A Retrospective Study of Pulmonary Actinomycosis in a Single Institution in China

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Abstract

Background: Actinomycosis is a rare indolent infectious disease caused by Actinomyces. Although pulmonary actinomycosis is thought to be more prevalent in developing countries, data from developing countries are scanty. This study was to reveal the current situation of pulmonary actinomycosis in developing countries and the difference from that in developed countries.

Methods: Patients fulfilling the inclusion criteria for pulmonary actinomycosis from Peking Union Medical College Hospital in China between January 2003 and December 2014 were retrospectively analyzed. Baseline characteristics, clinical symptoms, underlying diseases, diagnostic methods, pulmonary function test results, chest computed tomography (CT) tests, fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) tests, initial diagnosis, treatment and prognosis were retrieved from medical records and analyzed.

Results: Twenty-six patients were included in this study (mean age 52.0 ± 13.1 years). The ratio of male to female was 1.17:1. Most common clinical symptoms were cough (15/26), sputum (12/26) and hemoptysis (12/26). Chest CT findings presented as masses (13/26), nodules (10/26) and infiltrates (3/26). FDG-PET had an increased standardized uptake value and 4/6 patients were misdiagnosed as malignancy. Many kinds of antibiotics were used in the treatment of pulmonary actinomycosis and all got favorable results. Five patients receiving complete resection of the lesion were cured without postoperative use of antibiotic.

Conclusions: Pulmonary actinomycosis is a rare disease even in developing countries, and both misdiagnosis and missed diagnosis are common. FDG-PET seems useless in the differential diagnosis, and complete resection of the pulmonary lesion without postoperative antibiotic therapy might be enough to achieve cure.

Key words: Actinomycosis; Computed Tomography; Lung; Misdiagnosis; Treatment

Introduction

Actinomycosis is a rare, indolent and slowly progressing infectious disease caused by filamentous Gram-positive anaerobic bacteria, genus Actinomyces, belonging to the family Actinomycetaceae.¹ The human form of actinomycosis was first described in 1857,² while pulmonary actinomycosis was described 25 years later, accounting for 15%–20% of the total burden of actinomycosis.³

Actinomyces are commensals of the human oropharynx, gastrointestinal tract, and urogenital tract. Pulmonary actinomycosis probably results from aspiration of oropharyngeal or gastrointestinal secretions into the respiratory tract.⁴ The most common clinical complaints of pulmonary actinomycosis include cough, hemoptysis and sputum production.⁵ Fever, dyspnea and chest pain are also often seen. Chest computed tomography (CT) usually reveals pulmonary infiltrates or masses, and misdiagnosis for lung cancer or tuberculosis is common. Pulmonary actinomycosis usually presents a chronic course, and a long duration of therapy is usually needed.

The incidence of pulmonary actinomycosis has declined in recent years in developed countries as a result of better oral hygiene and susceptibility to a broad range of antibiotics.⁶ Pulmonary actinomycosis is thought to have a higher incidence in developing countries because of worse oral hygiene and more alcoholics. However, most data of pulmonary actinomycosis come from developed countries. As a matter of fact, data from developing countries are scanty, and only a case series from Thailand including 16 patients⁷ was reported in English literature. We performed this study in a developing country, China, with comparison with that in developed countries, to reveal the current situation of pulmonary actinomycosis in developing countries and the difference from that in developed countries.

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**METHODS**

**Patients**

Patients with the diagnosis of pulmonary actinomycosis at Peking Union Medical College Hospital from January 2003 to December 2014 were searched, and those fulfilling the following inclusion criteria were included in this study: (1) Pulmonary parenchymal abnormality on CT; and (2a) histopathological identification of actinomycosis from the tissues obtained by lung resection, percutaneous transthoracic lung biopsy, or bronchial biopsy; or (2b) culture of aseptic tissue, including lung tissue or pleural effusion; or (2c) histopathological identification of actinomycosis from expectorated mucus plug and remission achieved after therapy aiming at actinomycosis.

The following data were retrieved for analysis: Baseline characteristics, clinical symptoms, underlying diseases, diagnostic methods, pulmonary function test results, chest CT tests, fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) tests, initial diagnosis, treatment and prognosis. The study was approved by the Ethical Committee of Peking Union Medical College Hospital to use patient medical records, and patient confidentiality was ensured to be respected.

**Identification of actinomycosis**

Actinomycosis was identified with either of the following criteria: (1) Histopathological examination demonstrated a filamentous branching organism with or without sulfur granules by Hematoxylin and Eosin staining or Gomori’s Methenamine Silver staining. Meanwhile, a Gram staining with a positive result and a modified Kinyoun’s acid-fast staining with a negative result were also obtained. (2) Lung tissue or pleural effusion was sent for actinomycosis culture, which isolated *Actinomyces*.

**Statistical analysis**

Data were analyzed using Microsoft Excel 2010 (Microsoft Corp., Redmond, WA, USA) and SPSS version 19.0 software (SPSS Inc., Chicago, IL, USA). The data were expressed as mean values ± standard deviation or percentage.

**RESULTS**

**Baseline characteristics**

A total of 26 patients were included in this study. Men were mildly prevalent, and mean age was 52.0 years [Table 1]. All patients were human immunodeficiency virus – negative, and did not have any disease compromising body immunity. Smoking history and alcohol abuse were only noted in male patients, and underlying diseases were only occasionally seen [Table 1]. Elevated level of inflammatory markers, including white blood cell count, erythrocyte sedimentation rate and C-reactive protein, were only noted in a minority of patients, and only a few patients had obstructive ventilation dysfunction [Table 1].

![Table 1: Baseline characteristics of 26 patients with pulmonary actinomycosis](image)

| Characteristics                        | Number (%) or mean (range) |
|----------------------------------------|----------------------------|
| Male:female                            | 1.17:1                     |
| Age (years)                            | 52.0 ± 13.1 (18–75)        |
| History of smoking                     | 8/26 (30.8)                |
| History of alcohol abuse               | 5/26 (19.2)                |
| Co-morbidity (pulmonary)               |                            |
| Obstructive pulmonary disease          | 2/26                       |
| Healed pulmonary tuberculosis          | 1/26                       |
| ABPA                                   | 1/26                       |
| Bronchial foreign body                 | 1/26                       |
| Co-morbidity (nonpulmonary)            |                            |
| Hypertension                           | 7/26                       |
| Gingival disease                       | 3/26                       |
| GERD                                   | 2/26                       |
| Diabetes mellitus                      | 2/26                       |
| Maxillary sinusitis                    | 2/26                       |
| Subtotal gastrectomy                   | 1/26                       |
| Ischemic heart disease                 | 1/26                       |
| Rheumatoid arthritis                   | 1/26                       |
| Spontaneous abortion                   | 1/26                       |
| Laboratory findings and PFT            |                            |
| White blood cell count >10 × 10^9/L    | 1/20 (5.0)                 |
| ESR >20 mm/h                           | 5/12 (41.7)                |
| CRP >5 mg/L                            | 3/10 (30.0)                |
| FEV1/FVC <70%                          | 2/15 (13.3)                |

**Clinical symptoms**

Cough was the most common presentation, followed by sputum production and hemoptysis. Fever, short of breath and chest pain were also occasionally noted [Table 1]. Three patients were asymptomatic and pulmonary actinomycosis was found accidentally on routine health examination. The interval time from onset of initial symptoms to diagnosis ranged from 1 week to more than 6 years, and the mean interval time was around 10 months.

**Diagnosis modalities**

Pathological confirmation of actinomycosis from lung tissue was achieved in 23 patients, in whom 14 patients received wedge resection or lobectomy, 5 patients received percutaneous transthoracic lung biopsy, and 4 patients received bronchial biopsy. Two patients were diagnosed by pathological confirmation from expectorated mucus plug, and the last patient was diagnosed by actinomycosis culture of pleural effusion.
Different manifestations of pulmonary actinomycosis

Pulmonary actinomycosis presented as masses [Figure 1a], nodules [Figure 1c] and patchy infiltrates [Figure 1d] in 13, 10 and 3 patients separately. Solitary lesion was observed in 20 (76.9%) patients, while the other 6 patients presented as multiple lesions. Lesion margins in 3 patients with patchy infiltrates were ill-defined with ground glass opacities, and in the remaining patients, 18 patients had an irregular or spiculated edge, while the other 5 patients presented multiple smooth nodules. Mediastinal or hilar lymphadenopathy was seen in 15 (57.7%) patients. As the typical CT features of parenchymal actinomycosis, lesion located peripherally with pleural involvement was noted in 11 (42.3%) patients [Figure 1a–1c], cavity was seen in 6 (23.1%) patients [Figure 1c], and central low-attenuation was observed in 5 (19.2%) patients [Figure 1b]. Air bronchogram was noted in 5 (19.2%) patients. Calcification was noted in 3 (11.5%) patients.

Six patients received fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) examination. The maximum standardized uptake value ranged from 2.1 to 14.3. According to FDG-PET results, 4 patients were considered to have malignancy, while the other 2 patients were considered to have inflammation.

Initial diagnoses

A misdiagnosis was often made as the initial diagnosis. Lung cancer was the most common initial diagnosis, noted in 13 (50.0%) patients, followed by pulmonary tuberculosis (7 cases, 26.9%). Nontuberculosis pulmonary infection was suspected only in 6 (23.1%) patients. Calcification was noted in 3 (11.5%) patients.

Treatment and prognosis

In spite of our best effort, 6 patients were still lost to follow-up. In the remaining 20 patients, 5 patients diagnosed by surgery did not take any medicine after surgery in view of the complete resection of the lesion, and all of them were stable and uneventful at 2–3-year follow-up.

Other 15 patients (diagnosed by surgery in 7 patients and by other methods in the remainder) were treated with antibiotics for 3–18 months (2 patients for 3 months, and the others for equal or more than 6 months). Amoxicillin/clavulanic acid was used most commonly (6 patients), then moxifloxacin (4 patients), minocycline (3 patients), and penicillin G (2 patients). Some other antibiotics were also used occasionally, including ampicillin/subbactam, cefaclor, levofoxacin, clarithromycin and doxycycline (1 patient each). Five patients received combination therapy with 2 kinds of antibiotics. During follow-up ranging from 3 months to 3 years, all these patients were stable and remission was confirmed by chest CT.

Discussion

Our present study analyzes the data of pulmonary actinomycosis at a teaching hospital in China during the past 11 years, and as far as we know, this is the largest study of pulmonary actinomycosis in a single institution in China.

Pulmonary actinomycosis is seen at all ages, but mainly in adults. Most series described a peak incidence in the 4th and 5th decades.[8,12] All studies published in recent 5 years showed a mean age in the 5th,[5,8–10] as is seen in our study. Although lower than that reported in literature,[14] the prevalent incidence of infection in males is still noted in this study, which has been partly attributed to poorer oral hygiene and/or a higher incidence of facial trauma in males.[12,11]

With the improvement in oral hygiene, and early use of antibiotics, the presentation of pulmonary actinomycosis has changed from aggressive to less aggressive behavior in the past years. Cough, sputum and chest pain were reported to be the most common complaints in some studies undertaken in Europe,[8,12] but hemoptysis was more commonly seen in Asian series.[5,6,9,10,13] Our study also reveals a high incidence of hemoptysis, but only 1 case of chest pain, confirming the different clinical manifestations in different regions. Furthermore, the mean duration of symptoms in this study is much longer than that in recent literature, which might be explained by the fact that patients in developing China still lack consciousness for hospitalizing and/or actinomycosis is still not well recognized by Chinese clinicians.

The typical CT feature of parenchymal actinomycosis is a chronic segmental air-space consolidation containing necrotic low-attenuation areas with frequent cavity formation and peripheral enhancement,[14,17] but is only seen in <50% of patients in this study. Furthermore, imaging modalities in pulmonary

Chest computed tomography and fluoro-2-deoxy-D-glucose positron emission tomography results

Chest CT was performed in all patients. According to chest CT scan, pulmonary actinomycosis was bilateral in 2 patients. Among the remaining 24 unilateral patients, 11 cases were right-sided and 13 cases were left-sided.

According to FDG-PET results, 4 patients were considered to have inflammation.
Actinomycosis has been considered to be a medically treatable disease with good prognosis, sensitive to a lot of antibiotics, such as penicillin, tetracycline, erythromycin etc. Presumably due to the drug’s poor penetration, which is caused by avascularity and dense co-aggregations of actinomycosis known as sulphur granules, it is usually necessary to treat actinomycosis for a duration as long as 6–12 months. The thoracic form appears to require longer treatment courses compared to other forms. However, a few recent studies showed that a relatively brief course (2–3 months) of antibiotic therapy would be successful in pulmonary actinomycosis. In our study, 2 patients with mild illness are treated with antibiotics for 3 months and both get favorable outcome. Present data show that the optimal duration of antibiotic therapy for pulmonary actinomycosis still needs more investigation.

Surgery is usually performed to rule out lung cancer or to control severe symptoms such as hemoptysis Occasionally, surgery is considered when medical treatment has no effect. In this study, all patients receiving surgery are undiagnostic before surgery. What is interesting, 5 patients taking no antibiotic after surgery are all cured and no relapse is observed. It indicates that surgery solely might be enough to cure pulmonary actinomycosis if complete resection of the lesion is assured. From another point of view, a more thorough and comprehensive microbiological work up before surgical resection would be important so as to avoid unnecessary surgery. Moreover, although these patients taking no antibiotic after surgery are all cured, the potential danger of relapse should be paid attention to.

A few limitations are apparent in this study. First, as a rare disease, only 26 patients with pulmonary actinomycosis are included in this study, which will hamper the reliability of results. Second, some data from these patients are incomplete, such as inflammatory markers and pulmonary function tests. In spite of these defects, this study provides some important information about pulmonary actinomycosis in a developing country, and a comparison with that in developed countries will expedite the understanding for pulmonary actinomycosis.

In summary, pulmonary actinomycosis is a rare disease even in developing countries, and both misdiagnosis and missed diagnosis are common. FDG-PET seems useless in the differential diagnosis of pulmonary actinomycosis, and complete resection of the pulmonary lesion without postoperative antibiotic therapy might be enough to achieve cure.

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