CASE REPORT

Insufficient initial treatment but good recovery after diagnosis of pulmonary actinomycosis

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Abstract
Actinomycosis is an infrequent invasive bacterial disease. Although multiple different clinical features of actinomycosis have been described, pulmonary actinomycosis (PA) is a rare but challenging diagnosis and complete cure to make. Here we report the case of a 41-year-old Asian woman who had a mass-like consolidation in the right middle lung field. The lung lesion was exacerbated after initial treatment. After diagnosis of PA, thoracoscopic resection combined with intravenous and oral penicillin made a good recovery.

INTRODUCTION
Actinomycosis is an infrequent invasive bacterial disease that has been recognized for over a century. Actinomycetes spp. are filamentous anaerobic gram-positive bacilli, mainly belonging to the human commensal flora of the oropharynx, gastrointestinal tract and urogenital tract. To date, multiple different clinical features of actinomycosis have been described, as various anatomical sites (such as face, bone and joint, respiratory tract, genitourinary tract, digestive tract, central nervous system, skin and soft tissue structures) can be affected. Of note, in any site, actinomycosis frequently mimics malignancy, tuberculosis or nocardiosis, as it spreads continuously and progressively, and often forms a cold abscess [1, 2].

Pulmonary actinomycosis (PA) is a rare but challenging diagnosis to make. PA is commonly confused with other chronic suppurrative lung diseases and with malignancy [2]. Compared to cervicofacial actinomycosis, which is the most frequent form of actinomycosis and constitutes 50–60% of the total actinomycosis [2], PA is more difficult to treat due to inapplicable surgical incision and drainage and a high relapse rate [2–5].

Here, we report the case of a patient who complained of persistent coughing and a mild fever at her first visit. Chest radiograph revealed a mass-like consolidation in the right middle lung field. After exacerbation of both consolidation and opacity, bronchial brushing with bronchoscopy revealed actinomycosis. Surgical intervention combined with intravenous and oral penicillin made a good recovery.

CASE REPORT
A 41-year-old Asian woman, groomer by occupation, visited our office for persistent coughing for over a month. She had noticed a mild fever 2 weeks before the visit. Her past medical history was unremarkable. She had a 12-pack-year smoking history and a 20-year history of persistent alcohol use with daily use of beer.
Successful surgical intervention of pulmonary actinomycosis

Figure 1: Chest radiograph (postero-anterior view) revealing a mass-like consolidation in the right middle lung field with a poorly marginated, increased opacity in the right lower lung field at the first office visit.

Figure 2: (a) Chest radiograph (postero-anterior view) revealing slight improvement of the consolidation in the right middle lung field at 2 weeks of GRNX treatment. (b) Chest radiograph (postero-anterior view) revealing exacerbations of both consolidation and opacity in the right middle and lower lung fields 2 weeks after GRNX treatment.

(298-g alcohol units per week). Her physical examination at our office visit was unremarkable.

The baseline laboratory results were as follows: white blood cell (WBC) count, 9200/μL (neutrophils 76.0%, lymphocytes 20.9%, eosinophils 0.2%); hemoglobin, 11.9 g/dL; platelet count, 325 × 10^9/μL; blood urea nitrogen, 12 mg/dL; creatinine, 0.52 mg/dL; sodium, 142 mEq/L; potassium, 3.8 mEq/L; chlorides, 104 mEq/L; total protein, 6.8 g/dL; albumin, 3.6 g/dL; C-reactive protein (CRP), 3.36 mg/dL (↑); total bilirubin, 0.30 mg/dL; aspartate aminotransferase, 12 IU/L; alanine aminotransferase, 12 IU/L; lactate dehydrogenase, 162 IU/L; glucose, 120 mg/dL (↑); hemoglobin A1c, 5.1%; carcinoembryonic antigen, 2.7 ng/mL; carbohydrate antigen 19-9, 3.3 (↑) (0.0–0.9); Chlamydia pneumonia immunoglobulin A, 1.8 (↑) (0.0–0.9); Chlamydia pneumonia immunoglobulin G, 3.3 (↑) (0.0–0.9); and beta-D-glucan, 2.2 pg/mL. Urinary pneumococcal and Legionella antigens were negative.

Chest radiograph revealed a mass-like consolidation in the right middle lung field with a poorly marginated, increased opacity in the right lower lung field (Fig. 1). A computed tomography (CT) scan of the lung field revealed no underlying pulmonary disease except for consolidation in the right middle lobe as shown in Video 1 of the Supplementary material. The patient was treated with 400 mg/day of garenoxacin (GRNX) for 2 weeks after her refusal of bronchoscopy. Although the mass-like consolidation slightly decreased in size (Fig. 2a), it rather increased 2 weeks after GRNX treatment (Fig. 2b). WBC count and CRP also increased up to 12 100/μL (↑) and 9.68 mg/dL (↑), respectively. Bronchoscopy was performed after acceptance of an informed consent of the examination.

Hematoxylin and eosin (HE) stain of specimen obtained from right B4 by bronchial brushing with bronchoscopy at right B4, showing a gram-positive filamentous branching organism, indicating Actinomyces (magnification, ×100).

Figure 3: HE stain of specimen obtained by bronchial brushing with bronchoscopy at right B4, showing a gram-positive filamentous branching organism, indicating Actinomyces (magnification, ×1000).

Figure 4: (a) Chest radiograph (postero-anterior view) revealing the decreased but remaining consolidation in the right middle lung field at 3 weeks of PCG treatment. (b) Chest radiograph (postero-anterior view) revealing no consolidation and opacity in the right middle and lower lung fields 1 year after thoracoscopic resection of the right middle lobe.

Figure 5: (a) Actinomycosis-forming sulfur granules (HE stain; magnification, ×10). (b) Filamentous rods within sulfur granules of Actinomyces (Grocott stain; magnification, ×100).

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Hematoxylin and eosin (HE) stain of specimen obtained from right B4 by bronchial brushing with bronchoscopy revealed a gram-positive filamentous branching organism, indicating Actinomyces (Fig. 3). A total of 20 million units/day of benzylpenicillin (PCG) had been applied to the patient. At 2 weeks of PCG treatment, WBC counts and CRP were normalized, while the consolidation in the middle right lung field had shrunk but remained even 3 weeks of PCG administration (Fig. 4a). Finally,
thoracoscopic resection of the right middle lobe was performed after 4-week PCG treatment upon the acceptance of an informed consent of the surgery.

Histopathology of the resected lobe showed necrotic tissues surrounded by inflammatory granulations. The necrotic tissues included sulfur granules (Fig. 5a) that comprised filamentous rods of *Actinomyces* (Fig. 5b).

The patient received 6 months of oral amoxicillin following surgery. PA has not relapsed ~1.5 years after the surgery (Fig. 4b).

**DISCUSSION**

The peak incidence of PA was reported to be in the fourth and fifth decades of life. Men were more often affected than women, with a 3:1 ratio. PA mainly resulted from aspiration of oropharyngeal or gastrointestinal secretions. Consequently, individuals with poor oral hygiene, preexisting dental disease and alcoholism had an increased risk for developing PA [1]. These factors were likely to be predispositions of PA in our case. In fact, the patient had 15 treated teeth of total 26 teeth and 1 untreated cavity of a right maxillary cuspid, in addition to a 20-year history of persistent, daily alcohol use.

In the literature, a rate of treatment failure and recurrence of PA after antibiotics treatment was 15.1%, while that after surgical resections was 6.7% [4]. Therefore, durations of antibiotic treatment were recommended to be individualized, and termination of treatment could be considered 1 or 2 months after complete clinical and radiological disease resolution [3]. Early good responses to antibiotics could predict a successful treatment outcome [3, 4]. Furthermore, surgical interventions including surgical drainage are important for a complete cure of PA, which might shorten the duration of antibiotics treatment [1, 6]. Of note, a patient with relapses of PA was reported to take ~4 years of antibiotics treatment with a refusal of surgical interventions [5].

In our case, both GRNX and PCG treatments were insufficient for a complete resolution of the lung lesion (Figs 2a and 4a). PCG was effective for decreasing the size of the affected area but was not for the region of a right hilar nodule (Fig. 4a). Fluoroquinolones are usually considered to be inactive, but data are limited and controversial [1, 2]. In vitro studies showed that GRNX was effective for *Actinomyces* spp. (0.5 and 1 mg/L of minimum inhibitory concentration (MIC) 50; see [7] and [8], respectively), although MIC50s of GRNX for *Actinomyces* spp. were much higher than that for other anaerobic organisms [7, 8]. Therefore, it is still limited to determine whether GRNX is effective for a complete resolution of PA due to a short duration of the GRNX treatment and the involvement of necrotic tissues including sulfur granules (Fig. 5a) in the lung lesion in our case.

In summary, although PA was a challenging diagnosis to make, surgical intervention combined with intravenous and oral penicillin made a good recovery.

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**CONFLICT OF INTEREST STATEMENT**

None declared.

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**ETHICAL APPROVAL**

No ethical approval was required, as this was a clinical case.

**CONSENT**

Patient permission was obtained in writing.

**GUARANTOR**

Dr Toshiki Ito.

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