Multiple Lung Abscesses Caused by *Actinomyces graevenitzii* Mimicking Acute Pulmonary Coccidioidomycosis

Kentaro Nagaoka,a,b Koichi Izumikawa,a Yoshihiro Yamamoto,a Katsunori Yanagihara,a,b Kiyofumi Ohkusu,c and Shigeru Kohna

Department of Molecular Microbiology and Immunology,a and Department of Laboratory Medicine,b Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, and Department of Microbiology, Gifu University Graduate School of Medicine, Gifu, Japanc

*Actinomyces graevenitzii* is a newly recognized *Actinomyces* species that is seldom isolated from clinical specimens. A case of multiple pulmonary abscesses mimicking acute pulmonary coccidioidomycosis is described in this study, and the findings indicate that this organism is an opportunistic human pathogen.

CASE REPORT

A 38-year-old apparently healthy woman complained of fever and dry cough after visiting Los Angeles, CA. Her medical history did not reveal any specific illness, including acquired immune deficiency syndrome. She did not smoke or consume alcohol. During her 3-day stay, she visited the beach in California. On her way to the beach, she encountered a dust storm and inhaled a large amount of dust. Seven days after she returned to Japan (9 days after encountering the dust storm), she was admitted to a local hospital in Nagasaki owing to a progressive dry cough (clinical day 8). On admission, the vital signs of the patient were as follows: body temperature, 37.5°C; blood pressure, 99/64 mm Hg; pulse, 72 beats/min with a regular rhythm; SpO₂, 96% in a room air condition; and respiratory rate, 16 breaths/min. Cyanosis, cardiac murmur, and breath sounds were absent. Moreover, her liver, spleen and lymph nodes were not palpable. Her white blood cell count was 7.3 × 10⁹/ml, with a shift to the left (71% neutrophils), and her C-reactive protein value was 5 mg/dl (normal range, 0 to 0.3 mg/dl). The chest computed tomography (CT) images revealed multiple round lesions located on both lobes, with diameters of 0.5 to 1 cm (Fig. 1 and 2). The radiological findings strongly suggested metastatic tumors; hence, digestive tract endoscopy and positron emission tomography (PET) of the entire body were performed. No other lesions, except the lesions in the lungs, were performed. After 9 days of treatment (clinical day 35), her fever subsided, but the pulmonary lesions that were observed on radiological examination had not improved.

Primary culturing of bronchoalveolar lavage fluid (BALF) was performed with blood and chocolate agar plates. BALF (inoculum volume, 5 μl) was streaked onto the plate quantitatively and incubated at 37°C in 5% CO₂. Only molar-tooth-like colonies were observed in 3 days. Hemolysis around the colonies was not observed, and the quantitative culture yielded 1 × 10³ CFU/ml. The organism was a coryneform Gram-positive rod that did not produce catalase. On commercial biochemical testing (ID panel, Phoenix Automated Microbiology System; Becton, Dickinson Co., Ltd., Japan), the organism was initially identified as *Erysiploclthrix rhusiopathiae*, contrary to its colony characteristics. Upon repeated biochemical testing, the isolate was reidentified as *Arcanobacterium haemolyticum*. The microphotographs and colony characteristics of the organism isolated from the BALF are shown in Fig. 3. The MIC values of the tested antibiotics, including penicillin G, ampicillin, piperacillin, cefotaxime, cefitizoxime, ceftazidine, ceftriaxone, cefepime, imipenem, meropenem, erythromycin, and clarithromycin, were found to be less than 0.05 μg/ml. Only minocycline had an MIC value of 4 μg/ml. Results of the acid-fast staining and PCR testing of the patient’s BALF for *Mycobacterium tuberculosis*, *Mycobacterium avium*, and *Mycobacterium intracellulare* were negative.

Although a Gram-positive rod bacterium was isolated from the BALF cultures, the histological findings of the TBB specimen could reveal only nonspecific inflammation. Thus, there was a possibility of coinfection with other etiologic pathogens. The *Coccidioides* antibody was not detected on clinical day 32. However, owing to her unique travel history and radiological findings, we could not completely exclude the possibility of acute pulmonary coccidioidomycosis. Therefore, we performed an additional histological assessment and repetitive examinations for detection of
Coccidioides antibody to confirm the diagnosis. On clinical day 36, video-assisted thoracoscopic surgery (VATS) was performed to acquire lung tissue. During VATS, the nodule (30 mm) in the right lower lobe was resected and examined. On histological examination, lymphocyte infiltration, fibrous change, and several Masson bodies were found within the resected nodule, but no pathogen, including Coccidioides, was identified by pathological or microbiological examination. On clinical day 53, after confirming the result of VATS and obtaining negative results for the repetitive tests for serum antibody against Coccidioides, we replaced TAZ-PIPC and L-AMB with amoxicillin (AMPC) therapy at 2 g/day. After 2 months of administration, the pulmonary abscesses were no longer detected on radiological examination.

Because of the rarity of her clinical course, we performed molecular identification by PCR amplification and sequencing analysis of the 16S rRNA gene using DNA extracted from the isolates. The universal primers 8UA (5'-AGAGTTTGATCMTGGCTCA G-3') and 1485B (5'-ACGGGCGGTGTGTRC-3') were used, as described previously (9). We performed a sequencing analysis using a GenBank BLAST search and BiBi (http://pbil.univ-lyon1.fr/) phylogenetic tools. The sequence of the 16S rRNA gene showed 99.7% identity (1,403 bp over the entire 1,407-bp fragment) with that of the type strain Actinomyces graevenitzii (CCUG27294; GenBank accession no. AJ 540309). On the basis of this result, we identified the isolate as A. graevenitzii.

Actinomyces spp. are the most common commensal anaerobic bacterium in the human oral cavity, and 6 species of this genus are considered pathogenic in humans: A. israeli, A. naeslundii, A. odontolyticus, A. viscosus, A. meyeri, and A. gerencseriae (8, 13). Pulmonary actinomycosis is well known as a cause of chronic infection, and it constitutes 15% of the total burden of actinomycosis in humans (8). The clinical features usually include low-grade inflammation with indolent advancement, which is similar to the presentation of fungal infection or lung neoplasms (8). Several reports (7, 8, 15) found that 25% to 49% of cases of pulmonary actinomycosis were suspected to be lung malignancy upon hospital admission, and the mean duration of illness before a definitive diagnosis was 2 to 6 months. A diagnosis of pulmonary actinomycosis is often confirmed by histological findings, which reflect
chronic inflammation consisting of granulomatous change with sulfur granules (6). Bacterial confirmation of a clinicopathological diagnosis is usually obtained in <50% of cases owing to inadequate culturing techniques, previous antibiotic therapy, and bacterial overgrowth (1). Song et al. (15) found that positive culture results were obtained in only 3 of 40 cases of pulmonary actinomycosis. Thus, the diagnosis of conventional pulmonary actinomycosis requires a combination of several factors, including respiratory specimen culture, correlation with clinical and radiological features, histological findings, and response to antibiotic treatment.

In addition to these traditional actinomycotic forms, some coryneform anaerobic bacteria have also recently been assigned to the genus *Actinomyces* by the U.S. Centers for Disease Control and Prevention (4, 5). *A. graevenitzii* is a newly recognized *Actinomyces* sp. that was first isolated from 4 clinical human specimens in 1997 by Ramos et al. (11). It is a filamentous Gram-positive rod with no catalase production and is facultatively anaerobic with a distinct biochemical profile (11). Sarkonen et al. isolated *A. graevenitzii* from failed dental implant surfaces for their study on the distribution of *Actinomyces* spp. in 33 dental implant fixtures (12). Similar to other *Actinomyces* spp., *A. graevenitzii* is possibly a component of the oropharyngeal flora. Very little is known about the clinical features and pathogenesis of *A. graevenitzii* (14), and only 1 case report has described the disseminated infection of *A. graevenitzii*, which showed coinfection with *Mycobacterium tuberculosis* (16).

Our case presented different clinical features of conventional pulmonary actinomycosis, such as the rapid progression of lung lesions and the lack of specific histological features, including granulomatous change or presence of sulfur granules. Acute pulmonary coccidioidomycosis was first suspected because of the patient’s travel history to an area of coccidioidomycosis endemicity. The identification of *A. graevenitzii* using the molecular method described in this study was partially funded by a grant from the Global Centers of Excellence Program, Nagasaki University.

ACKNOWLEDGMENT

The identification of *A. graevenitzii* using the molecular method described in this study was partially funded by a grant from the Global Centers of Excellence Program, Nagasaki University.

REFERENCES