Actinomyces graevenitzii pulmonary abscess mimicking tuberculosis in a healthy young man

Smaranda Gliga MD1,2, Mathilde Devaux MD2, Marine Gosset Woimant MD2, Dominique Mompoint MD3, Christian Perronne MD PhD2, Benjamin Davido MD MS2

Pulmonary actinomycosis is a rare disease that is often misdiagnosed as tuberculosis or lung cancer. Actinomyces graevenitzii is a relatively new recognized Actinomyces species isolated from various clinical samples. The authors report a case of pulmonary actinomycosis caused by A graevenitzii. A computed tomography examination revealed an excavated consolidation in the middle right lobe of a previously healthy young man who presented with a long history of moderate cough. Cultures of the bronchoalveolar lavage fluid confirmed the diagnosis of pulmonary abscess caused by A graevenitzii. At the three-month follow-up consultation and, after six weeks of high-dose amoxicillin, the pulmonary lesion had completely disappeared.

Key Words: Actinomyces graevenitzii; Amoxicillin; Lung abscess; Pulmonary actinomycosis

Learning objectives:
● To understand the various steps used to identify and diagnose lung abscesses caused by A graevenitzii.

CanMEDS competency: Medical Expert

Pretest:
● What is the role of A graevenitzii in the pathogenesis of pulmonary actinomycosis?

● What are the different methods of laboratory diagnosis in pulmonary actinomycosis caused by A graevenitzii?

CASE PRESENTATION
A 35-year-old man of Italian origin, born and living in France presented to hospital with a one-week history of profuse night sweats and productive cough with dark brown sputum. He had a one-year history of moderate cough and had recently travelled to Sicily, Italy. There was no previous contact with a contagious tuberculosis case. He was not taking medication for any particular disease and had not been vaccinated before the first symptoms. He was exercising on a regular basis and had not lost weight in the past 12 months.

On clinical examination, his body temperature was 36.4°C with a pulse oximetry of 99%. There were neither pathological features nor dental diseases. Laboratory tests revealed a mild biological inflammation syndrome with a C-reactive protein level of 122.86 nmol/L and a normal white blood cell count of 5.9x10^9/L. The patient previously tested negative for HIV, pneumococcal and legionella antigens in the urine.

Three sputum smears were negative for acid-fast bacilli, and the mycobacterium tuberculosis polymerase chain reaction and interferon-γ release assay (Quantiferon-TB Gold In-Tube) were also negative. A tuberculin skin test showed a 6 mm area of induration (Bacille Calmette-Guérin vaccination in childhood). A pulmonary computed tomography (CT) scan revealed an excavated consolidation compatible with a pyogenic lung abscess or TB (Figure 1A).

On day 7 of hospitalization, direct examination of the middle lobe pulmonary samples collected after a bronchoscopy returned negative for acid-fast bacilli, fungi and bacteria (including specific cultures for Nocardia, Rhodococcus, Legionella and Aspergillus). No sulfur granules were observed in the bronchoalveolar lavage fluid (BALF); however, a subsequent aerobic culture revealed significant growth of A graevenitzii (>10^4 colony forming units/mL). Antimicrobial susceptibility testing revealed that the isolate was susceptible to penicillin, cephalosporins, aminoglycosides and rifampicin, and resistant to cyclins, fluoroquinolones, lincosamides and sulfonamides. Treatment initiated with amoxicillin 6 g daily was continued for six weeks.

A CT scan of the sinuses and a dental CT scan were performed to find an infectious route of entry, which revealed no abnormalities. After a three-week regimen, a pulmonary CT scan revealed complete regression of the cavity with persistence of a small consolidation.
Actinomyces israelii is considered pathogenic in humans: there are >30 species in the genus Actinomyces, six of which are usually considered pathogenic in humans: Actinomyces israelii, Actinomyces gerencseriae, Actinomyces naeslundii, Actinomyces odontolyticus, Actinomyces viscosus and Actinomyces meyeri (1).

A graevenitzii was first described in 1997 by Ramos et al (2). Similar to other Actinomyces, A graevenitzii is a component of the oropharyngeal flora and was isolated from the surfaces of failed dental implants. However, little is known about the clinical features and pathogenesis of this bacterium. Only a small number of cases have been published describing pulmonary infections due to A graevenitzii (3-5). Other usual sources of A graevenitzii isolates are from patients with osteomyelitis of the jaw, intra-abdominal lesion(s), and mouth and neck abscesses. To our knowledge, the present case is the first of pulmonary actinomycosis caused by A graevenitzii presenting as a single lung abscess, in the right apex, mimicking TB.

Pulmonary actinomycosis is a well-known cause of chronic pulmonary infection (1). The usual presentation is a slowly progressive pneumonia with fever, weight loss, cough, sputum and chest pain. Because clinical and radiological signs mimic malignancy and TB, it is often misdiagnosed and proper treatment is delayed. If the disease progresses to adjacent structures, life-threatening complications, such as massive hemoptysis or bronchoesophageal fistula, may occur. Important risk factors for thoracic actinomycosis include alcoholism, poor oral hygiene and underlying respiratory disease, all of which were absent in this patient.

Radiological aspects include a peripheral pulmonary nodule, mass or consolidation, all of which may or may not be cavitary or multifocal. In later stages, lung parenchyma may be destroyed and the infection may extend to the pleura or chest wall. Typical CT findings are reported as central areas of low attenuation within the consolidation in 62% to 75% of cases, and adjacent pleural thickening in 50% to 73% (6), which is consistent with the radiographic findings in the present case. Miliary presentations of the disease have also been reported.

Traditionally, diagnosis requires detection of sulfur granules by Gram-stain or histological examination. However, sulfur granules may occur in other infectious diseases such as nocardiosis and eumycetoma. Special stains, such as Gomori methenamine-silver, may be needed to show that the sulfur granules are composed of branching bacteria and not fungi, cocci or bacilli. Because of inadequate anaerobic culture, previous antibiotic therapy or overgrowth of concomitant organisms, direct bacterial confirmation by culture is difficult and achieved in <50% of cases (1). Culture of expectorated sputum or bronchoscopy aspirates are usually not successful, while fine-needle aspiration, tranbronchial biopsy and CT or ultrasound-guided biopsies lead to accurate diagnoses (1,6).

Because most Actinomycetales infections are polymicrobial in nature (7), a variety of other microorganisms are frequently found at infection sites in addition to Actinomyces species.

Regarding A graevenitzii, the pathogen was identified by quantitative culture of BALF (4,8), but most cases required an amplified 16S ribosomal DNA restriction analysis (2,3,5). In this case, diagnosis was obtained using quantitative culture of BALF. Nagaoka et al (4) argued that quantitative culturing of BALF is more reliable in differentiating respiratory tract pathogens from colonization related to pneumonia. They also showed that A graevenitzii had a faster growth rate (48 h to 96 h) than other Actinomyces species that can be cultured anaerobically for up to three weeks. The faster growth rate of A graevenitzii may account for a different clinical presentation than traditional Actinomyces species, including aggressive disease in previously healthy patients.

Penicillin G is considered to be the standard treatment for pulmonary actinomycosis (9). There are no guidelines regarding the duration of antibiotic treatment. In the past, high-dose intravenous penicillin was used for four to six weeks, followed by six to 12 months of oral penicillin A (amoxicillin). Recently, several investigators reported that shorter courses of treatment could be successful in pulmonary actinomycosis (7,9). However, treatments shorter than three months may lead to local complications or recurrence.

Some patients have been successfully treated with oral antibiotics only (amoxicillin) (7). In the present case, the outcome was favourable despite the high dose of oral amoxicillin for only six weeks.

To our knowledge, only two in vitro studies have reported Actinomyces species drug susceptibility (10,11). Recent reviews recommend that the first-line regimen consist of a beta-lactam with a beta-lactamase inhibitor (10,12). Because resistance of the contaminating bacteria is often the cause of treatment failure, a beta-lactamase inhibitor offers the advantage of coverage against penicillin-resistant aerobic and anaerobic copathogens.

For patients who do not respond to antibiotics, surgery is an option. Other indications for surgical treatment are exclusion of a malignancy, uncontrolled hemoptysis, drainage of an abscess or pleural empyema, decortication and the radical excision of sinus tracts (13).
The present case is uncommon because we report an atypical pulmonary abscess mimicking TB in a healthy patient with no comorbidities. More cases of pulmonary actinomycosis caused by *A. graevenitzii* and further information on this microorganism are needed to draw attention to this diagnosis when investigating pulmonary opacities. In cases in which actinomycosis is suspected, bacterial cultures of respiratory specimens should be performed. In cases in which cultures are negative, an amplified 16S ribosomal DNA restriction analysis is necessary.

**Post-test**

- What is the role of *A. graevenitzii* in the pathogenesis of pulmonary actinomycosis?

*A. graevenitzii* is a component of the oropharyngeal flora. Usual sources of *A. graevenitzii* isolates are failed dental implant surfaces, osteomyelitis of the jaw, intra-abdominal lesion, and mouth and neck abscesses. Only a small number of cases have been published describing pulmonary infections due to *A. graevenitzii* (multiple pulmonary abscesses, organizing pneumonia) in patients with and without comorbidities. There were also two cases of disseminated infection in immunosuppressed patients, suggesting that *A. graevenitzii* may also be an opportunistic agent.

- What are the different methods of laboratory diagnosis in pulmonary actinomycosis caused by *A. graevenitzii*?

Diagnosis requires detection of sulfur granules by Gram-stain or histological examination. Direct bacterial confirmation by culture is difficult and is achieved in fewer than 50% of cases. *A. graevenitzii* has a faster growth rate (48 h to 96 h) than other *Actinomyces* species. Generally, culture of fine-needle aspiration, transbronchial biopsy and CT or ultrasound-guided biopsies are more accurate than sputum and bronchoscopy culture for the diagnosis of actinomycosis. However, *A. graevenitzii* has been successfully identified using quantitative culture of BALF. When appropriate culture techniques are not available or there is a notion of previous antibiotic treatment, an amplified 16S ribosomal DNA restriction analysis can be very useful.

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