A Non-HIV-infected Man with Multiple Infections: Mycobacterium abscessus Lymphadenitis, Pulmonary Cryptococcosis and Tuberculous Osteomyelitis

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ABSTRACT

The authors present a case of nontuberculous mycobacterial infection, pulmonary cryptococcosis, tuberculous osteomyelitis and acute generalized exanthematous pustulosis. The patient was a 34-year-old man who had a history of chronic cough with bilateral neck mass for 4 months and developed left arm pain during hospitalization. He was diagnosed as tuberculous meningitis 7 months earlier and had enlarged bilateral cervical lymph nodes during treatment for tuberculosis. Pathologic examination of the excised cervical lymph node revealed caseous granulomatous inflammation, but his clinical was not improved after antimycobacterial treatment. The patient underwent bronchoscopy, cervical lymph node biopsy and bone biopsy. The cultures of cervical lymph node and sputum revealed Mycobacterium abscessus, the culture of bronchial fluid revealed Cryptococcus neoformans and the bone biopsy culture revealed Mycobacterium tuberculosis. After antimicrobial treatments, the patient showed a significant clinical improvement. In taking care of patients with disseminated NTM infection, multiple opportunistic infections need to be considered if clinical is not improved. (J Infect Dis Antimicrob Agents 2010;27:139-45.)

Note: This case had been presented and discussed in the Interhospital Case Conference on Infectious Diseases (ICCID), 6 May 2010, Bangkok, Thailand.

INTRODUCTION

Nontuberculous mycobacteria (NTM) are important causes of morbidity and mortality, often in the form of progressive lung disease.1 NTM are environmental organisms found in soil and water throughout the world.2-3 They are considered opportunistic pathogens, and several species are associated with human diseases such as pulmonary, skin/
soft tissue, lymphatic, or disseminated infection. These organisms have since been implicated in a large and increasing number of infections in both immunocompetent and immunocompromised hosts.

We originally described an unusual clinical presentation of 16 patients from northeastern Thailand infected with rapidly growing mycobacteria (RGM), primarily *Mycobacterium abscessus*. All of the patients presented with bilateral cervical adenopathy, and most patients had evidence of disseminated mycobacterial infection. These patients were non-HIV-infected; none had known underlying disease associated with immunosuppression. However, most of them had experienced previous or concurrent episode of opportunistic infections and reactive skin diseases. We later reported 129 cases of disseminated NTM infection, both RGM and slowly growing mycobacteria (SGM), with the same clinical entity. Some patients had reactive skin diseases such as Sweet’s syndrome, acute generalized exanthematous pustulosis (AGEP) and pustular psoriasis. Some patients are also infected with other intracellular opportunistic infections such as salmonellosis, cryptococcosis, penicilliosis and histoplasmosis. The cases with opportunistic cryptococcosis reported in the previous study presented with meningitis, osteomyelitis, septic arthritis or cellulites; none had pulmonary involvement.

We herein report a case with multiple infections: *M. abscessus* lymphadenitis, pulmonary cryptococcosis and tuberculous osteomyelitis. The patient also had reactive skin disease with AGEP.

**CASE REPORT**

A 34-year-old male farmer from Kalasin Province, Thailand, was referred to Srinagarind Hospital with treatment unresponsive pneumonitis of left lung. His ailment began 7 months prior to this admission when he was diagnosed with tuberculous meningitis based on cerebrospinal fluid examination findings. He had received antimycobacterial agents including isoniazid, rifampicin, pyrazinamide and ethambutol, and adjunctive corticosteroid therapy. However, he developed bilateral cervical lymphadenopathy during the treatment for tuberculosis. Pathologic examination of the excised cervical lymph node revealed caseous granulomatous inflammation with negative staining for acid-fast bacilli. Diagnosis of NTM infection was considered, the antimycobacterial treatment was changed to isoniazid, ethambutol, ofloxacin, and clarithromycin. However, lymphadenopathy persisted. In addition, he had developed chronic cough and left chest pain 4 months prior to admission. Left lower lobe pneumonia was demonstrated on the chest radiograph and computed tomography. All 3 specimens of sputum were negative for acid-fast bacilli. He had received ceftazidime for 2 weeks without improvement.

On admission at Srinagarind Hospital, the patient had full consciousness and mild distress. His vital signs were as follows: body temperature 37.0°C, blood pressure 125/66 mmHg, pulse rate 64/minute, and respiratory rate 22/minute. Multiple lymph nodes (5-10 mm in diameter) were palpated on both sides of the neck and the trachea was in midline. The physical examination of chest revealed decreased breath sounds, decreased vocal resonance, dullness on percussion, and fine crepitation at left lower lung field. Otherwise were unremarkable.

The initial hemoglobin concentration was 13.9 g/dL, and the white blood cell count was 22.69 x 10\(^9\)/L comprising of 76.8 percent neutrophils, 19.7 percent lymphocytes and 2.6 percent monocytes. The platelet count was 326,000 cells/mm\(^3\). Urinary examination showed trace albuminuria. The renal function and electrolytes were normal. The liver function test revealed mild elevation of alkaline phosphatase (210 U/L). A chest radiograph showed lobar pneumonia.
at left lower lung (Figure 1).

The investigations including anti-HIV antibody, anti-HCV antibody and serum cryptococcal antigen were negative whereas hepatitis B surface antigen was positive. Excisional biopsy of cervical lymph node was done for pathological examination and microbiological culture. The imprints of the lymph node revealed no organism. Sputum examinations were negative with acid-fast stain, Gram stain, and Wright stain.

Co-infection with other opportunistic infections especially fungal infections were suspected, so the patient had undergone bronchoscopy. Purulent discharge at left lingular segmental bronchus was found and the bronchial fluid examination revealed encapsulated round shaped yeast-like organism (Figure 2).

The cultures of both cervical lymph node and sputum grew *M. abscessus*. The bronchial fluid culture was positive for *C. neoformans*. The patient had received intravenous amphotericin B deoxycholate at 0.7 mg per kg per day for 14 days followed by fluconazole 400 mg/day. He also received imipenem 2 g per day, for 14 days along with clarithromycin and ofloxacin.

During the hospitalization, he developed erythematous plaque with pustular skin lesions over the extremities. Diagnosis of AGEP was suspected, so he received topical steroid therapy with clinical improvement. In addition, he had developed left arm pain. Plain film of the left arm demonstrated osteolytic lesion and periosteal reaction on the humeral shaft. Bone scan showed multi-foci of heterogeneous increased uptake at long bones and thoracolumbar spines suggested osteomyelitis, so the patient underwent bone biopsy of the left humeral shaft.

After treatment, the patient showed a significant clinical improvement and the last chest radiograph was presented in Figure 3. He was discharged from the
Figure 2. Bronchial fluid examination showed encapsulated round shaped yeast-like organism.

Figure 3. Chest radiograph on the 5th week after treatment showed a significant improvement.
hospital with take-home medications including fluconazole 400 mg per day, clarithromycin 1 g per day, and ofloxacin 400 mg per day for cryptococcosis and NTM infection. However, he experienced pathological fracture of left humerus 2 months after discharged home. On the follow-up date, the humeral bone biopsy culture grew *Mycobacterium tuberculosis* which was susceptible to isoniazid, rifampicin, ethambutol, streptomycin and ofloxacin. He was treated by closed reduction and slab application and the antimycobacterial treatment was changed to isoniazid, rifampicin, pyrazinamide, ethambutol, ofloxacin, and azithromycin.

**DISCUSSION**

In the present report, the patient demonstrated a typical presentation of a new clinical entity of unusual infection of NTM with other opportunistic infections. He was originally treated as tuberculous meningitis and lymphadenitis based on clinical, cerebrospinal fluid examination, and pathological findings of excised node. Then he was suspected of having NTM lymphadenitis by a primary physician when the lymphadenopathy persisted, not responded to antituberculous treatment. The empiric treatments for NTM, both RGM and SGM, were prescribed. Finally the primary physician referred him to our hospital after treated him for possible pulmonary melioidosis without clinical improvement. We made the definite diagnosis of pulmonary cryptococcosis, *M. abscessus* lymphadenitis and AGEP during admission. We suspected that his multiple bone lesions were caused by *M. abscessus* or *C. neoformans* which he had already been diagnosed. The mainstream treatments were focus on these organisms while tuberculosis was neglected. The tuberculosis treatment was discontinued after confirmation of NTM infection. This led to worsening symptoms of bone pain and pathological fracture later in this patient.

Besides the inadequate treatment, another possible reason may be the patient’s cell-mediated immune dysfunction.

Similar to our previous reports, this patient had multiple infections. It is remarkable that the patient was infected with multiple intracellular pathogens. These findings strongly suggest for cell-mediated immune dysfunction. Several recent reports demonstrated that anti-IFN-γ autoantibodies had been associated with disseminated NTM and other infections in 14 cases of non-HIV-infected patients. Surprisingly, 11 of 14 cases were Asian descents. We hypothesize that the patient had the same antibody defects. The mechanism underlying the immune defect in this patient is under investigation.

In the report of disseminated NTM from Thailand, 59 from 129 cases had 81 episodes of coinfection with other opportunistic infections (e.g. salmonellosis, 32 cases; cryptococcosis, 8 cases; penicilliosis, 8 cases; histoplasmosis, 5 cases). Among 8 cases co-infected with *C. neoformans*, there was no pulmonary involvement.

Pulmonary infection with *C. neoformans* is second only to meningoencephalitis. Despite there is evidence that *C. neoformans* virtually always infects the body through the respiratory tract, pulmonary disease is asymptomatic in the majority of cases. The varieties of clinical and radiologic manifestations related to this infection are established by the immunological status of the host. In the immunocompetent host, pulmonary cryptococcosis is usually asymptomatic, incidental findings in radiographic. In contrast, immunocompromised patients commonly have pulmonary involvement as part of disseminated disease and may occasionally have major respiratory symptoms that need further investigation.
M. abscessus causes a wide range of clinical diseases. Soft tissue infection by M. abscessus is typically caused by trauma with infected material, nonsterile surgical procedures, injections, implantations of foreign bodies, or in connection with tympanic tubes insertion. This mycobacterium is furthermore the infectious agent in over 80 percent of RGM chronic respiratory disease isolates. Such pulmonary disease is especially common in patients with cystic fibrosis. Various types of systemic immunosuppression may also predispose to disseminated M. abscessus infections; thus pulmonary disease and disseminated infection are generally linked with known predisposing host factors, while post-surgical or injection-associated infections or outbreaks are not.

We report a case of rapidly growing mycobacterial lymphadenitis. The infection should be considered when patients have concomitant reactive skin disease. The risk of coinfection with other opportunistic pathogens should also be recognized. To our knowledge, this is the first case report of pulmonary cryptococcosis in a non-HIV-infected patient coinfected with RGM and M. tuberculosis from Srinagarind Hospital.

References


