CASE REPORT

EMPYEMA THORACIS DUE TO NOCARDIOSIS AND *MYCOBACTERIUM TUBERCULOSIS* MIXED INFECTIONS IN AN AIDS PATIENT

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Abstract. A 26-year-old Thai man presented with progressive dyspnea for four months and right pleuritic chest pain two days before admission. The chest radiograph showed massive right pleural effusion. Thoracentesis was done, and the culture grew *Nocardia* spp as well as positive strain for acid-fast bacilli. An anti-HIV test was reactive, with a CD4 count of 12 cells/mm^3. The patient was treated with inter-costal tube drainage (ICD) inserted for empyema thoracis. The antimicrobials used trimethoprim-sulfamethoxazole and anti-TB drugs CAT-1 orally. One month later, anti-retroviral therapy with HAART was initiated. At follow-up after 6 months, he was healthy appearing, with a nearly normal chest radiograph.

INTRODUCTION

Nocardia asteroides is an aerobic gram-positive filamentous bacterium that has a worldwide distribution and can be cultured from the soil (Menendez *et al*, 1997). The diseases caused by this organism mainly manifest themselves by hematogenous dissemination with occasional abscesses or sinus tract formation. Nocardiosis has a greater propensity to occur in patients with AIDS and other immunosuppressed patients than does actinomycosis. Because most patients who develop nocardiosis are immunosuppressed (Aghasadeghi, 2005), the incidence of nocardiosis is increasing.

Tuberculous empyema is an uncommon disease characterized by purulent pleural fluid containing mycobacterial organisms (Sahn and Iseman, 1999). Tuberculous empyema usually occurs when an abscess ruptures into the pleural space. This catastrophic illness is often associated with bronchopleural and flank pus.

There are no case series reports on mixed empyema infections with nocardiosis and tuberculosis; most patients who develop nocardiosis empyema are immunosuppressed, especially many due to AIDS.

CASE REPORT

A 26-year-old Thai man was admitted to a provincial hospital in April 2008 with progressive dyspnea for 4 months. Four

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months before admission he experienced high-grade fever at night, severe malaise, loss of appetite and weight loss of about 6 kg in 3 months. He gave a history of having unsafe sex. Ten days before this admission, he was seen by a physician at a private hospital and had a chest x-ray that showed a right pleural effusion. He was prescribed medication for pulmonary tuberculosis (300 mg isoniazid, 450 mg rifampicin, 1,000 mg ethambutol, 1,250 mg pyrazinamide, and 50 mg vitamin B6). Sputum for AFB strain was negative for single test, an anti HIV test was positive with a CD4 count of 12 cells/mm^3. Two days prior to admission, he developed a progressive dry cough and right pleuritic chest pain. He visited the doctor who had prescribed his previous treatment and who then referred him to the provincial hospital for further management.

On admission at the provincial hospital, he had a temperature of 38.4ºC, a pulse rate of 105/minute, a blood pressure of 107/82 mmHg, a respiratory rate of 26/minute. He had flaring of alar-nasi, mild tachypnea, and markedly pale conjunctivae. The findings on respiratory examination showed no clubbing of the fingers and the trachea was midline. There was decreased expansion of the right chest, decreased breath sounds in right thoracic cavity, decreased vocal resonance, and tactile fremitus. Laboratory investigation revealed a hematocrit of 23.8%, a white blood cell count of 15.07 x 10^9/l, predominate neutrophils, and a platelet count of 369x10^9/l. A chest x-ray showed a massive right pleural effusion (Fig 1). Thoracentesis and the pleural fluid was a clear straw color; 800 ml was removed. Evaluation of the pleural fluid showed a total cell count of 290 cell/ml, a white blood cell count of 210 cell/ml; the differential showed 80% neutrophils and 20% mononuclear cells. The protein level was 4.8 g/dl, the sugar was 86 mg/dl, the LDH was 1,510 μ/l, the adenosine deaminase (ADA) was 42 IU/l, and a Gram stain and AFB stain showed no organisms. Sputum AFB smear for 3 days was negative.

The anti-TB drugs were continued and combined with ceftriaxone 1 g IV bid and trimethoprim-sulfamethoxazole. He was treated with a blood transfusion to correct his anemia. A chest x-ray five days later showed the pleural effusion was increasing. The thoracentesis was repeated and flank pus was obtained. An inter-costal drainage tube (ICD) was inserted. A pleural fluid culture for bacteria from the first thoracentesis was positive for *Nocardia* spp. Pleural fluid from the second thoracentesis on Gram' stain and modified AFB stain showed a gram-positive branching filament, and on AFB stain showed acid-fast bacilli. He was given the diagnosis of tuberculous and nocardia empyema. After 5 days of treatment, he improved clinically as seen by a resolution of his fever and a reduction in pus from his ICD tube (Fig 2). The patient was discharged from the hospital 7 days later. A chest x-ray one month later showed minimal blunting of the right costophrenic angle (Fig 3). He was started on HAART. On follow-up at 6 months, he appeared healthy. His chest radiograph was nearly normal (Fig 4), and his CD4 count had increased to 253 cells/mm^3.

This case report (limited to reporting symptoms, conditions, treatments, and outcomes), does not require formal institutional review board approval. However, the authors wish to affirm compliance with the principles of the Declaration of Helsinki, especially with respect to patient confidentiality.

DISCUSSION

Nocardiosis and tuberculosis are uncommonly found as a mixed infection. Nocardiosis should be suspected in patients with sub-

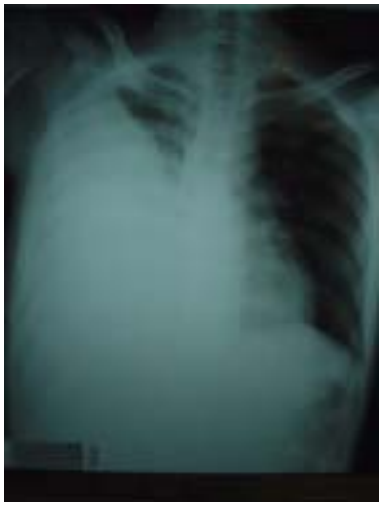

Fig 1-Chest x-ray on admission showing right pleural effusion.

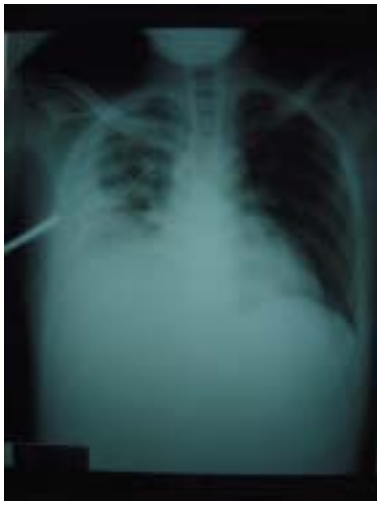

Fig 2-After intercostal drainage tube (ICD) insertion for treatment of empyema thoracis.

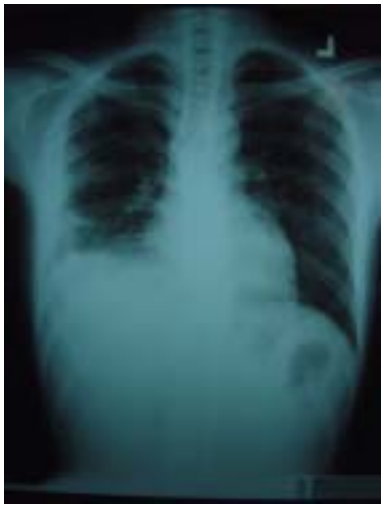

Fig 3-Chest x-ray after one month of treatment.

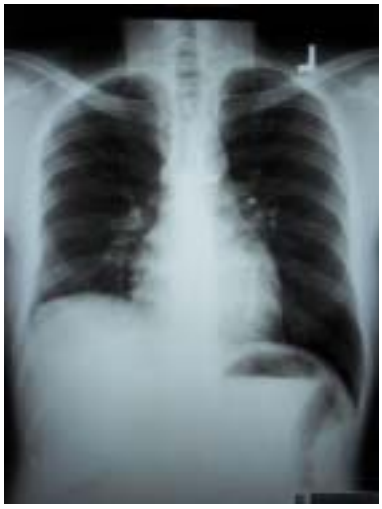

Fig 4-Chest x-ray after six month of treatment.

acute or chronic pulmonary infiltrates and pleural effusion, particularly if the patient is immunosuppressed. Support for the diagnosis is obtained from a Gram's stain of the sputum, bronchoscopic washings or pleural fluid revealing the typical gram-positive branching filamentous bacteria, or from an acid-fast stain revealing variably acid-fast filamentous bacteria (Sorrell *et al*, 2000). The definitive diagnosis is made by the demonstration of *N. asteroides* on aerobic bacterial culture from the sputum, bronchoscopic washings, or pleural fluid. Because *N. asteroides* is a slow-growing organism, when nocardiosis is suspected the bacterial cultures must be maintained for at least 2 weeks. Not all patients

have *N. asteroides* in the sputum. The lung is involved in about 75% of patients with nocardiosis (Uttamchandani *et al*, 1994), and as many as 50% of patients with pulmonary nocardiosis have a pleural effusion (Kramer and Uttamchandani, 1990). Patients with pleural effusions secondary to nocardiosis usually have associated parenchymal infiltrates. The pleural fluid, in patients with nocardiosis, is an exudate, which can range from serous fluid to flank pus. Pleural fluid cultures may or may not be positive for *N. asteroides*.

In a series of 20 patients with positive sputum cultures for *N. asteroides*, nine of the patients did not have radiographic abnormalities (Frazier *et al*, 1975). Chest radiographs of patients with pulmonary nocardiosis may demonstrate fluffy infiltrates, irregular densities, pleural empyema, single or scattered regular or irregular nodules, or masses which may have cavitates, single or multiple abscesses and interstitial, reticulonodular, alveolar or rarely miliary infiltrates (Kim *et al*, 1992; Lerner, 1996).

Nocardia species are ubiquitous environmental saprophytes, living in soil, organic matter, or water (Menendez *et al*, 1997). Animal-to-human, human-to-human, and vertical transmission have not been reported (Lerner, 1996; Bennett *et al*, 2007). They cause opportunistic infections among immunocompromised hosts, especially in patients with HIV infection, but may be diagnosed by modified AFB stain or by culture. It grows mostly on nonselective media used routinely for cultures of bacteria, fungi, and mycobacteria (Tantracheewathorn *et al*, 2004).

Tuberculosis is caused by bacteria belonging to the *Mycobacterium tuberculosis* complex. The disease usually affects the lung, although in up to one-third of cases other organs are involved. Mycobacteria belong to the family Mycobacteriaceae and the order Actinomycetales. Of the pathogenic species belonging to the *Mycobacterium tuberculosis* complex, the most frequent cause of human disease is *M. tuberculosis. M. tuberculosis* is a rod-shaped, non-spore-forming, thin aerobic bacterium, measuring about 0.5 mm by 3 mm. Mycobacteria, including *M. tuberculosis*, do not stain readily and are often neutral on Gram's staining (Kasper *et al*, 2004). The interaction of *M. tuberculosis* with the human host begins when droplet nuclei containing microorganism from infectious patients are inhaled. Radiographically, there may be an obvious pleural effusion, but frequently the chest radiograph shows only pleural thickening. A chest CT scan usually demonstrates a thick, calcific pleural rind and rib thickening surrounding loculated pleural fluid. Tuberculous empyema usually has a subacute or chronic illness characterized by fatigue, low-grade fever, and weight loss. Radiographically, there may be an obvious pleural effusion. The diagnosis is established with a diagnostic thoracentesis, which yields thick pus, for which an AFB smear is usually positive (Light, 2001).

This patient had prolonged fever, respiratory symptoms, weight loss for 4 months, and an underlying HIV infection with a CD4 count of 12 cells/mm^3. He was presumed to have contracted infection via inhalation. *Nocardia* grew on blood agar, which is a commonly used bacterial medium in the laboratory. The pleural fluid on AFB stain was positive. The hospital laboratory had a limitation of not being able to culture *M. tuberculosis* from the pleural fluid, due to an overgrowth with *Nocardia* spp on the medium culture.

Sulfonamides have been the mainstay of therapy for nocardiosis since the 1940s; trimethoprim-sulfamethoxazole is currently preferred in a dose of 15 mg/kg/day of trimethoprim and 75 mg/kg/day of sulfamethoxazole, either parenterally or orally. Treatment of pulmonary nocardiosis should be

continued for 6 to 12 months. Central nervous system disease requires treatment for 1 year, unless all apparent disease has been excised, in which case 6 months is sufficient. For immunocompromised patients with nocardiosis, therapy should be continued for 12 months (Tunkel *et al*, 1991). In some patients, including a few with advanced AIDS, much longer treatment would be necessary. Patients should be carefully followed during therapy and for at least 6 months after therapy is stopped for signs of relapse. With prompt diagnosis and appropriate treatment, more than 95% of patients are cured. Tuberculous empyema should be treated following the standard guidelines of WHO for short course therapy for 6 months, which has shown cure rates of about 98 % (Kochi, 1991; WHO, 2008). Anti-retroviral treatment should have been started earlier in this patient due to the CD4 count was too low to prevent infections.

REFERENCES

Aghasadeghi K. Nocardiosis: a case report [Webpage]. *Shiraz E-Med J* 2005; 6: np. [Cited 2005 Jan 5]. Available from: URL: http://semj.sums.ac.ir/vol6/jan2005/nocardiosis.htm

Bennett NJ, Domachowske J, Johann-Liang R. Nocardiosis [Webpage]. *MedeMed* 2007. [Cited 2007 Dec 7]. Available from: URL: http://emedicine.medscape.com/article/966919-overview

Frazier AR, Rosenow EC 3rd, Roberts GD. Nocardiosis : a review of 25 cases occurring during 24 months. *Mayo Clin Proc* 1975; 50: 657-63.

Kasper DL, Braunwald E, Hauser S, Longo D, Jameson JL, Fauci AS, eds. Harrison's principles of internal medicine. 16th ed. New York: McGraw-Hill, 2004: 934-58.

Kim OH, Yang HR, Bahk YW. Pulmonary nocardiosis manifested as miliary nodules in a neonate: a case report. *Pediatr Radiol* 1992; 22: 229-30.

Kochi A. The global tuberculosis situation and the new control strategy by WHO. *Tuberculosis* 1991; 72: 1-6.

Kramer MR, Uttamchandani RB. The radiographic appearance of pulmonary nocardiosis associated with AIDS. *Chest* 1990; 98: 382-5.

Lerner PI. Nocardiosis. *Clin Infect Dis* 1996; 22: 891-905.

Menendez R, Cordero P, Santos M. Pulmonary infection with *Nocardia* species: a report of 10 cases and review. *Eur Respire J* 1997; 10: 1542-6.

Light RM. Tuberculous pleural effusions. In: Pleural diseases. 4th ed. Philadelphia: Lippincott Williams Wilkins, 2001: 182-95.

Sahn SA, Iseman MD. Tuberculous empyema. *Semin Respir Infect* 1999; 14: 82-7.

Sorrell TC, Iredell JR, Mitchell DH. *Nocardia* species. In: Mandell GL, Bennett JE, Dolin, R, eds. Principles and practices of infectious diseases. 5th ed. Philadelphia: Churchill Livingstone, 2000.

Tantracheewathorn T, Lolekha S, Tantracheewathorn S. Nocardis pneumonia with empyema thoracis in a healthy neonate: a case report. *J Med Assoc Thai* 2004; 87: 438-41.

Tunkel A, Crane J, Hayden F. Pulmonary nocardiosis in AIDS. *Chest* 1991; 100: 295-6.

Uttamchandani RB, Daikos GL, Reyes RR, *et al*. Nocardiosis in 30 patients with advanced human immunodeficiency virus infection : Clinical features and outcome. *Clin Infect Dis* 1994; 18: 348-53.

WHO. Implementing the Stop TB Strategy: a handbook for national tuberculosis control programmes *WHO/HTM/TB/2008.401*. 2008.