditions.

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Table 1. Patient and disease characteristics

Patient number	*Sex*	*Age (years)*	*SUVmax*	*Localisation*	*Side - Lobe*	*Diagnosis*
1	F	36	5.4	Peripheral	Left - Lower	Tuberculosis
2	F	39.3	6.4	Central	Left - Upper	Tuberculosis
3	M	41	5.1	Central	Left - Lower	Tuberculosis
4	M	45	4.8	Peripheral	Right - Upper	Suture granuloma
5	M	46.5	3	Peripheral	Right - Lower	Suture granuloma
6	F	47	3	Peripheral	Left - Upper	Tuberculosis
7	F	49	3.6	Peripheral	Right - Upper	Aspergilloma
8	F	56	5.7	Peripheral	Left - Lower	Aspergilloma
9	F	56.9	3	Peripheral	Left - Lower	Sequestration
10	F	59.8	3.5	Peripheral	Right - Upper	Suture (stapler)
11	F	60.5	3.4	Peripheral	Right - Lower	BOOP
12	M	62.4	5.6	Peripheral	Left - Lower	Tuberculosis
13	F	63.5	15	Central	Left - Upper	Tuberculosis
14	M	67	3.0	Peripheral	Left - Upper	Hamartoma
15	F	67	5.7	Peripheral	Right - Lower	Anthracosis
16	M	70.4	3	Peripheral	Right - Lower	BOOP
17	M	71	8.8	Central	Right - Lower	Tuberculosis
18	F	73.5	4.75	Central	Left - Upper	Sarcoidosis
19	M	57	2.5	Central	Right - Middle	Hamartoma

SUV: standard uptake value, F: female, M: male, BOOP: bronchiolitis obliterans organizing pneumonia

Methods

Nineteen patients were retrospectively evaluated because of lung lesions. Their median age was 59.8 years (range 36-73.5) and 9 were female. Chest x-rays and thoracic CT scans were performed to all patients. Due to the abnormal appearance of the lesions on the radiologic images FDG-PETs were performed to all of these patients with a diagnosis suspicious for malignancy. The patients had SUVmax above the cut off value of 2.5, which is suggestive of malignancy. After the positive PET scan, all patients underwent major surgical or less invasive exploration for the accurate lesion diagnosis and proper treatment.

Results

The characteristics of the patients including age, gender, SUV, radiological location of the lesion, type of operation and final pathological diagnoses are shown in the Table 1.

The median SUV was 4.75 (range 2.5-15). Radiologic images depicted a mass (N=8) or solitary pulmonary nodules (N=11). Thirteen lesions were localized peripherally and 6 were central; 10 were located in the left lung (6 in the lower lobe and 4 in the upper lobe). Nine were found in the right lung with 5 in the lower lobe, 3 in the upper lobe, and 1 in the middle lobe.

Thoracotomy was performed in 18 patients and mediastinoscopy in 1 patient with mediastinal lymphadenopathy which was connected with a parenchymal nodule. Frozen sections of the lesions during surgery guided further actions for all patients. For benign lesions, wedge resections were performed (N=15). Lower lobectomies were performed in 3 patients because frozen sections implied possible malignancy. One had a previous history of urinary system malignancy and 2 had destroyed lobes due to granulomatous inflammations because of tuberculosis (Figure 1).

Another group of 3 patients had lesion with SUVs 3, 3.5 and 4.8, localized at their old operation sites, and all were finally diagnosed as suture granulomas (Figure 2). One of them was operated because of lung cancer where a linear stapler was used for fissure division during upper lobectomy. The second patient had bilateral lung cancers; bilateral upper lobectomies and a wedge resection in the right lower lobe were performed 8 months ago. The third patient was operated for pneumothorax with bullous lesions 15 years ago. In these 3 patients localizations of PET-positive lesions were compatible with the former operation zones.

The remaining patients had no operation

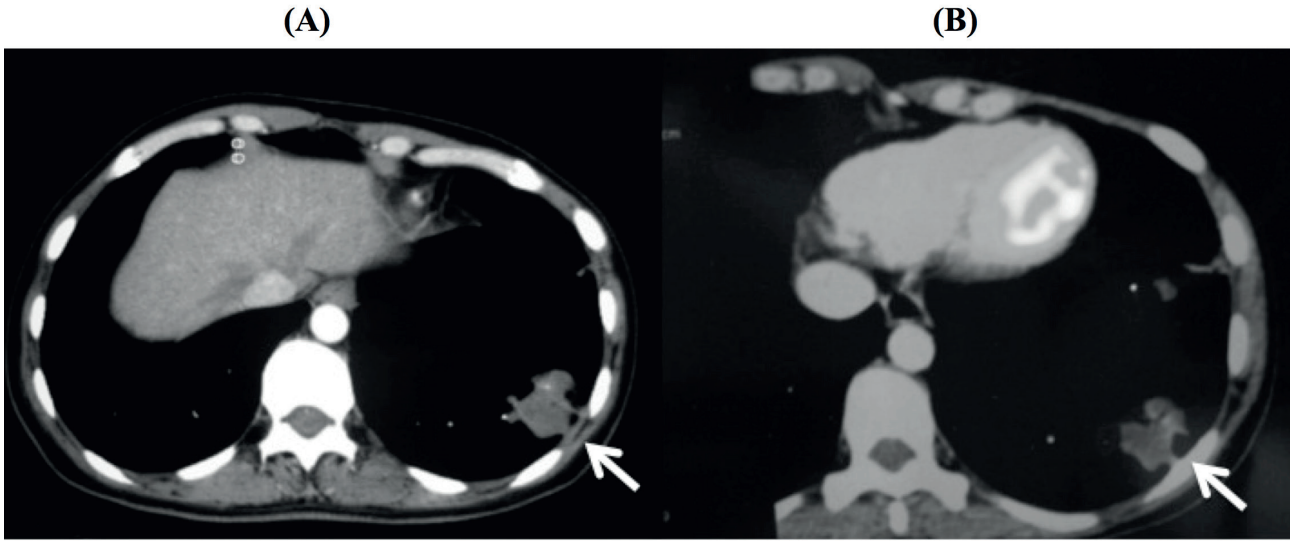

Figure 1. CT **(A)** and PET **(B)** scans. PET scan shows SUVmax 5.4 suggestive of malignancy. The lesion is shown by arrows. The final diagnosis was tuberculosis.

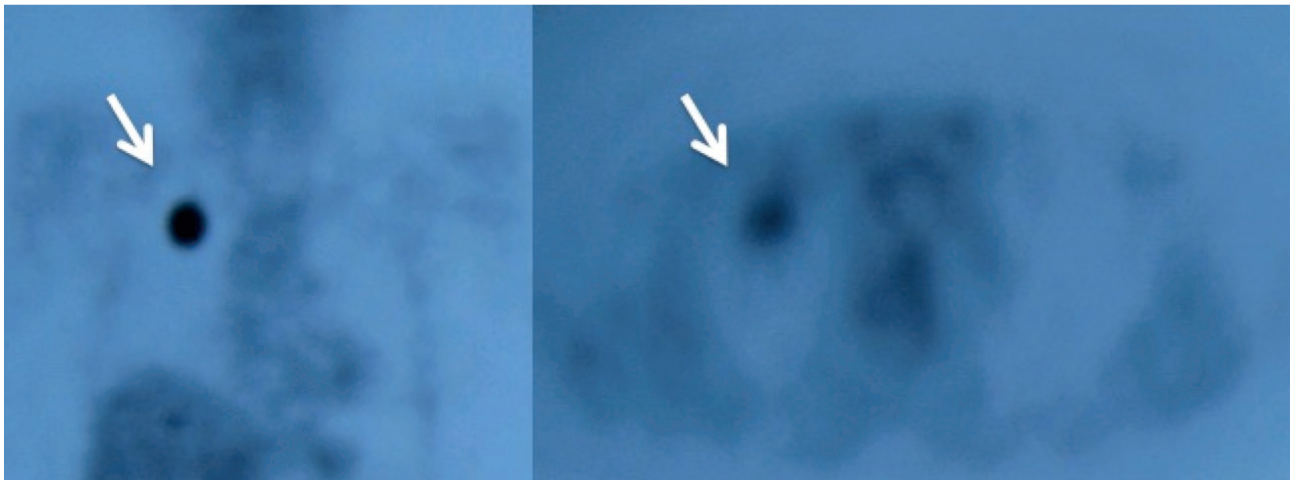

Figure 2. PET scan shows SUV max 3.5, suggestive of malignancy. The final diagnosis was suture granuloma (arrows).

related with lungs in their medical history. The final histological diagnoses were: tuberculosis (N=7), aspergilloma (N=2) (Figure 3), BOOP (N=2), sarcoidosis (N=1), sequestration (N=1), anthracosis (N=1) and hamartoma (N=2) (Figure 4).

Discussion

The problem of differential diagnosis of a solitary pulmonary nodule of undetermined nature is well known. Calcification or absence of growth over a 2-year period are highly suggestive of a benign lesion, but calcification or comparative chest radiographs are usually lacking. Diagnostic procedures like bronchoscopy are often nondiagnostic and a transthoracic needle-aspiration biopsy, if possible, may lead to some complications, such as pneumothorax and possible false-negative findings, leading to unacceptable expectations in patients with early-stage lung cancer [3].

Solitary pulmonary nodules arising during the postoperative follow-up of resected malignancies are commonly diagnosed as recurrences or new cancers [4]. Like our patients operated for PET positive results with high SUVs detected during the postoperative period initially thought as malignant.

Conventional imaging, including chest x-ray, thoracic CT, ultrasonography, and MRI, has a major role in the diagnosis, staging, and

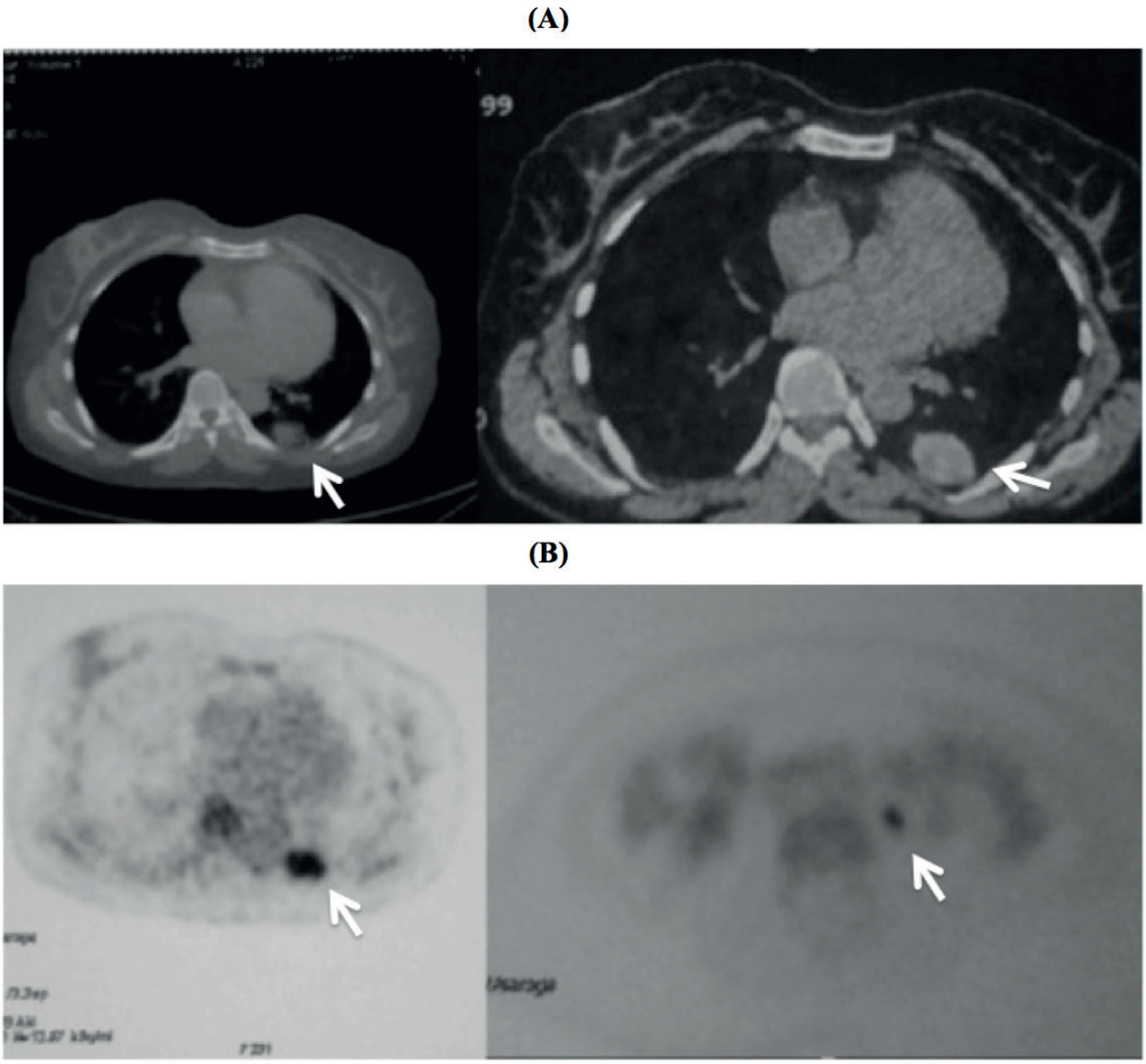

Figure 3. CT **(A)** and PET **(B)** scans. PET scan shows SUV max 5.7, suggestive of malignancy. The final diagnosis was aspergilloma (arrows).

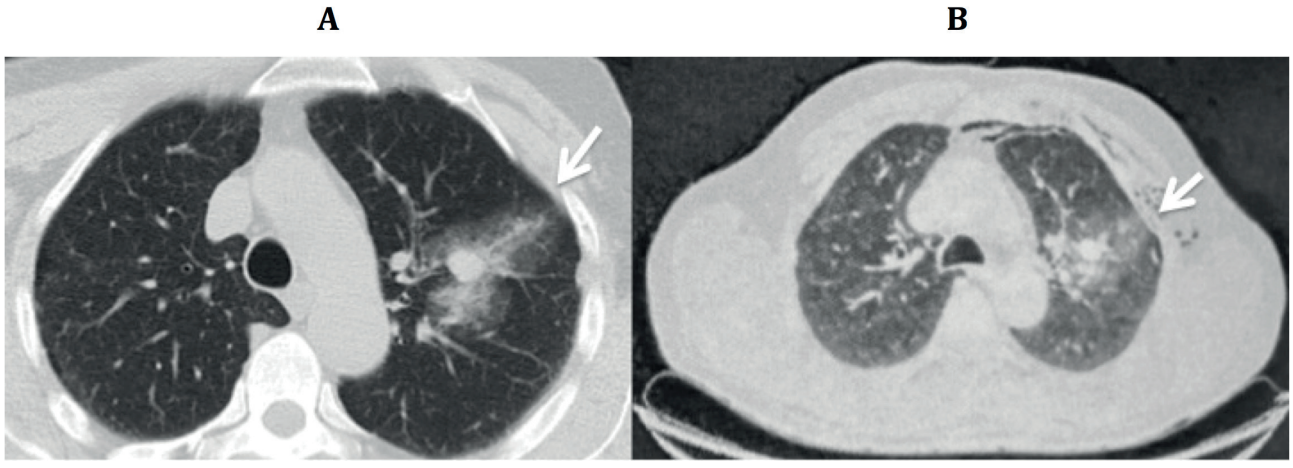

Figure 4. CT **(A)** and PET **(B)** scans. PET scan shows SUVmax 3, suggestive of malignancy. The final diagnosis was hamartoma (arrows).

follow-up of patients with lung cancer. A sensitive technique, CT, which is the most used one for detecting pulmonary lesions and for non-invasive staging in lung cancer, can not prove malignancy. Although these imaging methods allow for exquisite anatomic details, they usually do not provide a definitive diagnosis or staging. Therefore, invasive procedures with tissue sampling are often required [5,6].

Another imaging technique based on metabolic functions is 18F-FDG-PET which has been performed extensively in the evaluation of undetermined lung lesions. Based on well-designed prospective studies, it can be concluded that FDG-PET was proven to be accurate in differentiating benign from malignant lesions as small as 1 cm [7-11].

PET is a useful, non-invasive technique for observing changes of tumor metabolism. The advent of PET has made it possible to demonstrate sites of increased glycolysis due to cancer. Although malignant cells show an increased glucose turnover compared to normal tissues, this is not specific for malignant cells, but it is also observed in inflammatory tissues [12].

Today, most of the lung nodules are evaluated with CT and PET scans to diagnose the character of the lesions. PET has a sensitivity and specificity of 95 and 80% respectively in the detection of malignant solitary pulmonary nodules, compared to 50-60% of CT [13,14], but in slow-growing malignancies, such as bronchoalveolar carcinoma or carcinoid tumors, false-negative results can be taken. On the contrary, false-positive results are common in inflammatory lesions, especially in countries with high prevalence of tuberculosis [15,16].

False-positive PET scans deserve special attention. Most of these false-positive findings are related to inflammatory lesions such as bacterial pneumonia, pyogenic abscess or aspergillosis, granulomatous diseases, active sarcoidosis, tuberculosis, histoplasmosis, coccidioidomycosis, Wegener's disease or coal miner's lung, rather than true benign tumors such as hamartomas [11,17].

We had 15 patients with high SUVs whose final diagnoses were BOOP, aspergilloma, tuberculosis, sarcoidosis, anthracosis or hamartoma. Median SUV in our patients was 4.75 which suggested malignancy. Thus, chronicity of the non-neoplastic inflammatory lesions is not always correlated with low SUV uptake.

Therefore, in patients suspected for inflammatory disease, postoperative period of benign lesions, or with bilaterally positive FDG-PET findings, a false-positive result may be considered [17]. There is no evidence-based guideline about the proper follow-up procedures for the postoperative nodules following lung resection, especially for malignant lesions, so false-positive PET scans may lead to unnecessary surgical explorations as in our cases [18].

Foreign body reactions to suture materials is well known with non-absorbable sutures, such as silk and other polyfilament sutures. However, foreign body reactions to staplers is a very rare occurrence due to the inert nature of titanium used in modern stapler technology [18,19]. In our series one of the suture granulomas was due to the stapler. As in our cases, suture granulomas also may display a significantly high SUV on PET.

In conclusion, PET still does not seem to be the gold standard method in evaluating lung lesions for early detection of lung cancer, especially of small tumors. However, it contributes positively to the detection of malignancy in tumors of at least 1 cm in diameter. Exact diagnosis of benign or malignant pulmonary tumors by PET appears to complicate things when inflammatory lesions are present. A false-positive PET result may be considered in patients suspected of inflammatory disease. In addition, a foreign body reaction should be kept in mind for postoperative solitary lesions detected in the surgical region of patients with previous thoracic operation, especially with borderline SUV on PET scan.

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