Rapidly growing mycobacterial pulmonary infection in association with severe gastroesophageal reflux disease

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ABSTRACT

Pulmonary infection due to rapidly growing mycobacteria (Runyan group IV) is uncommon and may be overlooked or misdiagnosed. Esophageal disorders have been recognized as a potential risk factor predisposing for this infection. A 35-year-old Sri Lankan patient, with severe gastroesophageal reflux disease and a hiatus hernia, contracted a pulmonary infection with *Mycobacterium fortuitum-chelonae*. He had severe airway obstruction and focal bronchiectasis, and responded to treatment with ciprofloxacin and clarithromycin. The case is reported to alert clinicians to the pathogenic potential of these organisms and to the prompt institution of appropriate chemotherapy once infection is recognized.

Keywords: Atypical mycobacteria, mycobacteria other than tuberculosis, gastroesophageal reflux disease.

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Atypical mycobacteria (also known as mycobacteria other than *Mycobacterium tuberculosis* (MTB) or MOTT) are commonly thought of as colonizers in the immunocompetent subject and only rarely have been recognized as pathogens. Studies from different countries have reported an increase in the isolation of MOTT over the last decade, exceeding that of MTB.[1-5] Infections by these organisms were also documented, occurring mainly in patients who were immunosuppressed, such as those with malignancy, organ transplantation, or human immunodeficiency virus (HIV). However, infections were also observed in immunocompetent patients with or without certain associated risk factors.[1-6] An example of this is pulmonary infection by Runyan group IV mycobacteria which has been reported infrequently to cause an insidious progressive infection which may go on for some time before being recognized and managed properly.[2,3,6] The following is a report of such a case which highlights some of the difficulties that may be encountered in managing patients with MOTT.

Case Report. A 35-year-old Sri Lankan male was seen for a pulmonary assessment prior to possible surgery for severe gastroesophageal reflux disease (GERD). He had a cough for 13 years, but did not seek medical attention as it was mild, intermittent and did not affect his activities. The previous year he had been admitted to a local private hospital for a week with severe pneumonic illness. Sputum culture grew a *Streptococcus* species. Sputum smears were negative for acid fast bacilli (AFB), but culture was not requested. His chest radiograph and computed tomographic scan (CT) were reported as showing bronchopneumonia, fibrotic changes and bronchiectasis in the lingula. He received parenteral antibiotics and had some improvement, but since that time his cough has been much worse and productive. He remained quite active in his work and denied fever, night sweats or weight loss, but he reported dyspnea on climbing one flight of stairs. He has history of severe GERD, which was diagnosed endoscopically and treated with proton pump inhibitors. He also had an atrial

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septal defect, and was assessed previously by cardiologists who recommended no intervention at that time. His job was administrative and he smoked occasionally until he stopped completely 13 years previously. On examination, he was well nourished, afebrile and had no clubbing. His chest examination showed signs of hyperinflation and wheezes. Investigations showed that his full blood count, electrolytes, renal and liver profiles were within normal range. A radiograph and CT of the chest showed hyperinflation, scattered bronchiectatic changes in both lungs and fibrosis of the lingual and posterior segment of the left lower lobe (**Figure 1**). The mediastinum was shifted to the left and pulmonary arteries were enlarged. Spirometry showed that forced expiratory volume in the first second (FEV1) was 1.8 L (43% of the predicted), forced vital capacity (FVC) was 2.5 L (49% of the predicted) and FEV1/FVC was 72.5 (89% of predicted). There was no significant change after administration of bronchodilator. Upper gastro-intestinal endoscopy showed reflux changes grade III and a large sliding hiatus hernia. He was maintained on dietary and non-dietary measures as well as his anti-reflux therapy. Sputum smear showed AFB, and accordingly 4 of the first line anti-tuberculous drugs were started. However, later the culture grew mycobacterial species that was identified as *Mycobacterium fortuitum-chelonae* (MFC) complex, which was resistant to the standard anti-tuberculous drugs and sensitive to Ciprofloxacin and Clarithromycin (Bioscintia Laboratory Germany). His previous anti-tuberculous drugs were discontinued and he was started on ciprofloxacin and clarithromycine, each at 250 mg twice a day. At the same time, a repeat sputum stain was again positive for AFB and the culture grew MFC. Follow up over 5 months has shown an improvement in his symptoms, chest radiograph and lung function (FEV1 increased to 2.2 L and FVC to 2.7 L 2 months later). Repeat sputum smears showed very few positive AFB organisms and subsequently negative smears and cultures.

Discussion. Reports from many countries (for example Japan, USA, Canada) have shown an increasing frequency of isolation of MOTT, in many centers exceeding that of MTB.[1-3] Likewise, in Saudi Arabia, MOTT constituted nearly two thirds of mycobacterial isolates and MTB the remaining 3rd.[4,5] While in many instances this merely indicated contamination or colonization, definite pathogenic role of MOTT in causing pulmonary infection was shown in a variable proportion of patients in these reports.[1-5] Since many of these studies were carried out in tertiary care centers, the isolates were mostly from immunosuppressed patients. However, pulmonary infection with MOTT was also seen in patients with minor risk factors or no apparent immune defect or risk factor. For example, Ellis and Qadri found 2 patients with pulmonary infection due to MFC.[4] One patient was a smoker and the other had chronic obstructive pulmonary disease.

In the present case report, pulmonary infection with MFC was documented, satisfying the clinical, radiological and bacteriological diagnostic criteria outlined by the American Thoracic Society (ATS).[7] He had persistent respiratory symptoms, and radiologically he had infiltrates, nodules and multi-focal bronchiectasis, which is typical for MOTT. Unlike tuberculosis, cavities are not commonly seen.[6] In addition, his sputum smears were positive and MFC was isolated on multiple occasions. The isolate was sensitive to Clarithromycin and Ciprofloxacin (which suggests the species to be *Mycobacterium fortuitum*), to which he responded clinically and radiologically. This case demonstrates the insidious indolent nature of the infection that was overlooked

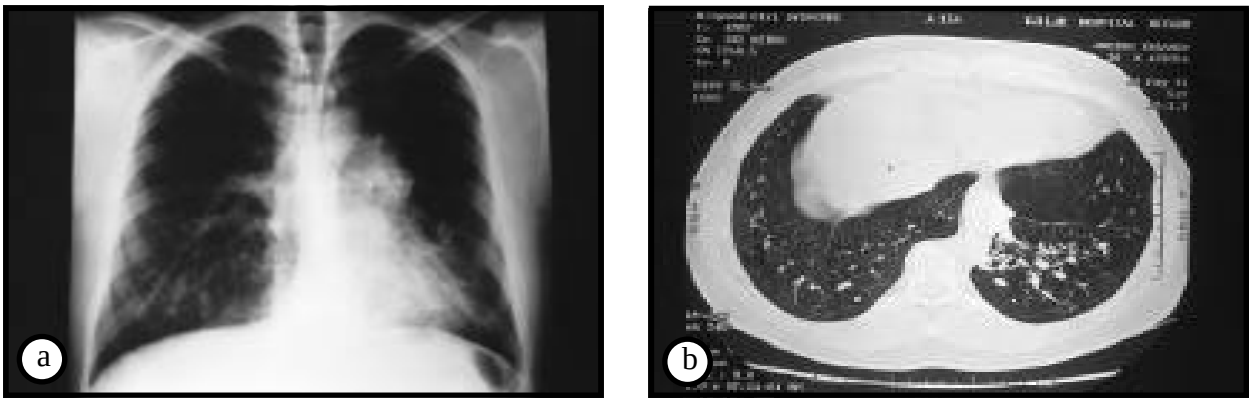

Figure 1 - Chest radiograph showing **(a)** hyperinflation, interstitial changes in the ligula and enlarged pulmonary arteries. These abnormalities are also seen on the computed tomography **(b)** which additionally shows areas of focal bronchiectasis.

despite specialized medical evaluation and investigation. Difficulties in establishing infection may have resulted because of the non-specific picture of the disease and unfamiliarity with this uncommon infection. Negative sputum smears at the onset of the disease may be misleading to the clinician.[2,3] On the other hand, positive smears and cultures may be disregarded as colonizers or contaminants.[6] Alternatively, if facilities for species identification are not available (as in many hospitals in Saudi Arabia), patients may be treated with anti-tuberculous drugs to which these organisms are resistant.[4] In addition, unnecessary isolation may be also imposed, which may be psychologically disturbing to the patients.[4] If the infection is recognized, a response of a variable degree to appropriate antibiotics occur,[6] but significant residual pulmonary damage may persist. Our patient developed bronchiectasis and severe airway obstruction, with no explanation other than the possible contribution of the associated GERD. Fatalities due to the rapidly growing mycobacteria were reported rarely.[8,9]

Pulmonary infection with the rapidly growing mycobacteria was observed to occur in association with gastroesophageal disorders. Hadjiliadis et al reported 2 patients and reviewed the literature from 1966 to 1997.[9] In a total of 20 patients, the most common esophageal disorder was achalasia (11 patients), followed by lipoid pneumonia (4 patients), and the remaining 5 had miscellaneous disorders. Our patient had severe GERD and a hiatus hernia, which was observed in one patient in that review.[9]

In conclusion, physicians need to be aware of the occurrence of pulmonary infection with MOTT in patients who are not necessarily immunocompromised, but may have certain risk factors, such as esophageal disorders. Griffith and Wallace believe that "there are probably many unrecognized cases for every case that has been identified".[6] There is also a need to support laboratory facilities for identification and antimicrobial susceptibilties of mycobacterial species (including a local reference laboratory). Further studies on the epidemiologic and pathogenic role of MOTT in Saudi Arabia are warranted.

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