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Clinical and radiological characteristics of pulmonary actinomycosis mimicking lung malignancy

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SUMMARY

INTRODUCTION: Pulmonary actinomycosis, clinically and radiologically, mimics abscess, tuberculosis, and lung malignancy, resulting in misdiagnosis or delay in diagnosis. In this study, we analyzed the clinicoradiological features of pulmonary actinomycosis, the presence of any differences between clinical prediagnosis and radiological diagnosis, and whether imaging modalities help distinguish pulmonary actinomycosis from lung cancer.

METHODS: A total of 22 patients who had a histopathological diagnosis of actinomycosis in a tertiary health center participated in this study. Of these, 14 had positron-emission tomography/computed tomography.

RESULTS: In all, 81.8% of the patients were males. The diagnostic procedures employed for the diagnosis of actinomycosis were surgery in 54.5% of patients, fiberoptic bronchoscopy in 36.4% of patients, and rigid bronchoscopy in 9.1% of patients. Radiological and clinical prediagnosis showed malignancy in 31.8 and 40.9% of patients, respectively. The mean of the maximum standardized uptake value was 6.33±3.6 on positron-emission tomography/computed tomography. Kappa compliance analysis revealed that clinical and radiological diagnoses were significantly compatible with each other and that radiological pre-diagnoses were not superior to clinical diagnoses (κ=0.701 and p<0.001).

CONCLUSION: Pulmonary actinomycosis shows high metabolic uptake in positron-emission tomography/computed tomography, and this may mislead clinicians for a diagnosis of malignancy. Our results suggest that positron-emission tomography/computed tomography does not help distinguish pulmonary actinomycosis from lung malignancy and does not provide a clear diagnostic benefit to the clinician, so pathological diagnosis is necessary.

KEYWORDS: Actinomycosis. Neoplasms. Tomography. Positron-emission tomography.

INTRODUCTION

Actinomycosis is a disease caused by Gram-positive anaerobic, non-acid-resistant bacteria belonging to the Actinomycetaceae family. These bacteria are present in normal human flora and are often isolated from mucosal surfaces of the oral cavity, gastrointestinal tract, and female genital tract[1].

Actinomycosis often involves the cervicofacial region but can involve all systems in the body. Unusual areas of involvement include the pulmonary tract, abdominopelvic region, central nervous system, skin, heart, and genitourinary tract. Infection occurs when *Actinomyces* in normal flora invade the mucosa that gets damaged due to various predisposing factors. Predisposing factors include poor oral hygiene, gingival disorders and surgery, diabetes mellitus (DM), and chronic respiratory disorders such as bronchiectasis[2].

Approximately 15% of cases with actinomycosis have pulmonary involvement. When lungs are involved, diagnosis of actinomycosis is difficult since it clinically and radiologically mimics abscess, tuberculosis, and lung cancer, resulting in misdiagnosis or delay in the diagnosis[3]. Pulmonary actinomycosis (PA) usually presents with cough, fever, chest pain, and, rarely, hemoptysis[2]. PA can present with lung consolidation, nodules, cavity formation, or a mass in the lung, mimicking lung cancer. It is often difficult to distinguish actinomycosis from malignancy due to its nonspecific clinical, radiological, and laboratory findings. Recent studies have reported that PA cases are often clinically prediagnosed as pulmonary malignancy[4,5,6,7]. Actinomycosis results in intense hypermetabolic regions in positron-emission tomography/computed tomography (PET-CT), as in malignancy[8].

In this study, we analyzed the clinicoradiological features of PA, the presence of any differences between clinical prediagnosis and radiological (PET-CT, thorax CT) diagnosis, and whether imaging modalities help distinguish PA from lung cancer.

METHODS

This study included a total of 22 patients who had a histopathological diagnosis of actinomycosis in a tertiary health center between

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2014 and 2019. Of them, 14 patients had PET-CT. The symptoms, comorbidities, predisposing factors, posteroanterior chest X-ray (CXR) findings, and the most common clinical prediagnoses, CT and/or PET-CT findings and radiological pre-diagnoses, the maximum standardized uptake values (SUV_{max}) of the lesion on PET-CT, diagnostic methods, and fiberoptic bronchoscopy (FOB) findings of the patients were obtained from the medical records of the hospital. Institutional Medical Education Board reviewed and approved the protocol of this retrospective study (approval date February 12, 2019; decree no.: 617).

The data were analyzed with the SPSS version 26.0 (IBM Corp., NY, USA) package program. Categorical variables were presented as percent and frequencies. The compliance of continuous variables to normal distribution was analyzed with the Shapiro-Wilk test. Continuous variables with a normal distribution were presented as mean±standard deviation, and continuous variables without a normal distribution were presented as median and interquartile range. Compatibility of radiological and clinical diagnoses was studied with Cohen's kappa analysis. All p-values were two-tailed and $p<0.05$ was considered statistically significant.

RESULTS

A total of 18 (81.8%) male and 4 (18.2%) female cases were included in the study. The median age of all patients was 53 years (interquartile range=48.5–67.75 years). Eight (36.4%) patients were current or former smokers. The median smoking pack-year was 20.5 (interquartile range=20–37.5 pack-years) (Table 1).

Analysis of the comorbid conditions and predisposing factors of the patients revealed that 10 (45.4%) patients had cystic bronchiectasis and a history of surgery due to bronchiectasis, 5 (22.7%) patients had DM, 4 (18.2%) patients had hypertension, 2 (9%) patients had surgery due to lung cancer, and 1 (4.5%) patient had tooth extraction previously.

The most frequent symptom in our patients [15 (68.2%)] was cough. The frequencies of the symptoms are shown in Table 1.

The diagnostic procedures employed for the diagnosis of actinomycosis were surgery in 12 (54.5%) patients, FOB in 8 (36.4%) patients, and rigid bronchoscopy in 2 (9.1%) patients. In FOB plus rigid bronchoscopy examinations (n=10), more than one finding was observed in each patient. These findings were narrowing of the bronchus by external pressure (30%), irregular mucosa (50%), granulation tissue (20%), endobronchial lesion (EBL) at the site of the surgical stump (20%), suture material at the site of the surgical stump (20%), and aspirated foreign body (a piece of bone) (20%).

Table 1. Demographic and clinical characteristics of the patients.

Male gender, n (%)	18 (81.8)
Age, years, median (IQR)	53 (48.5–67.75)
Smoking history, n (%)	8 (36.4)
Diabetes mellitus, n (%)	5 (22.7)
Hypertension, n (%)	4 (18.2)
Surgery due cystic bronchiectasis, n (%)	10 (45.4)
Surgery due to lung malignancy, n (%)	2 (9)
Tooth extraction, n (%)	1 (4.5)
Cough, n (%)	15 (68.2)
Sputum production, n (%)	8 (36.4)
Dyspnea, n (%)	8 (36.4)
Hemoptysis, n (%)	8 (36.4)
Back chest pain, n (%)	5 (22.7)
Weight loss, n (%)	4 (18.2)
Fever, n (%)	4 (18.2)
Foul breath, n (%)	1 (4.5)

IQR: interquartile range.

A total of 19 (86.4%) patients had CXR. Of these, in 7 (36.8%) patients, CXR was interpreted as normal. CXR findings are shown in Table 2. The lesions were located in the left lower lobe in 8 (36.4%) patients, right upper lobe in 5 (22.7%) patients, right lower lobe in 5 (22.7%) patients, right middle lobe in 2 (9.2%) patients, left upper lobe in 1 (4.5%) patient, and left lingular segment 1 (4.5%) patient on thorax CT (Table 2).

The most frequent finding on thorax CT was the presence of a mass, which is evident in 7 (31.8%) patients. The other findings were cavity (n=4, 18.2%), lymphadenopathy (n=7, 31.8%), consolidation (n=3, 13.6%), effusion (n=3, 13.6%), infected bronchiectasis (n=3, 13.6%), nodule (n=2, 9.1%), EBL (n=2, 9.1%), atelectasis (n=2, 9.1%), and ground-glass appearance (n=1, 4.5%).

A total of 14 (63.6%) patients had PET-CT. The findings on PET-CT were as follows: collapse consolidation in 4 (28.6%) patients, EBL in 3 (21.4%) patients, mass in 3 (21.4%) patients, nodule in 2 (14.3%) patients, and cavity in 2 (14.3%) patients (Table 2). The highest SUV_{max} on PET-CT was 11.77, and the mean SUV_{max} was 6.33±3.6.

The radiological prediagnosis was malignancy in 7 (31.8%) patients, pneumonia in 7 (31.8%) patients, infected bronchiectasis in 4 (18.2%) patients, benign lesions in 3 (13.6%) patients, and a recurrent malignant lesion in 1 (4.5%) patient. The clinical diagnoses of the patients were as follows: malignancy in 9 (40.9%) patients, pneumonia in 5 (22.7%) patients, infected bronchiectasis in 4 (18.2%) patients, recurrent malignant lesion in 2 (9.1%) patients, tuberculosis in 1 (4.5%) patient, and

empyema in 1 (4.5%) patient. The kappa compliance analysis determined that clinical and radiological diagnoses were statistically significantly compatible with each other, and radiological prediagnoses did not show superiority over clinical diagnoses (κ=0.701 and p<0.001). Table 3 shows the compliance analysis of clinical and radiological diagnoses.

In this study, malignancy was reported in 7 (31.8%) patients as the radiological pre-diagnosis, and a pre-diagnosis of recurrent malignancy was reported in 1 (4.5%) patient, while the clinical diagnosis was malignancy in 9 (40.9%) patients and recurrent malignancy in 2 (9%) patients. Kappa compliance analysis revealed that clinical and radiological diagnoses were statistically significantly compatible with each other, and radiological pre-diagnoses were not superior to clinical diagnoses (κ=0.701 and p<0.001).

Table 2. Radiological findings.

Chest radiography findings (n=19), n (%)	
Normal	7 (36.8)
Effusion	4 (21.1)
Cystic bronchiectasis	4 (21.1)
Infiltration	2 (10.5)
Cavity	1 (5.3)
Consolidation	1 (5.3)
Site of the lesion on CT (n=22), n (%)	
Left lower lobe	8 (36.4)
Right upper lobe	5 (22.7)
Right lower lobe	5 (22.7)
Right middle lobe	2 (9.2)
Left lingular segment	1 (4.5)
Left upper lobe	1 (4.5)
Lesion defined on PET-CT (n=14), n (%)	
Collapse-consolidation	4 (28.6)
Endobronchial lesion	3 (21.4)
Mass	3 (21.4)
Nodule	2 (14.3)
Cavity	2 (14.3)

PET-CT: positron-emission tomography/computed tomography.

DISCUSSION

Our study analyzed the past 5-year cases with a histopathological diagnosis of PA in a tertiary Pulmonary Training and Education Hospital, and as far as we know, it is the largest study performed on PA cases in a single institution in our country.

Actinomycosis is a rare, chronic, and slowly progressing bacterial infection caused by several members of the *Actinomyces* family. *Actinomyces israelii* is the most common human pathogen among six pathogenic species of *Actinomyces* spp. Although it often causes infection in oral and cervicofacial regions, other regions can also become infected in immunocompromised individuals. PA is mainly caused by aspiration of oropharyngeal or gastrointestinal secretions into the respiratory tract[9].

In cases of endobrochial actinomycosis, bronchiectasis, and chronic obstructive pulmonary disease, corticosteroids, broncholithiasis and endobronchial foreign bodies (e.g., chicken bone and fish bone, grape seed, bean, dental prosthesis, and surgical suture material) are predisposing factors and increase the risk of *Actinomyces* colonization[2,10].

The most common symptoms are fever, weight loss, cough, sputum, chest pain, and hemoptysis. It mimics malignancy or tuberculosis with these nonspecific symptoms and clinical and radiological findings[11].

Pulmonary actinomycosis occurs at any age, but it is more frequent in adults. More frequent infection in men has been

Table 3. Compliance analysis of clinical and radiological diagnoses.

Radiological diagnosis	Clinical diagnosis					
	Malignant	Recurrent malignant	Pneumonia	Infected bronchiectasis	Tuberculosis	Empyema
Malignant	7	0	0	0	0	0
Recurrent malignant	0	1	0	0	0	0
Pneumonia	0	0	5	0	1	1
Infected bronchiectasis	0	0	0	4	0	0
Benign lesions	2	1	0	0	0	0
Total	9	2	5	4	1	1

κ=0.701 and p<0.001.

attributed in part to poor oral hygiene[2,12]. In our study, the majority of the patients were males (n=18, 81.8%).

The main predisposing factors are poor oral hygiene, gingival diseases, surgery, chronic respiratory system disorders such as bronchiectasis, and DM[2]. Among our patients, one patient had a pulmonary cavity and hemoptysis following a tooth extraction, two patients had a history of surgery for lung malignancy causing immunosuppression, and five patients had DM.

The most common clinical symptoms of PA are cough, chest pain, and dyspnea. These nonspecific symptoms make the diagnosis of PA difficult and may often lead to a misdiagnosis of malignancy rather than an infection[9]. Cough, sputum production, and chest pain were reported as the most common complaints in various European studies[13]; however, hemoptysis was more common in Asian series[5].

In our study, the most common complaints of the patients were cough, sputum production, dyspnea, hemoptysis, back chest pain, weight loss, fever, and foul breath, with cough being the most common (n=15) and foul breath being the least common symptom (n=1).

There is no specific and diagnostic imaging modality for PA. Misdiagnosis for malignancy, tuberculosis, or other infections is quite common without a microbiological or histopathological confirmation of the disease[14]. In this study, CXR was normal in 36.8% of the patients, and other findings were nonspecific. The most common site of lesion on thorax CT was the left lower lobe (n=8, 36.4%) and the least frequent site of lesion was the left upper lobe (n=1, 4.5%). The most frequent radiological findings in descending order were mass, cavity, lymphadenopathy (LAP), consolidation, and EBL, comprising 90.9% all radiological findings. As seen, malignancy comes to mind as the first clinical prediagnosis.

In this study, a specimen for histopathologic diagnosis of PA was obtained with rigid bronchoscopy and FOB in 10 patients, and more than one bronchoscopy finding was recorded in the same patient. Considering findings during surgery, stenosis of the bronchus with external compression (n=3, 10%), mucosal irregularity (n=5, 10%), granulation tissue (n=2, 10%), and EBL at the site of the surgical stump (n=2, 10%) suggest lung malignancy as a clinical prediagnosis; however, the presence of the suture material at the site of the surgical stump (n=2, 10%) and aspirated foreign body (a piece of bone) (n=2, 10%) exclude a malignant lesion.

CT and bronchoscopy findings suggesting lung malignancy directed clinicians to order a PET-CT, and 14 (63.6%) patients had PET-CT. SUV_{max} in PET-CT was evaluated according to the cutoff value of SUV_{max}>2.5, which predicts a malignant lesion[15]. There was no pathological uptake on PET-CT in 1 patient, SUV_{max} was <2.5 in 2 patients, and SUV_{max} was >2.5 in 11 (78.5%) patients.

Our patients' PET-CT findings were as follows: collapse consolidation (n=4, 28.6%), EBL (n=3, 21.4%), mass (n=3, 21.4%), nodule (n=2, 14.3%), and cavity (n=2, 14.3%). Mediastinal and hilar LAP was detected in 6 (14%) patients on PET-CT, and the highest SUV_{max} detected in an LAP was 8.52. Actinomycosis, like malignancy, has intense hypermetabolic features and intense FDG uptake; the highest SUV reported in the literature is 33.1[8]. The highest SUV_{max} detected in our patients was 11.77, and the mean SUV_{max} of the lesions was 6.33±3.6.

Since clinical and FOB findings directed the clinician to a clinical diagnosis of malignancy, PET-CT was ordered to support the clinical diagnosis. In this study, it was found that radiological diagnosis was malignancy in 31.8% (n=7) of the patients, and recurrent malignancy in 4.5% (n=1) of them. As a clinical diagnosis, 40.9% (n=9) of our patients were diagnosed with a malignancy, and 9.1% (n=2) of them were diagnosed with a recurrent malignancy. The kappa compliance analysis showed that the clinical and radiological diagnoses were statistically significantly compatible with each other and that the radiological prediagnosis was not superior to the clinical prediagnosis (κ=0.701 and p<0.001).

The kappa compliance analysis performed for all malignancy cases for clinical (n=2) and radiological (n=1) recurrent malignancy diagnoses revealed that the clinical and radiological diagnoses were consistent with each other (κ=0.681 and p<0.001).

It was decided that PET-CT was not useful in terms of predicting malignancy and supporting the clinical diagnosis, and the clinical and radiological diagnoses were found to coincide.

It has been reported that there is a high rate of initial misdiagnosis for malignancy unless PA is confirmed by microbiological or histopathological means[14].

Clinicians should be aware of the predisposing factors of the clinical picture of PA (infection following oral-dental infection, failed tooth extraction, or poor oral-dental hygiene) and that actinomycosis may mimic malignancy in various conditions[10].

There are several limitations in this study: the inclusion of only 22 patients with PA due to the rarity of those cases, the fact that only 14 of the patients had PET-CT, and the lack of inflammatory markers and pulmonary function tests. These may hamper the reliability of the results. Despite these limitations, we believe this study provides important information about the clinical and radiological characteristics of PA.

CONCLUSION

Pulmonary actinomycosis is a rare disorder, the lesion shows high metabolic uptake in PET-CT, and this may mislead clinicians

for a diagnosis of malignancy. Our results suggest that PET-CT does not help distinguish PA from lung malignancy and does not provide a clear diagnostic benefit to the clinician, so the pathological diagnosis is necessary.

THE INSTITUTIONAL BOARD APPROVAL

Health Sciences University Atatürk Chest Diseases and Thoracic Surgery Education and Research Hospital, Medical Education Board approval (decision date February 12, 2019, and number 617).

AUTHORS' CONTRIBUTIONS

HB, FBT, ET: Conceptualization, Data curation, Formal Analysis, Methodology, Writing – original draft. **AFU, DÇ:** Conceptualization, Data curation, Formal Analysis, Methodology, Writing – review and editing.

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