Brief Report

Pulmonary actinomycosis mimicking lung cancer on positron emission tomography

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Abstract:

Pulmonary actinomycosis frequently mimics lung malignancy on radiologic imaging studies. Positron emission tomography-computed tomography (PET-CT) is a useful diagnostic modality for differentiating lung malignancy from benign diseases. However, few studies evaluated PET-CT findings of pulmonary actinomycosis. Therefore, it is unclear whether PET-CT is helpful to distinguish lung malignancy from benign lung disease when pulmonary actinomycosis is clinically suspected. We investigated PET-CT findings in 11 patients with pathologically confirmed pulmonary actinomycosis. The median maximal standardized uptake value (SUV) on PET-CT of pulmonary actinomycosis was increased to 5.5 (interquartile range, 4.2–8.8), which was higher than the threshold value of 2.5 indicating malignancy. Pulmonary actinomycosis without central necrosis demonstrated higher maximal SUV of 7.5 (4.9–12.2) compared to 4.8 (3.2–5.6) of ones with central necrosis. PET-CT might be not helpful in differentiating lung malignancy from benign lesions when pulmonary actinomycosis is clinically suspected.

Key words:

Actinomycosis, diagnosis, lung neoplasms, positron emission tomography

Actinomycosis is an indolent, slowly progressive infection caused by anaerobic or microaerophilic bacteria, primarily from the genus *Actinomyces*.[1] There is pulmonary involvement in approximately 15% of all actinomycosis cases, and it usually develops due to aspiration of organisms from the oropharynx. Pulmonary actinomycosis commonly presents with productive cough, fever, and chest pain, and rarely presents with hemoptysis.[1]

Severe manifestations of pulmonary actinomycosis were common in the preantibiotic era, ranging from empyema to sinus fistula.[2] The presentation of pulmonary actinomycosis became less severe with improvements in oral hygiene and increased availability of antibiotics.[1] Pulmonary actinomycosis commonly presents as a consolidation, nodule, or mass that frequently mimics lung malignancy.[3-6] It is often difficult to differentiate pulmonary actinomycosis from lung malignancy due to nonspecific clinical and laboratory findings. Recent studies also showed that lung cancer is the most common initial diagnosis of pulmonary actinomycosis made by attending physicians.[3-6] Typical chest computed tomography (CT) findings of actinomycosis show chronic segmental airspace consolidations that contain low-attenuation areas with peripheral enhancement,[7] similar to the findings of necrotic lung malignancy.[8]

Positron emission tomography (PET)-CT with 18-fluorodeoxyglucose (FDG) is a useful imaging modality to differentiate benign pulmonary lesions from malignant lesions.[9] However, pulmonary infections such as tuberculosis and histoplasmosis can have high metabolic uptake on PET-CT, which may cause false positive results.[10] Despite some case reports, there is scarce information on the PET-CT findings of pulmonary actinomycosis.[11-13] Thus, we aimed to investigate the PET features of pulmonary actinomycosis and whether PET is helpful to distinguish pulmonary actinomycosis from lung malignancy.

Subjects and Methods

This study included 12 patients who were diagnosed with pulmonary actinomycosis

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by pathology and had available PET-CT results at a single referral hospital in Seoul, South Korea, from October 1994 to January 2016. Tissue specimens were obtained from surgical biopsy, bronchoscopic biopsy, or percutaneous core biopsy. After excluding one patient who underwent PET-CT scan at another hospital and did not have a maximal standardized uptake value (SUV), 11 patients were included in this study. The medical records were reviewed for presenting symptoms, comorbidities, diagnostic procedures, and duration of antibiotic treatment. Maximal SUV was obtained using formal reading. Following CT scan, an emission scan was obtained from the thigh to the head for 2.5 min per frame in 3-dimensional mode. Attenuation-corrected PET images (vortex size, 3.9 mm × 3.9 mm × 3.3 mm) were reconstructed from the CT data using a 3-dimensional ordered-subset expectation maximization algorithm (20 subsets, 2 iterations).[14] Abnormal FDG uptake beyond expected normal tissue was defined as SUV >2.5, which is commonly used as a threshold indicative of malignancy.[15] The CT findings of pulmonary actinomycosis were classified into three categories: parenchymal, bronchiectatic, and endobronchial patterns. The parenchymal patterns were further classified as lobar, segmental, and subsegmental patterns according to the extent of consolidation.[9] The presence of central low density within the consolidation was also investigated. The ethics committee of our institution reviewed and approved the protocol of this retrospective study (IRB No. 2016-06-104).

Data are presented as medians and interquartile range (IQR) for continuous variables and as numbers (percentages) for categorical variables. Continuous variables were compared using the Mann–Whitney U-test, and categorical variables were compared using Pearson's Chi-square test or Fisher's exact test. All tests were two-sided, and $P < 0.05$ was considered statistically significant. Data were analyzed using IBM SPSS Statistics for Windows, version 23.0 (Armonk, NY, USA).

Results

The baseline characteristics of the study participants are summarized in Table 1. Of 11 patients, eight (72.7%) patients were male, with a median age of 52 years (IQR, 47–70 years). The median body mass index was 23.6 kg/m^2 (IQR, 21.6–24.4 kg/m^2). Six patients (54.5%) were either current or ex-smokers. Common comorbidities included chronic obstructive pulmonary disease ($n = 3$, 27.3%), hypertension ($n = 2$, 18.2%), and diabetes mellitus ($n = 2$, 18.2%). Cough ($n = 6$, 64.5%) was the most common presenting symptom, followed by sputum ($n = 4$, 36.4%) and hemoptysis ($n = 3$, 27.3%). The median forced expiratory volume in 1 s was 2.6 L (95.0% predicted). With respect to diagnostic procedures, surgical biopsies were performed in eight (72.7%) patients, bronchoscopic biopsy was performed in one (9.1%) patient, and percutaneous core needle biopsies were performed in two patients (18.2%).

Table 2 and Figure 1 depict radiologic features and PET-CT findings of pulmonary actinomycosis. The largest diameter on CT scan was 4.3 cm (median; IQR, 2.5–5.3 cm). All patients had parenchymal patterns, consisting of lobar type in four (36.4%) patients, segmental type in four (36.4%) patients, and subsegmental type in three patients (27.2%). Central low density within the consolidation on chest CT was observed in five patients (45.5%). The median of maximal SUV was 5.5 (IQR, 4.2–8.8) on PET. Whereas 90.9% of patients (10/11) had maximal SUV over 2.5, one patient had maximal SUV of 2.2. Although consolidative lesions with central low density had longer diameter (5.1 cm vs. 3.4 cm, $P = 0.177$) on CT scan and lower maximal SUV (4.8 vs. 7.5, $P = 0.082$) on PET-CT compared to those without central low density, these differences were not significant.

Table 1: Baseline characteristics of 11 patients with pulmonary actinomycosis

	Total (n=11)
Age (years)	52.0 (47.0-70.0)
Male sex (%)	8 (72.7)
Body mass index (kg/m^2)	23.6 (21.6-24.4)
Smoking	
Current or ex-smokers (%)	6 (54.5)
Pack-years	25 (17.5-32.5)
Comorbidities (%)	
Chronic obstructive pulmonary disease	3 (27.3)
Hypertension	2 (18.2)
Diabetes mellitus	2 (18.2)
Malignancy	1 (9.1)
Symptoms (%)	
Cough	6 (54.5)
Sputum	4 (36.4)
Hemoptysis	3 (27.3)
Pulmonary function test	
FEV_1/FVC (%)	74.0 (66.0-79.0)
FEV_1 (L)	2.6 (2.3-3.3)
FEV_1%predicted (%)	95.0 (85.0-111.0)
Diagnostic procedures (%)	
Surgical biopsy	8 (72.7)
Bronchoscopic biopsy	1 (9.1)
Percutaneous core needle biopsy	2 (18.2)

Data are presented as n (%) or medians (IQR). FEV_1 = Forced expiratory volume in 1 s, FVC = Forced vital capacity, IQR = Interquartile range

Regarding treatment, eight patients (72.7%) underwent lung resection, including lobectomy ($n = 7$) and wedge resection ($n = 1$). Postoperative antibiotic treatment was initiated in five patients for a median of 2.0 months (IQR, 1.6–4.9 months). During a median of 22.0 months of follow-up duration (IQR, 15.6–55.9 months), no recurrence was observed in any patient regardless of postoperative use of antibiotics.

Discussion

To the best of our knowledge, this is the first study investigating PET-CT findings of pulmonary actinomycosis with the largest number of patients. In agreement with previous case reports,[11-13] more than 90% of patients with pulmonary actinomycosis in this study had maximal SUV >2.5, which is the cutoff value indicating malignancy. Thus, our study strongly suggests that PET-CT might not be useful in differentiating pulmonary actinomycosis from lung malignancy. Furthermore, our study indicates that clinicians should be cautious when evaluating the need for lung resection surgery due to high uptake on PET-CT when pulmonary actinomycosis is clinically suspected.

Table 2: Radiological and positron emission tomography findings of patients with pulmonary actinomycosis

	Total (*n*=11)	With central necrosis (*n*=5)	Without central necrosis (*n*=6)	*P* value
CT findings				
Largest diameter (cm)	4.3 (2.5-5.3)	5.1 (3.8-6.8)	3.4 (1.5-4.7)	0.177
Subsegmental consolidation (%)	3 (27.2)	0	3 (50)	0.247
Segmental consolidation (%)	4 (36.4)	2 (40)	2 (33.3)	
Lobar consolidation (%)	4 (36.4)	3 (60)	1 (16.7)	
PET findings				
Maximal SUV	5.5 (4.2-8.8)	4.8 (3.2-5.6)	7.5 (4.9-12.2)	0.082

Data are presented as *n* (%) or medians (IQR). CT = Computed tomography, PET = Positron emission tomography, SUV = Standardized uptake value, IQR = Interquartile range

PET-CT findings of actinomycosis in organs other than lung have been discussed in previous studies.[16,17] However, only few case reports are present for PET-CT findings of pulmonary actinomycosis.[11-13] Thus, limited information on PET-CT findings of pulmonary actinomycosis might lead to unnecessary lung resection in patients with pulmonary actinomycosis due to the concern of lung cancer caused by high FDG uptake on PET-CT. For example, some of our patients underwent surgical resection despite typical CT scans suggestive of pulmonary actinomycosis (lobar, subsegmental, or segmental consolidation with central necrosis), since the attending physicians considered that high FDG uptake on PET-CT favored lung malignancy over pulmonary actinomycosis. This is partly due to the lack of information on PET-CT findings of pulmonary actinomycosis. Our study showed that most cases of pulmonary actinomycosis have high FDG-uptake on PET-CT and will provide informative data that clinicians should not use PET-CT findings to discriminate lung cancer from benign disease when pulmonary actinomycosis is suspected.

Pulmonary actinomycosis is an uncommon and indolent pulmonary infection caused by *Actinomyces* species, which frequently mimics lung malignancy.[18] Pulmonary actinomycosis can be diagnosed by demonstration of sulfur granules in pus or histopathologic section of a specimen,[19] which is usually obtained from transbronchial biopsy, percutaneous needle biopsy, or surgical resection.[1,20] It has been studied that transbronchial biopsy is less successful in providing diagnostic material compared with surgery.[18,21] However, since pulmonary actinomycosis responds well to antibiotic treatment, less invasive procedures such as transbronchial biopsy or percutaneous needle biopsy are preferred to surgical resection.

The typical CT feature of pulmonary actinomycosis is airspace consolidation containing necrotic low-attenuation area, which is more common than bronchiectatic and endobronchial actinomycosis.[8] Since cases of pulmonary actinomycosis with PET-CT performed during diagnostic workup were included in this study, parenchymal actinomycosis similar to lung mass might have been selected for in this study. Approximately half of CT images showed a central necrotic low-attenuation area and tended to reveal lower metabolic uptake on PET-CT compared to consolidations without a central low-attenuation area. In the central necrotic portion, low bacterial load and less severe inflammation may result in low maximal SUV on PET-CT.

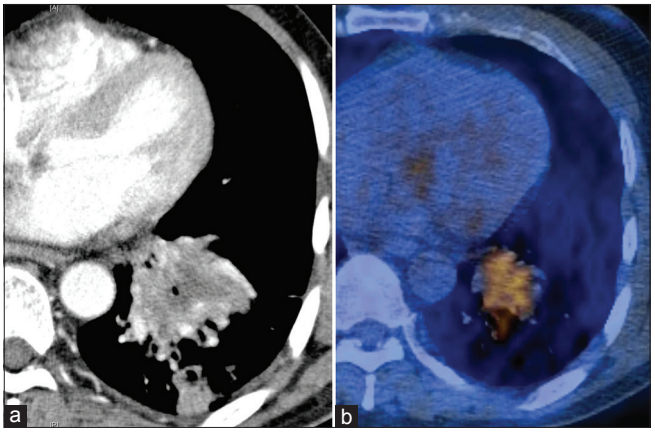

Figure 1: A 59-year-old male with pulmonary actinomycosis. (a) Chest computed tomography scan shows consolidation with necrotic low-attenuation area. (b) positron emission tomography-computed tomography scan shows high metabolic uptake in lesion (maximal standardized uptake value 4.2)

Long-term postoperative antibiotics have been recommended even after complete resection for pulmonary actinomycosis.[1] However, some studies showed that pulmonary actinomycosis did not recur despite a short-term course of antibiotic treatment or no antibiotic treatment following complete resection of pulmonary actinomycosis.[3,22,23] In agreement with the results of previous studies,[3,22,23] no recurrent cases were observed in eight patients after short-term antibiotic treatment ($n = 5$) or no treatment ($n = 3$) following complete resection of pulmonary actinomycosis. Although the optimal antibiotic duration after resection in pulmonary actinomycosis is not established, the results of our study and previous studies[3,22,23] suggest that a brief course of postoperative antibiotics might be enough in cases of completely resected pulmonary lesions.

Our study has several limitations. First, this study was performed in a referral center in South Korea. Second, considering the retrospective nature of this study, there might be a selection bias. Third, although we suggest that short-term antibiotic treatment might be sufficient in cases undergoing complete resection of pulmonary actinomycosis, the number of patients in this study was relatively small. Studies with larger numbers of patients are needed to further investigate antibiotic treatment.

Conclusions

Pulmonary actinomycosis demonstrates high metabolic uptake on PET-CT. Our study suggests that PET-CT would not be

helpful in differentiating pulmonary actinomycosis from lung malignancy.

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Conflicts of interest
There are no conflicts of interest.

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