Presentation of pulmonary tuberculosis and actinomyces co-infection as a lung mass: a literature review and unique case report

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Abstract

Parenchymal lung infections occasionally present with clinical symptoms and radiological findings similar to lung malignancy. Pulmonary actinomycosis is a rare condition of its own right, let alone in coexistence with tuberculosis. We report a case of a man presenting with hemoptysis alongside a chest computed tomography compatible with lung cancer. The diagnosis, after removal of a large endobronchial mass with flexible bronchoscopy and cryon, was a concomitant infection with *Mycobacterium tuberculosis* and *Actinomyces odontoliticus*. In the literature, there are few reported cases with concomitant tuberculosis and actinomycosis. To our knowledge, such radical treatment without surgical intervention has not been reported in the past.

Introduction

Lung infections mimicking malignancy is an uncommon presentation. Thoracic actinomycosis can masquerade as primary or metastatic lung cancer and in some cases, infection and cancer may even coexist. Actinomycosis occurs in humans worldwide and is usually caused by *Actinomyces israelii*, an anaerobic or microaerophilic, non-spore-forming, gram-positive rod. The extension of the infection in large bronchi is a rare manifestation of the disease. Most infections with *Actinomyces* spp. are polymicrobial [1]. However, cases with concomitant actinomycosis and tuberculosis appear to be rare. We present a case of a *Mycobacterium tuberculosis* co-infection with actinomycosis that presented as a large endobronchial mass. Written consent was obtained from the patient whose personal data were fully anonymized to protect the identity of the individual. This meets the requirements by the Ethics Committee of Evaggelismos General Hospital that approved the present case report. This case report aims to describe a case of co-infection of *A. odontoliticus* and *M. tuberculosis* presenting as an endobronchial mass in the greater context of the published literature, as well as highlight the challenges inherent in the diagnosis and management of this particular co-infection.

Case Report

A 62-year-old Caucasian male presented with a 20 days history of low grade fever, night sweats, shortness of breath, productive cough with blood-tinged sputum and weakness. He was a carpenter by occupation and an ex-smoker. His medical history revealed a previous pulmonary tuberculosis infection when he was 17 years old that was inappropriately treated. Additionally, the patient’s history included bronchiectasis and chronic obstructive pulmonary disease (COPD) over the last 10 years that has been well controlled with combined inhalation therapy of corticosteroids and long acting beta-receptor agonists. He was also allergic to penicillin and clindamycin. There was neither travel history nor exposure to animals and no alcohol use.

Ten days prior to admission, he had been examined for the same symptoms by his family doctor and following a chest X-ray he received clarithromycin for community acquired pneumonia. The symptoms did not resolve and he was referred to our hospital. Physical examination upon admission, revealed blood pressure 130/85 mmHg, heart rate 90/min, respiratory rate 20/min and body temperature 37.6°C. In addition, lung auscultation was pathological with crackles over the lower lobes bilaterally, diminishing vesicular breath sound over the right middle lobe (RML) and wheezing. Arterial blood gases did not reveal respiratory failure (pH 7.39, PaO₂ 78 mmHg, PaCO₂ 38 mmHg). Initial abnormal laboratory parameters included platelet count of 502,000/µl and C-reactive protein 1.1 mg/dl. Extensive laboratory tests for HIV, HBV, HCV and malignancy were negative. Computed tomography (CT) of the...
thorax revealed a well-defined mass in the middle lobe extending to the right lower lobe with surrounding airspace disease (Figure 1 A,B).

The patient underwent flexible fiberoptic bronchoscopy. A pale, polypoid and dense lesion was noted in the proximal portion of the right lower lobe bronchus. The lesion obstructed approximately 80% of the bronchial lumen also causing obstruction of the orifice of the right middle lobe due to pressure (Figure 2). Diffuse bleeding from the hypertrophic mucosa, purulent secretions and significant bronchomalacia were also noted. As the lesion was quite hard and we could not get large chunks for biopsy, we used cryoadhesion with a cryoprobe, and eventually we removed more than 70% of the lesion.

Histologically, the biopsy specimens were negative for cancer and Grocott-Gomori methenamine-silver nitrate stain revealed aggregates of Gram positive filamentous, branching bacteria with the characteristic “sulphur granules” of Actinomyces spp (Figure 3). The organism was initially identified by the hospital laboratory as Actinomyces spp and was then sent to a reference laboratory for definitive identification. The DNA of the isolate was subjected to 16S rRNA gene sequencing via PCR and the isolate was finally identified as A. odontoliticus. In addition, bronchoalveolar lavage culture for M. tuberculosis was positive. A diagnosis of bronchial actinomycosis concomitant with tuberculosis was made and therapy with INH - RIF - ETB - PZA for 8 weeks following INH - RIF for 18 weeks and doxycycline 200 mg per day for 12 months was started. After 2 months of antituberculous therapy and oral doxycycline, the patient underwent a repeat CT that showed a significant resolution of all lesions in the lung (Figure 1C). At that time, the repeat bronchoscopy revealed minor residual disease at

![Figure 1. CT scans of the thorax. A,B) On admission, showing a right-middle-lobe lesion with surrounding airspace disease. C) Substantial resolution of the pulmonary lesion after 2 months of combined antibacterial and antituberculous therapy.](image)

![Figure 2. Bronchoscopic views. A) On admission, showing polypoid lesion in the proximal portion of the right lower lobe bronchus also causing obstruction of the orifice of the right middle lobe. B) Minor residual disease at the entrance of the lateral basal bronchus after 2 months of combined antibacterial and antituberculous therapy.](image)
the entrance of the lateral basal bronchus (Figure 2B). The bronchus was completely opened by the use of cryoadhesion with cryoprobe. Continuous follow up of the patient for 3 years showed no signs of recurrence of the disease.

**Discussion**

Actinomycosis is an infectious disease caused by filamentous, gram-positive, non–acid-fast, anaerobic-to-microaerophilic bacteria. Except *A. israelii*, which is the most common pathogen in humans, there are several other pathogens such as *A. naeslundii*, *A. odontoliticus*, *A. meyeri*, *A. gerencseriae* and *A. graevenitzii*, which are less common causes of actinomycosis [2,3]. The most common clinical forms of actinomycosis are cervicofacial (40-60%), thoracic (10-20%), and abdominal/pelvic (20-30%) [2,3].

Pulmonary actinomycosis is a rare disease and is often clinically confused with other pulmonary diseases like malignancy and chronic infections because commonly presents like pulmonary mass or infiltrate. The main problem is to differentiate the disease from lung cancer. The presence of an air bronchogram within a mass lesion in a chest CT should suggest the possibility of a non-neoplastic process. Other pulmonary findings in chest CT have been described including multiple nodular appearances, cavitations, pleural thickening, pleural effusions and hilar or mediastinal lymphadenopathy [2,3].

In the literature there is no clear explanation for the predisposing factors and the role of immune system in actinomycosis. A pivotal step in the pathogenesis of actinomycosis is the disruption of the mucosal barrier so patients with poor dental hygiene, facial trauma, oral surgery, head and neck radiotherapy are in increased danger [1].

Firstly, concomitant actinomycotic infections may be underdiagnosed or underreported since it does not necessarily signify clinical disease. Secondly, the process of aerobic culture will negatively select most *Actinomyces* spp. [8]. Thirdly, clinically important *Actinomyces* species are not always identified because the differentiation process is laborious and expensive, while commercial identification kits may not include recently discovered *Actinomyces* species. Finally, it has been proposed that *Actinomyces* species are “incompatible” with tuberculous co-infection because they possess bacterial properties that hinder the growth of *M. tuberculosis* [18].

The endoscopic appearance of endobronchial actinomycosis can range from an irregularly raised mucosa or swelling to a mass that causes partial or complete occlusion of a bronchus [19]. An important point in endobronchial actinomycosis is the clinical appearance which resembles other endobronchial pathologies. In many cases non-specific symptoms such as cough, fever and recurrent pneumonias have been commonly reported. The above clinical symptoms in conjunction with a chest radiograph that resemble a spectrum from benign infection to malignancy make the diagnosis between malignancy, lung abscess and tuberculosis difficult and challenging. In general, bronchoscopy may not be diagnostic in every case of pulmonary actinomycosis [20]. However, it should be performed as part of the differential diagnosis that also includes neoplasms or infections with similar radiological

![Figure 3. Grocott-Gomori methenamine-silver nitrate stain showing filamentous, branching aggregates and characteristic “sulphur granules” of *Actinomyces* spp.](image-url)
or clinical characteristics. Especially in the case of endobronchial actinomycosis, the diagnostic capacity of flexible bronchoscopy increases substantially. In this clinical setting bronchoscopy may also provide a window of opportunity to completely remove the endobronchial mass or at least decrease the burden of the disease while acting as a therapeutic adjunct. Nevertheless, co-infection of actinomycosis or clinical characteristics. Especially in the case of endobronchial actinomycosis, the diagnostic capacity of flexible bronchoscopy increases substantially. In this clinical setting bronchoscopy may also provide a window of opportunity to completely remove the endobronchial mass or at least decrease the burden of the disease while acting as a therapeutic adjunct. Nevertheless, co-infection of M. tuberculosis and Actinomyces spp represents a rare, but difficult challenge in clinical practice. This highlights the importance of timely diagnosis and treatment to avoid interventions requiring considerable time, effort and risk to the patient.

### Table 1. Summary of previously reported cases of Actinomyces co-infection with M. tuberculosis.

| Age (yr) | Ethnicity       | Comorbidity                                         | Thoracic lesion                | Actinomyces species     | Treatment                              | Outcome                      |
|----------|-----------------|-----------------------------------------------------|--------------------------------|-------------------------|----------------------------------------|------------------------------|
| Bisero et al. (2016) | 13              | Caucasian                                           | None                           | Pneumonia, thoracic wall abscess | Unknown                               | Penicillin, RHZE              | Recovery                    |
| Tietz et al. (2005) | 43              | African-American                                    | Coronary artery disease, hypertension | Pneumonia, cavity A. graevenitzii          | Amoxicillin, RHZE                  |                              | Recovery                    |
| Stein et al. (1983) | 12              | African-American                                    | None                           | Cavity, thoracic wall abscess A. israelii    | Penicillin, RHE                    |                              | Recovery                    |
| Chakravarty and Fernandez (1977) (patient #1) | 22              | Asian Indian                                        | None                           | Cavity A. israelii                | Penicillin, HS, PAS                  |                              | Recovery                    |
| Chakravarty and Fernandez (1977) (patient #2) | 30              | Asian Indian                                        | None                           | Bilateral cavities A. israelii       | Penicillin, HS                      |                              | Recovery                    |
| Lee (1966) | 35              | African-American                                    | None                           | Cavity, pleural empyema Unknown | Penicillin, unknown tuberculosis treatment, lung resection |                              | Recovery                    |
| Bates and Cruickshank (1957) (patient #1) | Unknown | Caucasian                                          | Unknown                         | Empyema A. israelii               | Unknown antibiotics, thoracoplasty   |                              | Recovery                    |
| Bates and Cruickshank (1957) (patient #2) | Unknown | Caucasian                                          | Unknown                         | Empyema A. israelii               | Unknown antibiotics, thoracoplasty   |                              | Death from amyloidosis       |
| von Arnim (1949) | 42              | Caucasian                                           | None                           | Cavity, substernal abscess Unknown | Neosarsephenamine, Sulphonamides, incision and drainage of abscesses |                              | Death from pulmonary haemorrhage |

R, rifampin; H, isoniazid; Z, pyrazinamide; E, ethambutol; S, streptomycin; PAS, para-aminosalicylic acid.

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