Hidden Diagnosis of Tuberculous Pleurisy Masked by Concomitant *Pseudomonas oryzihabitans* Bacteremia

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The clinical presentations of tuberculous pleurisy are usually nonspecific and have an insidious course, thus resulting in diagnostic challenges. *Pseudomonas oryzihabitans* is a nonfermenting, oxidase-negative, catalase-positive, Gram-negative bacillus that has rarely been encountered as a human pathogen. We present the case of a 30-year-old male patient who exhibited intermittent fever despite antibiotic treatment for *Pseudomonas oryzihabitans* bacteremia for 6 days. Tuberculous pleurisy was finally diagnosed by histopathologic and microbiologic studies. He recovered after a 2-week antibiotic course and 6-month antituberculosis treatment. *Key words: Pseudomonas oryzihabitans; bacteremia; tuberculous pleurisy.* [Respir Care 2012;57(2):298–301. © 2012 Daedalus Enterprises]

Introduction

Tuberculosis remains a major health problem worldwide. Extrapulmonary involvement is observed in less than 30% of all tuberculosis patients.[1] Tuberculous pleurisy has an insidious course and nonspecific presentation, thus resulting in difficulties in diagnosis and subsequent treatment delays. Polymerase chain reaction of *Mycobacterium tuberculosis* (TB-PCR) is a rapid method for diagnosing pleural tuberculosis.[2] However, if a patient is co-infected with other pathogens and the initial TB-PCR result is negative, diagnosis of pleural tuberculosis may be delayed. Here, we present the case of a patient with tuberculous pleurisy concomitant with *Pseudomonas oryzihabitans* bacteremia, who was successfully treated with antibiotics and antituberculosis treatment.

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Case Report

A previously healthy 30-year-old man had experienced right pleuritic chest pain for one week, 2 months prior to this admission. He visited an emergency department and underwent a chest radiography examination (Fig. 1) that revealed increased lung markings in the right lower lung zone. Other laboratory parameters were within normal limits. Acute bronchitis was diagnosed by the emergency physician. His symptom was relieved by nonsteroidal anti-inflammatory drug treatment. He had high fever, chills, and right chest pain 2 days before admission to our hospital.

On admission, his blood pressure was 112/77 mm Hg, pulse rate was 108 beats/min, respiration rate was 18 breaths/min, and body temperature was 38.6°C. A physical examination revealed decreased breathing sounds in the right lung field. Laboratory findings were as follows: white cell count 9.3×10^3 cells/mL, proportion of neutrophils 80.5%, proportion of lymphocytes 10.1%, hemoglobin 15.9 g/dL, platelets 273×10^3 cells/mL, and C-reactive protein 6.85 mg/dL.

Chest radiography disclosed a right-sided pleural effusion (Fig. 2), and diagnostic thoracentesis was performed. Pleural effusion samples were obtained, and cell counting, biochemistry, pH evaluation, Gram staining, bacterial culture, acid-fast staining, *M. tuberculosis* culture (conventional Lowenstein Jensen medium), and TB-PCR were performed. The findings indicated lymphocyte predominance and revealed a yellow, turbid exudate. Empyema was sus-
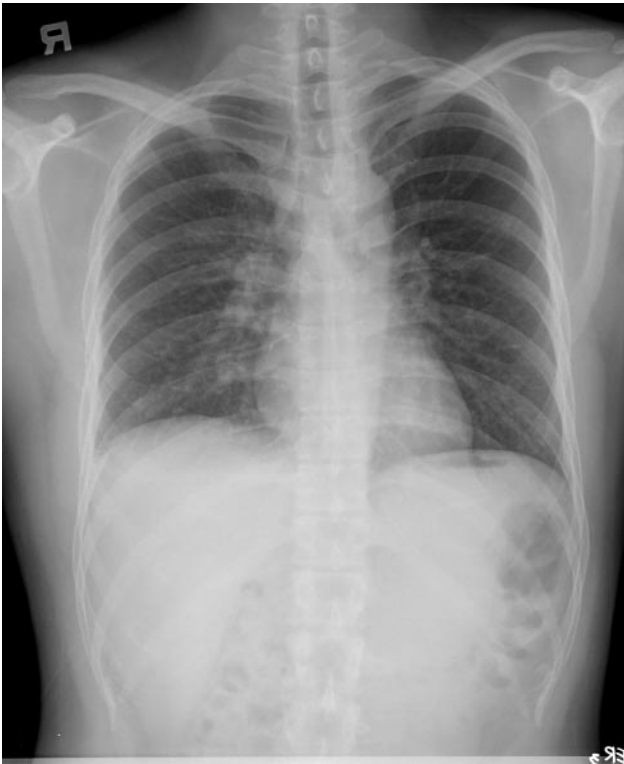
Fig. 1. Chest radiograph showing increased lung markings in the right lower lung zone (obtained 2 months before admission).
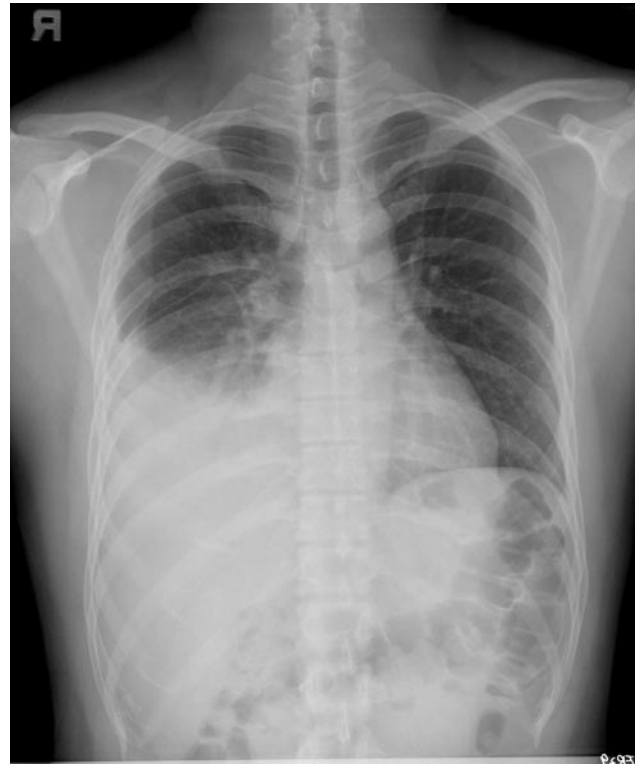

Fig. 2. Chest radiograph showing right-side pleural effusion (obtained on the day of admission).

pected because of the low pH value, and a chest tube was inserted. Ceftazidime (2 g) was administered intravenously every 8 hours. Two days later, a Gram-negative bacillus was detected in the blood culture and finally identified as *P. oryzihabitans* (susceptible to amikacin, gentamicin, ciprofloxacin, ceftriaxone, ceftazidime, and imipenem). The patient exhibited intermittent fever under antibiotic treatment for 2 days, but the sputum and pleural fluid findings for bacteria, including *M. tuberculosis* (acid-fast stain and PCR), were all negative. A diagnostic procedure of video-assisted thoracoscopy with pleural biopsy was performed on the third day because of high suspicion of tuberculous pleural effusion. Multiple small white nodules scattered over the lung surface and parietal pleura regions were noted. Biopsy samples were sent for histopathologic examination, bacterial culture, and tuberculosis study. The pathological findings were suggestive of chronic granulomatous inflammation of the pleural tissue, with multinucleated giant cell formation, and TB-PCR of pleural tissue was still negative. Antituberculosis agents were given on the seventh day, based on pathological findings. The chest tube was removed on the tenth day, and the patient was discharged on the thirteenth day.

The patient was followed up in the out-patient department. Because *P. oryzihabitans* infection most commonly

occurs in immunocompromised patients, we also examined the patient's immune status, including administration of a human immunodeficiency virus screen test and cell immune function tests, including tests of T lymphocyte subsets (CD3, CD4, CD8, and CD4/CD8 ratio). The human immunodeficiency virus screen test was negative, and the CD4/CD8 ratio was 0.64 (normal limit 1–2). Finally, 2 months after the patient was discharged, pleural effusion culture for *M. tuberculosis* was found to be positive. The patient recovered after a 2-week course of antibiotics and antituberculosis treatment (intensive phase: rifampin, pyrazinamide, isoniazid, and ethambutol; maintenance phase: rifampin, isoniazid, and ethambutol) for 6 months. Follow-up chest radiography indicated that pleural effusion was resolved, with mild pleural thickening (Fig. 3).

Discussion

P. oryzihabitans, previously known as *Flavimonas oryzihabitans*, *Chromobacterium typhiflavum*, and Centers for Disease Control and Prevention (CDC) group Ve-2, is a nonfermenting, oxidase-negative, catalase-positive, Gram-negative bacillus that has rarely been encountered as a human pathogen.[3] Although it had been isolated from various tissues in humans, *P. oryzihabitans* was not impli-

Fig. 3. Chest radiograph showing resolution of pleural effusion with mild pleural thickening (obtained 8 months after admission).

cated as a pathogenic organism until 1977, when the first case of infection was reported.[4] Since that time, *P. oryzihabitans* infections have been reported in association with bacteremia, wound infections, peritonitis, endophthalmitis, and meningitis.[5–9] *P. oryzihabitans* bacteremia mostly occurs in immunocompromised patients such as those receiving long-term steroid therapy,[10] those with liver cirrhosis[11] or malignancy,[12] and those who have undergone bone marrow transplantation.[13] The presence of foreign material, including indwelling intravascular catheters and artificial grafts, also plays a major role. Here, we report a unique case of bacteremia caused by *P. oryzihabitans* that occurred in a patient with tuberculous pleurisy.

Tuberculosis is the prototype of infections that require a cellular immune response for their control. Mycobacterial antigens have a unique ability to promote the expression of inhibitory cytokines, and it has been suggested that suppression of CD4 cell responses contributes to immunosuppression, deactivation of macrophage effector function, and disease progression in tuberculosis.[14] Hence, tuberculosis patients are susceptible to secondary infectious agents, particularly pathogens that require cell-mediated immunity for infection control. Co-infection with *M. tuberculosis* and cytomegalovirus,[15] severe acute respiratory syndrome-associated coronavirus,[16] *Chlamydia trachomatis*,[17] *Bartonella quintana*,[18] and cutaneous leishmaniasis[19] has been reported. However, no study has reported co-infection with *M. tuberculosis* and *P. oryzihabitans*. To the best of our knowledge, we present the first case of tuberculous pleurisy concomitant with *P. oryzihabitans* bacteremia in an adult.

Immunocompromised patients are predisposed to *P. oryzihabitans* infection. Qian et al[20] identified 11 cases of *F. oryzihabitans*-positive cultures from microbial cultures collected over a 4-year period. Among them, 8 patients had bacteremia, and the other 3 patients had pleurisy, soft tissue infection, and peritonitis, respectively. In 9 patients, peripheral blood showed abnormalities in T lymphocytes and natural killer cells, and their CD3, CD4, and CD4/CD8 ratios were lower than the normal value. Therefore, immune function abnormality was commonly observed in *P. oryzihabitans* infections. The CD4/CD8 ratio in our patient was also below the normal value, as observed in previous results. In this patient, the scenario for co-infection with *M. tuberculosis* and *P. oryzihabitans* is summarized as follows. The patient acquired *M. tuberculosis* infection before admission. *M. tuberculosis* infection resulted in cell-mediated immunity dysfunction, and his T lymphocyte CD4/CD8 ratio was lower than normal, facilitating infection by *P. oryzihabitans*.

A diagnosis of tuberculous pleurisy should be considered in any patient with an exudative pleural effusion. However, it can be difficult to establish the diagnosis using only conventional methods. Direct examination of pleural fluid using Ziehl-Neelsen staining has quite low sensitivity.[21] Although culture is more sensitive, it is time-consuming. PCR is a rapid method for diagnosing pleural tuberculosis and decreasing the time required to identify the organism in the clinical specimens. However, in some studies, the sensitivity of pleural effusion TB-PCR was only 50–70%.[22,23] So tuberculosis PCR of pleural biopsy sample was suggested in some situations. Its sensitivity could increase to 90%.[24]

PCR of pleural effusions and tissue for *M. tuberculosis* were both negative in this patient, thus delaying tuberculosis diagnosis and treatment. Potential explanations include the presence of a low number of tuberculous bacilli or the presence of an amplification inhibitor in the samples. Definite diagnosis was finally achieved by pathologic examination and culture of pleural fluid for *M. tuberculosis*.

Tuberculous pleurisy remains diagnostically challenging. This case indicates the necessity of testing for occult infection if the clinical response is insufficient during administration of appropriate antibiotic treatment for definite bacteremia. Tuberculous pleurisy should be considered even if the initial TB-PCR sample is negative when the patient has an exudative pleural effusion. Pleural biopsy for histopathologic examination is suggested, which will prevent delays in tuberculosis diagnosis and treatment.

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