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# Clinical features and treatment outcomes of pulmonary actinomycosis

N.T. HOCA[1], M.B. BERKTAŞ[2], Y. SÖYLER[2], C. CELEP[2], F.B. TANRIKULU[3]

[1]Department of Chest Diseases, Faculty of Medicine, Gazi University, Ankara, Turkey
[2]Department of Chest Diseases, [3]Department of Pathology, Health Sciences University, Atatürk Sanatorium Training and Research Hospital, Ankara, Turkey

**Abstract. – OBJECTIVE: Pulmonary actinomycosis is a rare and chronic infectious disease that mimics malignancy and is frequently misdiagnosed. There are few reports that address the clinical characteristics of pulmonary actinomycosis. The objective of this research is to evaluate the clinical features, radiological findings, diagnostic approaches and treatment outcomes of pulmonary actinomycosis.**

**PATIENTS AND METHODS: Thirty-seven patients with pulmonary actinomycosis histopathologically diagnosed from 2009 to 2021 were analyzed retrospectively.**

**RESULTS: The mean age at presentation was 53.7 (±13.3) years. Frequent symptoms were cough and hemoptysis. The median diagnosis time from the first symptoms was 60 days (interquartile range 18-195). Pulmonary comorbidity was found in 59.5% of cases. The most common thorax computed tomography finding was mass or nodule. The low-attenuation center within the mass or consolidation was observed in 40% of the lesions. The median maximal standardized uptake value of lesions on positron emission tomography (PET) was 6.5 (interquartile range 2.7-10.3). In the majority of cases (97.3%), the diagnosis of pulmonary actinomycosis was not suspected at admission, and 56.8% of patients were misdiagnosed with lung cancer. The mean duration of antibiotic therapy was 9.4 days (range 3-22) with intravenous antibiotics and 64.7 days (range 5-270) with oral antibiotics. Four patients died due to concomitant comorbidities. Eight cases were lost to follow-up. All other cases were fully cured.**

**CONCLUSIONS: Pulmonary actinomycosis mimics other diseases, often lung cancer. Clinicians should consider the diagnosis of actinomycosis when they detect a mass or consolidation, especially with a low-attenuation center. PET/CT appears not to be useful for differential diagnosis. A shorter course of antibiotic therapy than traditionally recommended appears to be sufficient.**

*Key Words:*
Actinomycosis, Actinomyces, Misdiagnosis, Hemoptysis, Treatment, Lung cancer.

## Introduction

Actinomycosis is a rare, slowly progressive, suppurative and granulomatous disease induced by the *Actinomyces* species, which is a gram-positive, anaerobic or microaerophilic facultative bacterium that colonizes in the human oropharynx, gastrointestinal system or urogenital system[1,2]. The frequency of all forms of actinomycosis has clearly decreased in recent years due to both relatively improved oral hygiene and early administration of antibiotic therapy whenever an infection is suspected, particularly in developed countries[3]. The common clinical forms of actinomycosis are cervicofacial (55%), abdominal and pelvic (20%) and pulmonary (15%), and rare forms are found in the skin, the brain and the limbs (10%)[4,5]. The primary source of pulmonary actinomycosis is the aspiration of oropharyngeal contents or gastric secretion. Rarely, direct spread from local infections or hematogenous spread can enhance the development of actinomycotic lesions in the lungs. Since the spread of an actinomycotic lesion occurs despite anatomic barriers, invasion into the pleura can result in empyema[2]. If not promptly diagnosed and treated, the disease may extend through the chest wall, cause a pleuro-cutaneous fistula and destruct the vertebrae and ribs[6].

The diagnosis of pulmonary actinomycosis can be challenging. The mean duration of symptoms before a definitive diagnosis is nearly six months[7]. Signs and symptoms of pulmonary actinomycosis include dry or productive cough, fever, shortness of breath, chest pain, hemoptysis



*Corresponding Author:* Nevin Taci Hoca, MD; e-mail: nevintacihoca@yahoo.com

and weight loss[8,9]. Acceptable specimens are obtained from sinus drainage, deep needle aspirate or biopsy. Sputum specimens are inappropriate as actinomyces are normal oral commensal[10]. Delayed diagnosis or misdiagnosis of lung cancer, tuberculosis, lung abscess, empyema, endemic mycosis or aspergilloma is common even among experienced specialists[7]. Increased awareness of the disease may facilitate diagnosis and avoid undesirable complications, including unnecessary surgery in patients under investigation for insistent pulmonary lesions. This study highlights the importance of considering the possibility of rare infections in malignant-looking pulmonary lesions or unresolved pneumonia. Here we review the clinical features, radiological findings, diagnostic approaches and treatment outcomes of the disease based on our 12 years of experience.

## Patients and Methods

### Study Design and Patients

Adult patients diagnosed with pulmonary actinomycosis between January 2009 and January 2021 in our institution serving as a regional center for chest diseases and thoracic surgery in a large metropolitan area were included in this retrospective study. All patients had pathological confirmation based on histopathological findings of sulphur granules on hematoxylin-eosin staining or positive branching filamentous organisms on Gomori methenamine silver staining. Samples were obtained by bronchoscopic forceps biopsy, cryo-biopsy, percutaneous transthoracic fine needle aspiration biopsy or surgical resection. The time from the first symptoms to diagnosis was recorded.

Exclusion criteria were: age under eighteen, medical records without sufficient data, previous diagnosis of actinomycosis before admission to our institution and identified *Actinomyces* species from pathological examination of bronchoscopic lavage without clinical and radiological findings of infection.

The written informed consent requirement was waived due to the retrospective nature of the study, and the data were analyzed anonymously. The study was approved by the Local Clinical Research Ethics Committee with the protocol number 2012-KAEK-15/2429.

The medical charts of all patients were reviewed, and the data were retrieved in a standardized form. Collected information included demographic characteristics, comorbidities, smoking history, presenting symptoms, laboratory findings, pulmonary function, diagnostic procedures, treatment modalities and durations and clinical outcomes. Thorax computed tomography (CT) scans and fluoro-deoxy-glucose positron emission tomography (FDG-PET/CT) findings were also evaluated. A lymph node measuring more than 1 cm in the transverse diameter was considered as lymph node enlargement. Radiological lesions were classified as consolidation or ground-glass opacity, mass or nodules, bronchiectasis, atelectasis, cavitation, pleurisy or pleural thickening and lymph node enlargement. Areas of central low attenuation in the lesions were also investigated. Endobronchial lesion appearances were noted in patients evaluated by bronchoscopy.

Therapeutic response was defined as cure/complete recovery when clinical symptoms improved, and complete radiological resolution or fibrotic inactive radiologic lesions were detected. Treatment failure was defined as the persistence or progression of the lesion determined by radiological evaluation or the presence of uncontrolled symptoms despite medical and/or surgical therapy.

### Statistical Analysis

Data were presented as mean and standard deviation (SD) or median and interquartile range (IQR) for continuous variables according to the distribution of data and as numbers (percentages) for categorical variables. Continuous variables were compared with the Mann-Whitney U test. All $p$-values were two-sided, and $p < 0.05$ was considered an indicator of statistical significance. Analyses were executed using Statsoft's Statistica for Windows, version 8.0 (Tulsa, OK, USA).

## Results

### Patient Characteristics and Clinical Findings

37 patients were included in this study. Patients' characteristics are summarized in Table I. The mean ± SD age at the time of pulmonary actinomycosis diagnosis was 53.7 ± 13.3 years. The male:female ratio was 4.3:1. 23 patients were non-smokers at presentation (62.2%). 8 (21.6%) patients were heavy drinkers (alcohol consumption > 4 times/week). None of the 37 patients had used long-term systemic corticosteroids. All of the patients were human-immunodeficiency-virus-negative.

**Table I.** Baseline characteristic features of 37 patients with pulmonary actinomycosis.

| Variables | Number (%) or mean (standard deviation) |
|---|---|
| Age, years | 53.7 (13.3) |
| Gender, male | 30 (81.1) |
| Nonsmoker | 23 (62.2) |
| History of alcohol abuse (> 4 times/week) | 8 (21.6) |
| Duration of symptoms, median (IQR), day | 60 (18-195) |
| Comorbidity (pulmonary) | |
| COPD | 7 (18.9) |
| Bronchiectasis | 6 (16.2) |
| Asthma | 3 (8.1) |
| Pulmonary sequelae following tuberculosis | 3 (8.1) |
| Lung cancer | 2 (5.4) |
| Obstructive sleep apnea | 1 (2.7) |
| Comorbidity (Non-pulmonary) | |
| Diabetes mellitus | 10 (27.0) |
| Hypertension | 4 (10.8) |
| Coronary arterial disease | 3 (8.1) |
| Chronic renal disease | 1 (2.7) |
| Chronic liver disease | 1 (2.7) |
| Symptoms | |
| Cough | 16 (43.2) |
| Hemoptysis | 13 (35.1) |
| Dyspnea | 11 (29.7) |
| Sputum production | 9 (24.3) |
| Chest pain | 6 (16.2) |
| Weight loss | 4 (10.8) |
| Fatigue | 2 (5.4) |
| Laboratory findings | |
| WBC, median (IQR), /μL × $10^3$ | 9,400 (3,295-15,505) |
| Hematocrit, % | 39.5 (5.1) |
| CRP, Median (IQR), mg/L | 22.6 (7.1-94.5) |
| ESR, mm/hour | 53.3 (26.2) |
| Pulmonary function tests ¶ | |
| $FEV_1$, L | 2.69 (0.91) |
| $FEV_1$, % | 75.4 (22.3) |
| $FEV_1$/FVC | 77.1 (8.6) |

WBC: White blood cell count, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, $FEV_1$: Forced expiratory volume in the first second, FVC: Forced vital capacity, IQR: interquartile range. ¶Available from 21/37 patients.

Pulmonary comorbidity was found in 22 (59.5%) patients, mainly as chronic obstructive pulmonary disease (18.9%), bronchiectasis (16.2%), asthma (8.1%), pulmonary sequelae following tuberculosis (8.1%), lung cancer (5.4%) and obstructive sleep apnea (2.7%). Non-pulmonary comorbidities found included diabetes mellitus (27%), hypertension (10.8%), coronary arterial disease (8.1%), chronic renal disease (2.7%) and chronic liver disease (2.7%).

The most frequent symptoms at admission were cough (43.2%), hemoptysis (35.1%) and shortness of breath (29.7%). Massive hemoptysis, defined as the expectoration of more than 200 ml of blood within a day, occurred in three (8.1%) patients. The median time from the onset of initial symptoms to diagnosis was 60 days (IQR 18-195). As inflammatory biomarkers, 18 (48.6%) patients had elevated levels of leukocytes (> 10.2 x $10^3$/mL), 30 (81.0%) patients had increased levels of C-reactive protein (CRP) (> 5 mg/L) and 34 (91.9%) patients had elongated erythrocyte sedimentation rate (ESR) (> 20 mm/hour), as shown in Table I.

### *Radiological Findings*

The most frequent thorax CT findings were mass or nodule (54.1%), consolidation (43.2%) and mediastinal and/or hilar lymph node enlargement (43.2) (Table II). A low-attenuation center within the mass or consolidation was observed in 40% of the lesions. Findings on thorax CT of certain patients with pulmonary actinomycosis are shown in Figure 1. PET/CT was performed for the detection of cancer in 18 (48.6%) patients who

**Table II.** Chest CT findings of patients.

| Finding | Number (%) |
|---|---|
| Mass or nodule | 20 (54.1) |
| Consolidation | 16 (43.2) |
| Mediastinal and/or hilar lymph node enlargement | 16 (43.2) |
| Ground glass opacity | 9 (24.3) |
| Cavity | 8 (21.6) |
| Pleural thickening | 7 (18.9) |
| Bronchiectasis | 6 (16.2) |
| Pleurisy | 6 (16.2) |
| Atelectasis | 4 (10.8) |

had lesions mimicking lung cancer in radiological imaging studies. The median maximum standardized uptake value (SUV) of the lesions on PET/CT was 6.5 (IQR 2.7-10.3), which was higher than the threshold value of 2.5 that is commonly used as indicative of malignancy with controversy[11,12]. According to PET/CT findings, 17 patients had malignancy, while only one patient had an infection or inflammation. Lesions with central low density had a higher maximal SUV of 7.2 (3.4-16.7) compared to the lesions without central low density, which had a maximum SUV of 5.8 (0.8-10.2). However, the difference was statistically insignificant ($p$=0.18).

### Initial Suspected Diagnosis

In the majority of cases (97.3%), the diagnosis of pulmonary actinomycosis was not suspected at admission. According to the clinical characteristic features and imaging findings, lung cancer was initially the most suspected (56.7%), followed by pneumonia (10.8%), hydatid cyst (an endemic parasitic disease in our region) (8.1%), bronchiectasis (5.4%), pulmonary tuberculosis (5.4%), aspergillosis (5.4%), actinomycosis (2.7%), empyema (2.7%) and foreign body aspiration (2.7%).

### Diagnostic Modalities

For pathological diagnosis, specimens were obtained surgically in 18 (48.6%) patients, by fiberoptic bronchoscopic biopsy in 17 (45.9%) patients and by transthoracic fine needle aspiration in 2 (5.4%) patients. 13 patients had endobronchial lesions. There was right hemithorax predilection (10/3 right/left). In addition, a foreign body was detected in 5 patients. The surgical procedures performed were lobectomy in 8 (44.4%) patients, wedge resection in 5 (27.8%) patients, video-assisted thoracoscopic biopsy in four (22.2%) patients and pneumonectomy in one (5.5%) patient (Figure 2). The indication for surgery was the investigation of suspected or concurrent lung malignancy in 7 (38.9%) patients, the resection

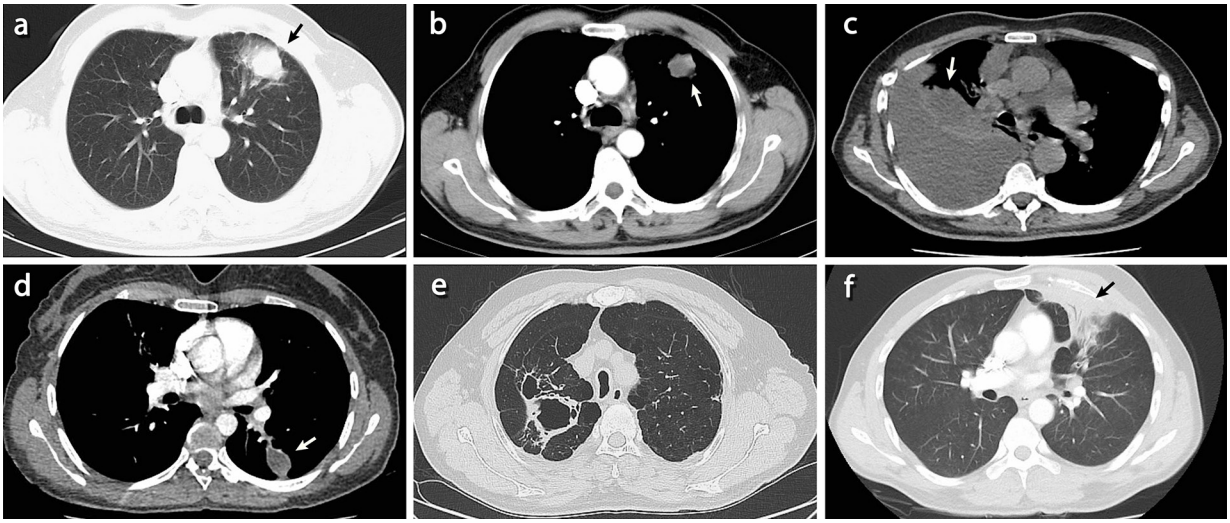


**Figure 1.** Different manifestations of pulmonary actinomycosis on chest computed tomography. **a,** An irregular mass (*arrow*) is seen on the periphery of the left upper lobe in one patient, and (**b**) a low-attenuation center within the mass (*arrow*) is noted with mediastinal window setting. **c,** A central mass lesion is in the right hilar region, obliterating the intermediary bronchus, with indistinguishable borders from the hilar lymph node and collapsed lung, and pleural effusion (*arrow*) in one patient. **d,** 2×2.5 cm sized pleural-based, well-contoured cystic lesion (*arrow*) in the superior segment of the left lower lobe in one patient. **e,** Cavity lesion and bronchiectasis in the right upper lobe that causes pleural retraction and parenchymal distortion in one patient and (**f**) consolidation area with air bronchogram extending from the hilus to the pleura (*arrow*) in the superior lingula segment in another patient.

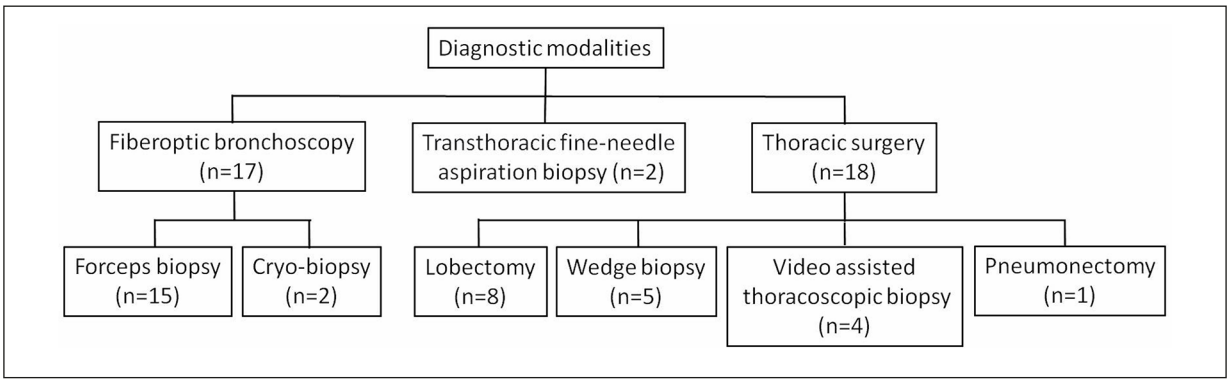


**Figure 2.** Diagnostic modalities of the patients.

of bronchiectasis to control hemoptysis in three (16.7%) patients, aspergilloma or cavitary lesion refractory to medical therapy in three (16.7%) patients, the decortication of thickened pleura in 3 (16.7%) patients and cystectomy in 2 (11%) patients.

After bronchoscopic or surgical interventions, 5 (13.6%) patients were diagnosed with concomitant foreign body aspiration, 2 (5.4%) patients with non-small-cell lung carcinoma, 1 (2.7%) patient with a hydatic cyst and 1 (2.7%) patient with aspergillosis.

### Therapeutic Approach

Patients were treated with several antibiotics after pulmonary actinomycosis diagnosis. Penicillin derivatives (penicillin G and ampicillin-sulbactam) were the most used (73.0 %), followed by cephalosporins (cefuroxime, ceftriaxone) (13.5%), macrolides (clarithromycin) (5.4%), quinolone (levofloxacin, moxifloxacin) (5.4%) and imipenem/cilastatin (2.7%). Metronidazole was combined with other antibiotics in four patients due to coinfection. The mean duration of treatment was 9.4 days (range 3-22 days) with intravenous antibiotics and 64.7 days (range 5-270 days) with oral antibiotics. The median duration of treatment was 22 days (IQR 15-60) in patients diagnosed with surgical biopsy and 60 days (IQR 17-90) in patients diagnosed with non-surgical biopsy. Although the patients diagnosed with surgical biopsy seemed to have received the antibiotic therapy for a shorter duration than patients diagnosed with a non-surgical biopsy, there was no statistically significant difference between the two groups ($p$=0.62).

Patients were followed for a median of 12 months (IQR 4-43). 4 patients died (2 due to complications of comorbid diseases, 1 due to concurrent adenosquamous lung carcinoma, and 1, who was 88 years old and very fragile and who had chronic obstructive pulmonary disease, atherosclerotic cardiac disease and bronchial foreign body aspiration, died two weeks after the cryoextraction of the foreign body and pulmonary actinomycosis diagnosis due to a neurological disorder). 8 patients were lost to follow-up. All other patients were fully cured.

## Discussion

In the present study, we analyzed the clinical features and treatment outcomes of patients with pulmonary actinomycosis diagnosed in a tertiary education and research hospital in the past 12 years. Pulmonary actinomycosis often mimics malignancy and various other suppurative infections. Diagnosis is difficult since both clinical presentations and radiological findings are nonspecific, and the culture of the bacterium requires special methods. Therefore, investigations generally take many months before accurate treatment can be started.

In our series, the mean age at presentation was 53.7±13.3 years, and male predominance was observed, which was consistent with other series[13,14]. Pulmonary comorbidity was found in nearly 60% of our cases. Chronic obstructive pulmonary disease, bronchiectasis and pulmonary sequelae following tuberculosis were the most common underlying pulmonary disorders. Patients with pulmonary sequelae due to tuberculosis and chronic lung disorders, such as bronchiectasis, emphysema and chronic bronchitis, are considered to be at risk of pulmonary actinomycosis[15,16]. 5 (13.5%) patients in our study were associated with foreign

body aspiration as confirmed by bronchoscopy. Diabetes mellitus, which is another risk factor for pulmonary actinomycosis, was found in 10 (27%) patients.

The most frequent symptoms of pulmonary actinomycosis are nonspecific: cough, sputum, hemoptysis, dyspnea, fever, chest pain, night sweats and weight loss[13]. In our study, cough occurred in most cases, followed by hemoptysis and dyspnea. Hemoptysis was more commonly seen in the Asian series[17,18]. Our study found hemoptysis in one-third of the patients. In previous reports[7,18], the mean duration of symptoms was six months (ranging from one month to two years). The mean duration of symptoms in this study was much shorter than in recent literature, which might be explained by the fact that bronchoscopy or surgical biopsy were completed promptly because lung cancer is the most suspected initial diagnosis.

For inflammatory biomarkers, 48.6% of patients had elevated levels of leukocytes, 81% had increased levels of CRP and 92% presented with elongated ESR. This corresponds to the general manifestation of pneumonia and is not specific to the diagnosis of actinomycosis.

Radiological appearances were generally nonspecific and related to the duration of the disease[17,19]. The most frequent radiological findings were mass, nodule, mediastinal and/or hilar lymph node enlargement and consolidation, as consistent with other series. Typical CT manifestations reported as central-low attenuation within the consolidation or mass were present in 40% of lesions in our series. Pulmonary actinomycosis initially appears as a small, peripheral parenchymal nodule with or without interlobular septal thickening. The parenchymal nodule progressively turns into segmental air-space consolidation; then, if antimicrobial therapy is insufficient, central-low attenuation areas with cavity forms occur[19]. In the late stage, the pulmonary parenchyma may be destroyed, and the disease may extend across the fissures to an adjacent lobe, pleura or chest wall with abscess formation. Other findings are bronchiectasis, pleural thickening, mediastinal or hilar lymphadenopathy, pleural effusion and empyema. Sometimes the infection exists as a mass or a cavitary lesion that can mimic lung cancer or pulmonary tuberculosis[6,19,20]. In our series, lung cancer was initially the most suspected (56.7%), followed by pneumonia (10.8%).

In recent literature, only a few reports[21-23] have described the use of PET/CT in the differential diagnosis of pulmonary actinomycosis. In our study, most of the patients (94.4%) with pulmonary actinomycosis had high FDG uptake on PET scans. When the lesions with central-low attenuation were compared to those without central-low attenuation, there was no statistically significant max SUV difference ($p$=0.18) as in previous reports[23]. This study strongly suggests that PET/CT might not be useful for differentiating lung malignancy from pulmonary actinomycosis.

In most series[13,17,24], clinicians have not suspected pulmonary actinomycosis at admission due to its symptoms and radiological findings often being unspecific. Even when the clinical suspicion is high, microbiological confirmation can still be difficult because the specimen that is used for the identification of *Actinomyces* must be collected under strict anaerobic conditions, and coinfections are common, as previously reported[17]. In a previous study[13] from China involving 145 patients with pulmonary actinomycosis, the authors reported that only 5 cases (3.4%) had an accurate initial diagnosis, while other patients were misdiagnosed with lung cancer (41.4%), tuberculosis, pyogenic abscess, pneumonia, asthma or bronchiectasis. In another study by Kim et al[17] with histopathologically confirmed pulmonary actinomycosis, the initial diagnosis was accurate only in 6 (6.4%) patients. Pulmonary actinomycosis is stated to be a 'great imitator'[24]. In this report, pulmonary actinomycosis was initially suspected in just one case (2.7%) but was undiagnosed by a microbiological method. Up to 90% of the cases were initially diagnosed as lung cancer or other infectious diseases, such as pneumonia, pulmonary tuberculosis, hydatic cyst, empyema or aspergillosis. On the other hand, the coexistence of actinomycosis with lung cancer, hydatic cyst, aspergilloma and foreign body aspiration, as seen in a few of our cases, leads to more challenges for diagnosis and treatment. *Actinomyces* species tend to colonize devitalized tissues, which commonly occurs within necrotic malign neoplasms, tuberculosis, bronchiectasis and pyogenic abscesses[7]. Coinfection with other organisms is common[2,25,26]. The frequency of concomitant infection varies between 75% and 95%[2]. In our study, pulmonary actinomycosis was accidentally detected in 2 patients with lung cancer, one patient with hydatid disease and one with aspergillosis. To the best of our knowledge, this is the first case in which pulmonary actinomycosis has been diagnosed concomitantly with hydatid disease in a patient. Due to the lack of literature, the

association between these two diseases is yet to be determined. There are rare case reports[27,28] of pulmonary actinomycosis found concomitantly with pulmonary aspergillosis and lung cancer. In literature[13,15,17,29], most diagnoses have been based on pathological examination. Definitive diagnosis depends on the pathological findings of granulomatous inflammation with sulphur granules and branching filamentous organisms in accordance with the growth of *Actinomyces* species in tissue cultures. Sulphur granules are highly suggestive but not pathognomonic for the diagnosis of actinomycosis[13,16]. In this study, specimens were obtained mostly by surgical biopsy (48.6%) and bronchoscopic biopsy (45.9%) for pathological diagnosis. 13 patients had endobronchial lesions located predominantly on the right side. Bronchoscopic findings of endobronchial actinomycosis may resemble a wide spectrum of lung diseases with endobronchial involvement. Therefore, actinomycosis should be included in the differential diagnosis of any types of endobronchial lesions. An accompanying foreign body was detected during the bronchoscopic intervention in 5 patients. Mucosal breaches are secondary to foreign body impaction, causing *Actinomyces* species to colonize. Our findings demonstrate that greater attention should be paid to those who are suffering from foreign body aspiration as it might lead to pulmonary actinomycosis.

*Actinomyces* species are generally susceptible to penicillin and other beta-lactam group antibiotics, as well as many agents used against gram-positive anaerobic microorganisms, yet they are resistant to metronidazole[30]. The principle of prolonged antibiotic treatment has traditionally been recommended based on clinical experiences. Kolditz et al[31] reported that antibiotic therapy for less than three months in medically treated patients without prior surgical debulking might be associated with recurrence or local complications. However, several investigators[10,32] have successfully healed pulmonary actinomycosis patients with relatively short courses of antibiotics. The duration of antibiotic therapy could presumably be shortened in patients on whom optimal surgical resection of infected tissues has been performed[16]. According to a previous report by Choi et al[32], actinomycosis is best treated with individualized therapeutic modalities that depend on factors such as the clinical and radiological responses at the beginning of the therapy, the initial burden of the disease and the performance of the resectional surgery. In a report[14] of 68 patients with pulmonary actinomycosis, there was no significant difference in the treatment outcomes depending on pulmonary comorbidities, systemic disease, the extension of the pulmonary lesion, whether the initial treatment was surgical and the duration of antibiotic therapy or whether intravenous antibiotics were given. The treatment duration should be individualized to the patient based on clinical and radiographic responses. The trend towards a brief course of antibiotics, as described in literature, was observed in our study.

Pulmonary actinomycosis often has a good prognosis if diagnosed early and treated properly. Park et al[14] reported an overall cure rate of 86.8%, a failure rate of 8.8% and a relapse rate of 4.4% for pulmonary actinomycosis. They stated that prolonged antibiotic therapy cannot guarantee a successful outcome or absence of relapse. In another study[15], an 85% cure rate was reported in 40 cases of pulmonary actinomycosis. In this study, patients were followed for a median of 12 months (IQR 4-43); 4 patients died due to comorbidities, 8 patients were lost to follow-up and all other patients were fully cured.

### *Limitations and Strengths*

The main limitation of the present study is that it is a retrospective analysis. However, due to the sporadic occurrence of pulmonary actinomycosis, prospective trials might not be practically feasible. The other limitations are the inclusion of patients diagnosed only by histopathological examination, the absence of microbiological culture data, a relatively short follow-up period and the loss of 8 patients to follow-up. We could not ascertain whether recurrence of pulmonary actinomycosis occurred in our patients in the long term. Despite these limitations, this study highlights the diversity of clinical and radiological presentations of pulmonary actinomycosis, as well as provides important information about the effectiveness of relatively short courses of antibiotic treatment. This information may increase clinicians' awareness of this uncommon disease.

## Conclusions

Pulmonary actinomycosis is a rare disease that can mimic or complicate malignancy or other chronic suppurative pulmonary infections. The utilization of PET/CT to rule out malignancy seems nonessential. Pulmonary actinomycosis should be considered part of differential diag-

noses in patients confronted with unresolving pneumonia that extends across anatomic barriers, malignant-looking radiologic lesions and especially endobronchial lesions detected concomitantly with a foreign body during bronchoscopy. The prognosis of actinomycosis is excellent, with low mortality when treated properly. Pulmonary actinomycosis is best treated with individualized therapeutic modalities that depend on factors such as the clinical and radiological responses at the beginning of the therapy, the initial burden of the disease and the performance of the resectional surgery. Relatively short-term antibiotic regimens may achieve successful outcomes.

### Conflict of Interest
The Authors declare that they have no conflict of interests.

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### Informed Consent
The written informed consent requirement was waived due to the retrospective nature of the study, and data were analyzed anonymously.

### Ethics Approval
The study was approved by the Local Clinical Research Ethics Committee with the following protocol number: 2012-KAEK-15/2429.

### Authors' Contribution
Nevin Taci Hoca designed the research, analyzed and interpreted the data, drafted the article, Bahadır M. Berktaş analyzed and interpreted the data and performed the research, Yasemin Söyler attained data and performed the research, Canan Celep attained data and performed the research, Fatma Benli Tanrıkulu attained data and performed the research. All authors participated in the intellectual content of the manuscript.

### ORCID ID
Nevin Taci Hoca: 0000-0002-6803-4181; Bahadır M. Berktaş: 0000-0003-4984-3829; Yasemin Söyler: 0000-0002-0507-0767; Canan Celep: 0000-0002-3846-7947; Fatma Benli Tanrıkulu: 0000-0002-6072-644X.

## References

1) Wong VK, Turmezei TD. Actinomyces. BMJ 2011; 343: d6099.
2) Könönen E, Wade WG. Actinomyces and related organisms in human infections. Clin Microbiol Rev 2015; 28: 419-442.
3) Russo TA. Agents of actinomycosis. In: Mandell GL, Bennett JE, Dolin Red (eds). Principles and Practice of Infectious Disease. New York, Churchill Livingstone, 1995; 2645-2654.
4) Hinnie J, Jaques BC, Bell E, Hansell DT, Milroy R. Actinomycosis presenting as carcinoma. Postgrad Med J 1995; 71: 749-750.
5) Yung BC, Cheng JC, Chan TT, Loke TK, Lo J, Lau PY. Aggressive thoracic actinomycosis complicated by vertebral osteomyelitis and epidural abscess leading to spinal cord compression. Spine 2000; 25: 745-748.
6) Kim TS, Han J, Koh WJ, Choi JC, Chung MJ, Lee JH, Shim SS, Chong S. Thoracic actinomycosis: CT features with histopathologic correlation. Am J Roentgenol 2006; 186: 225-231.
7) Mabeza GF, Macfarlane J. Pulmonary actinomycosis. Eur Respir J 2003; 21: 545-551.
8) Machi T. Chest pain with induration of the chest wall. Postgrad Med J 1998; 74: 283-285.
9) Petroianni A, Conti V, Terzano C. A thoracic mass infiltrating the chest wall. Eur Rev Med Pharmacol Sci 2011; 15: 345-348.
10) Hsieh MJ, Liu HP, Chang JP, Chang CH. Thoracic actinomycosis. Chest 1993; 104: 366-370.
11) Hong R, Halama J, Bova D, Sethi A, Emami B. Correlation of PET standard uptake value and CT window-level thresholds for target delineation in CT-based radiation treatment planning. Int J Radiat Oncol Biol Phys 2007; 67: 720-726.
12) Kwee TC, Cheng G, Lam MGE, Basu S, Alavi A. SUVmax of 2.5 should not be embraced as a magic threshold for separating benign from malignant lesions. Eur J Nucl Med Mol Imaging 2013; 40: 1475-1477.
13) Zhang M, Zhang XY, Chen YB. Primary pulmonary actinomycosis: a retrospective analysis of 145 cases in mainland China. Int J Tuberc Lung Dis 2017; 21: 825-831.
14) Park JY, Lee T, Lee H, Lim HJ, Lee J, Park JS, Cho YJ, Park YS, Lee CH, Lee SM, Yoon HI, Yim JJ, Yoo CG, Kim YW, Han SK, Lee CT, Lee JH. Multivariate analysis of prognostic factors in patients with pulmonary actinomycosis. BMC Infect Dis. 2014; 14: 10.
15) Song JU, Park HY, Jeon K, Um SW, Kwon OJ, Koh WJ: Treatment of thoracic actinomycosis: a retrospective analysis of 40 patients. Ann Thorac Med 2010, 5: 80-85.
16) Valour F, Sénéchal A, Dupieux C, Karsenty J, Lustig S, Breton P, Gleizal A, Boussel L, Laurent F, Braun E, Chidiac C, Ader F, Ferry T. Actinomy-

cosis: etiology, clinical features, diagnosis, treatment, and management. Infect Drug Resist 2014; 7: 183-197.

17) Kim SR, Jung LY, Oh IJ, Kim YC, Shin KC, Lee MK, Yang SH, Park HS, Kim MK, Kwak JY, Um SJ, Ra SW, Kim WJ, Kim S, Choi EG, Lee YC. Pulmonary actinomycosis during the first decade of 21st century: cases of 94 patients. BMC Infect Dis 2013; 13: 216.

18) Sun XF, Wang P, Liu HR, Shi JH. A Retrospective Study of Pulmonary Actinomycosis in a Single Institution in China. Chin Med J 2015; 128: 1607-1610.

19) Han, JY, Lee, KN, Lee, JK, Kim YH, Choi SJ, Jeong YJ, Roh MS, Choi PJ. An overview of thoracic actinomycosis: CT features. Insights Imaging 2013; 4: 245-252.

20) Cheon JE, Im JG, Kim MY, Lee JS, Choi GM, Yeon KM. Thoracic actinomycosis: CT findings. Radiology 1998; 209: 229-233.

21) Qiu L, Lan L, Feng Y, Huang Z, Chen Y. Pulmonary Actinomycosis Imitating Lung Cancer on (18)F-FDG PET/CT: A Case Report and Literature Review. Korean J Radiol 2015; 16: 1262-1265.

22) Tanaka S, Araki H, Yoshizako T, Kitagaki H, Isobe T. Pulmonary Actinomycosis Mimicking Pulmonary Cancer on Fluorine-18 Fluorodeoxyglucose PET-CT. Cureus. 2020; 12: e12306.

23) Choi H, Lee H, Jeong SH, Um SW, Kown OJ, Kim H. Pulmonary actinomycosis mimicking lung cancer on positron emission tomography. Ann Thorac Med 2017; 12: 121-124.

24) Grzywa-Celińska A, Emeryk-Maksymiuk J, Szmygin-Milanowska K, Czekajska-Chehab E, Milanowski J. Pulmonary actinomycosis- the great imitator. Ann Agric Environ Med 2017; 25: 211-212.

25) Bonnefond S, Catroux M, Melenotte C, Karkowski L, Rolland L, Trouillier S, Raffray L. Clinical features of actinomycosis: A retrospective, multicenter study of 28 cases of miscellaneous presentations. Medicine (Baltimore) 2016; 95: e3923.

26) Tietz A, Aldridge KE, Figueroa JE. Disseminated coinfection with Actinomyces graevenitzii and Mycobacterium tuberculosis: case report and review of the literature. J Clin Microbiol 2005; 43: 3017-3022.

27) Huang CW, Lee MA, Lu RH, Peng HC, Chao HS. A case of pulmonary aspergilloma and actinomycosis. J Med Microbiol 2011; 60: 543-546.

28) Zayed Y, Osterholzer D, Armstrong E, Azher Q, Bachuwa G. Pulmonary actinomycosis and tracheal squamous cell carcinoma: A rare simultaneous presentation of both in a single patient. Respir Med Case Rep 2019; 27: 100855.

29) Elzein F, Kharraz R, Arab N, Alotaibi F, Almohaya A, Almutairy A. A case series of actinomycosis from a single tertiary care center in Saudi Arabia. IDCases 2019; 15: e00521.

30) Wade WG, Könönen E. Propionibacterium, Lactobacillus, Actinomyces, and other non-sporeforming anaerobic gram-positive rods. In Versalovic J, Carroll KC, Funke G, Jorgensen JH, Landry ML, Warnock DW (ed), Manual of clinical microbiology, ASM Press, Washington, DC 2011; 817-833.

31) Kolditz M, Bickhardt J, Matthiessen W, Holotiuk O, Hoffken G, Koschel D: Medical management of pulmonary actinomycosis: data from 49 consecutive cases. J Antimicrob Chemother 2009; 63: 839-841.

32) Choi J, Koh WJ, Kim TS, Lee KS, Han J, Kim H, Kwon OJ. Optimal duration of IV and oral antibiotics in the treatment of thoracic actinomycosis. Chest 2005; 128: 2211-2217.