

Pulmonary and Vertebral *Mycobacterium avium* Disease in a HIV-negative 71-year-old Man A Case Report

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SUMMARY

Nontuberculous mycobacteria (NTM) caused pulmonary disease is on increase worldwide, especially in countries with decreasing time trend of tuberculosis incidence. NTM skeletal affection is rare. *Mycobacterium avium* related disease, with still unclear clinical and radiologic features, is in current focus of both clinicians and researchers.

An exhausted severely ill 71-year-old man was admitted on emergency due to cough, dyspnea and lumbar back pain to be diagnosed with terminal phase *M. avium* disease. Three sputum smears were positive for acid fast bacilli and *M. avium* was identified with hybridization reaction by means of *GenoType*[®] *MTBC* (*Hain*). Apart from pulmonary disease, com-

pressive fractures of the 12th thoracic and 1-4th lumbar vertebrae were detected. We found age, chronic alcoholism, previous professional exposure, tobacco smoking, chronic obstructive pulmonary disease and previous tuberculosis as risk factors for NTM disease in the HIV-negative patient. Despite combined antibiotic treatment, disease had lethal outcome. This case report might contribute to clinicians' awareness and improved knowledge on this sort of pathology, and lead to earlier diagnosis with possibly better disease outcome.

Keywords: *Mycobacterium avium*, pulmonary infection, vertebral infection.

INTRODUCTION

Nontuberculous mycobacteria (NTM) are increasingly recognized as important pathogens in subjects with and without immunodeficiency [1]. Although the number of case reports which document the spectrum of NTM related disease in otherwise healthy individuals is on increase, clinical and radiographic features of *M. avium complex* (MAC) disease are not clear enough, including their extrapulmonary manifestations [2, 3].

Risk factors for pulmonary MAC disease in immunocompetent individuals include cigarette smoking with associated chronic obstructive pulmonary disease (COPD), bronchiectasis, prior tuberculosis or other mycobacteriosis, alcoholism, pulmonary alveolar proteinosis and professional exposure such as those in coal mining and farming [3-5]. Especially use of inhaled corticosteroids highly increase risk of NTM pulmonary disease [3]. One third of the patients reported alcohol abuse and 38% smoked heavily [5]. Discovery that MAC strains can be recovered from cigarettes, suggests that cigarettes may be a source of the bacteria and not only risk factor related to tobacco smoke consequent immune suppression [6-8]. We aimed to share details of

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M. avium pulmonary and vertebral disease as an emerging pathology, diagnosed only in terminal phase of the illness.

■ CASE REPORT

A 71-year-old man, retired worker in metal industry, former smoker (43 pack/years until seven years ago), was admitted on emergency for dyspnea, cough, lumbar back pain, and fatigue. History taking revealed that the subject also suffered from chronic alcoholism and COPD. At the age of 48 years, he was diagnosed pulmonary tuberculosis and successfully treated following standardized anti-tuberculosis drug regimen. Both his father and uncle died from pulmonary tuberculosis. On admission, he was conscious, asthenic, tachypneic (25/min), with signs of mild cyanosis and cardiac failure, without peripheral lymphadenopathy.

Breath sounds were changed bilaterally. Heart rate: 130/min; arterial blood pressure: 110/70 mmHg; body mass index: 20.52. Peripheral blood laboratory findings showed erythrocyte sedimentation rate: 90/hour, WBC: $13.8 \times 10^9/L$, γ -GT: 139 U/L (normal <55), direct bilirubin 6.7 $\mu\text{mol/L}$ (normal <3.4), s-albumin: 32g/L (normal 34-55) and the rest was within normal range. Arterial blood gas analysis revealed partial respiratory insufficiency (PaO₂: 7.5kPa, SAT O₂: 93%). Standard chest x-ray on admission is shown at Figure 1a and details of computed tomography (CT) findings are presented at the Figures 1c and 1d. On vertebral radiography (Figure 1b), signs of compressive fracture of the 12th thoracic and 1-4th lumbar vertebrae were found. Three sputum smears were positive for acid fast bacilli (AFB) and *M. avium* was identified with hybridization reaction by means of *GenoType[®] MTBC (Hain)*. Therapy with clarithromycin, rifampicin and eth-

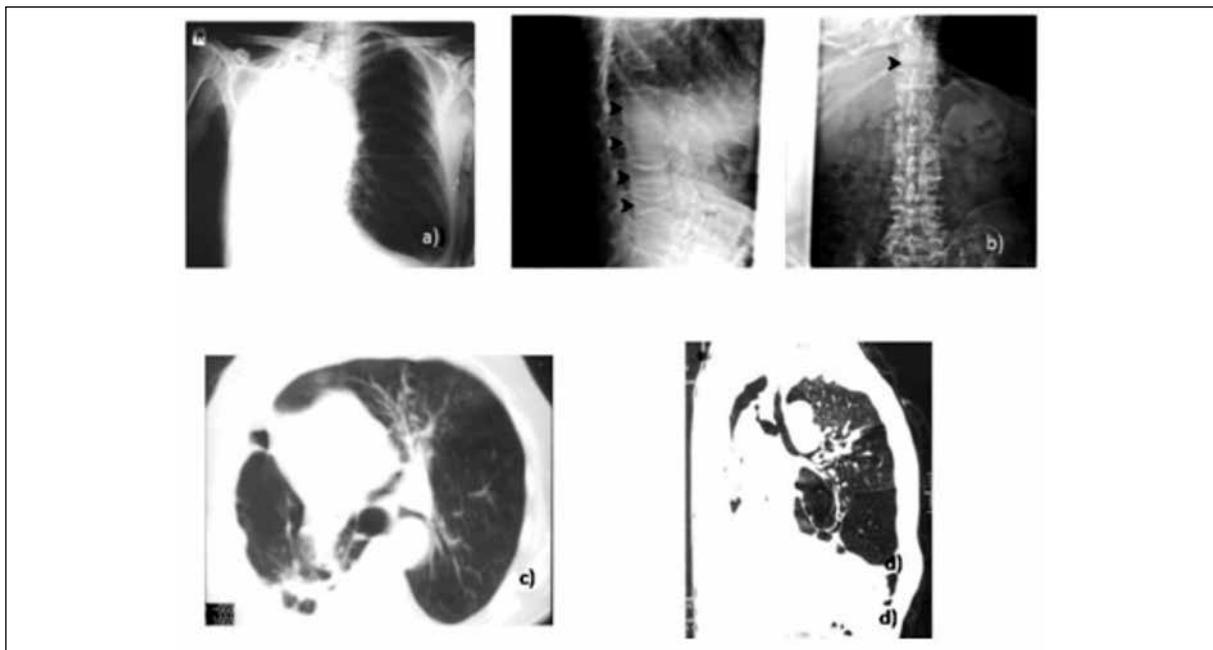


Figure 1 a-d - Radiographic findings in patient with *M. avium* disease (a-d).

a) Standard chest x-ray on admission: complete atelectasis/fibrothorax on the right side and signs of hyperinflation of the left lung; b) Radiograph of the vertebrae, standard and profile projection: signs of compressive fracture of the 12th thoracic and 1-4th lumbar vertebrae; c) Chest computed tomography (CT), axial view; d) Chest computed tomography (CT), sagittal view: widening of the pleura, especially its paracostal basal parts with small pleural effusion on the right side (c), compensatory hyperinflation with centro-lobular emphysema, and subpleural paramediastinal bullous formations up to 50 mm in diameter (d). Magistral airways are wider with tubular bronchiectasis. There is no pleural exudation or infiltration on the left side, but numerous basal adhesions are seen. Small homogenous paratracheal lymph nodes on the right side are up to 15 mm in diameter.

ambutol started but general condition and respiratory failure continually worsened to the lethal outcome, which happened two weeks later.

■ DISCUSSION

We presented a case of an advanced NTM pulmonary disease in HIV-negative patient caused by *M. avium* detected in terminal phase, associated with vertebral destruction and lethal outcome. Lethal outcome and disseminated *M. avium* disease has also been reported in an immune deficient 10-year-old boy with idiopathic CD4+ lymphocytopenia and juvenile laryngeal papillomatosis caused by human papillomavirus infection [9].

NTM bone infections in HIV-negative patients are rare [10, 11]. Japanese authors recently reported on three such cases detected over 14-year period at a tertiary level institution [12]. In two of them, a 66- and a 71-year-old men, *M. avium* was the cause. In two of the cases, apart from vertebrae, pubic, pelvic bone, sternum, ribs and scapula have been affected. The group also identified at least one precondition that led to infection in the patients - idiopathic CD4-positive lymphocytopenia, pneumosilicosis and/or anti-interferon- γ autoantibody syndrome.

It is evidence based that chronic respiratory disease, including COPD, is a strong risk factor for NTM pulmonary disease in adults [3]. Risk factors for pulmonary *M. avium* complex disease in HIV-negative individuals are many as mentioned before [5, 7]. Our presented HIV-negative patient was an elderly, former cigarette smoker with COPD and history of pulmonary tuberculosis and chronic alcoholism. Cigarettes and previous exposure at the working place of metal industry environment could be possible sources of NTM colonization with later infection/disease [3-6].

Changes in epidemiology with increased incidence and prevalence of NTM infections have led to studies and development of methods for improved recovery, rapid detection and identification of causative agents. It is extremely important for both diagnostics and treatment to discriminate tuberculous and nontuberculous mycobacteria. Nowadays, time-consuming biochemical analyses are replaced by fast and exact molecular genetic diagnostics. In our presented case, *M. avium* was identified by one of test systems for reliable

differentiation of mycobacteria of *M. tuberculosis* complex from NTM at the molecular level.

In 2007, the American Thoracic Society (ATS) and Infectious Disease Society of America (IDSA) published new diagnostic guidelines for NTM disease, bacteriological criteria have become simpler compared to the 1997 ATS diagnostic criteria, and consequently, diagnosis rate significantly increased [12]. Our presented case met all the clinical and radiologic criteria including repeated demonstration of *M. avium* in sputum samples [12, 13]. Due to severe patient's condition, vertebral osteomyelitis was documented only by clinical symptoms and standard radiographies similarly to a case recently reported by Japanese authors [12].

When it comes to therapy approach in *M. avium* complex infections, many different antibiotics and the combinations have been used in trials including those with liposome-encapsulated drugs [15]. The reports were uniform in demonstrating that combinations including macrolides (*e.g.*, clarithromycin or azithromycin), rifabutin, or both were effective in clearing *M. avium* complex infection and abolishing disease symptoms [16]. New studies are needed to elucidate the most potent therapy protocols and laboratories should offer drug sensitivity testing for NTM.

NTM pulmonary infections, including those with *M. avium* complex, are expected to be more and more actual in clinical practice in the future [17]. Our case report with highlighted risk factors, clinical and radiographic features of the disease might be a contribution to better understanding of this sort of pathology. Increased clinicians' awareness on NTM related disease could lead to earlier diagnosis and better disease outcome.

Conflict of interest: none

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