Original article

Clinical Significance of Environmental Mycobacteria Isolated From Respiratory Specimens of Patients With and Without Silicosis

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A R T I C L E  I N F O

Article history:
Received 6 March 2015
Accepted 15 July 2015
Available online 12 February 2016
Keywords:
Silicosis
Nontuberculous mycobacteria
Environmental mycobacteria

A B S T R A C T

Objective: To describe the clinical, functional and radiographic differences of respiratory disease caused by environmental mycobacteria in patients with and without silicosis.

Method: Retrospective, observational study in patients with nontuberculous mycobacteria isolated in the Hospital Meixoeiro (University Hospital of Vigo) microbiology laboratory between January 2007 and December 2013. Patients were grouped according to the presence or absence of silicosis and mycobacterial lung disease, using American Thoracic Society criteria.

Results: In 156 cases, at least one species of environmental mycobacteria had been isolated from the respiratory culture. A total of 71% were identified in men, 40 (25.6%) of whom had silicosis. Sixty patients (38.5%) met American Thoracic Society microbiological criteria: 62.5% of the silicosis group and 30.2% of the non-silicosis group. The most common species were Mycobacterium avium complex, Mycobacterium genavense and Mycobacterium chelonae. American Thoracic Society criteria for environmental mycobacterial disease were met in 34 (22.7%) patients: 14 in the silicosis group and 20 in the non-silicosis group. Treatment was administered in 24 cases, with better bacteriological eradication levels in the non-silicosis group.

Conclusions: In our series, a history of silicosis was related with a higher incidence of environmental mycobacterial disease. The causative species in the majority of cases in our setting was Mycobacterium avium complex, followed by Mycobacterium genavense. Patients with silicosis showed lower cure rates after treatment.

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Significado clínico de las micobacterias ambientales aisladas en muestras respiratorias en pacientes con silicosis y sin silicosis

R E S U M E N

Objetivo: Describir las diferencias clínicas, funcionales y radiográficas de la enfermedad respiratoria por micobacterias ambientales (MA) en pacientes con silicosis y sin silicosis.

Palabras clave:
Silicosis
Micobacterias no tuberculosas
Micobacterias ambientales


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Introduction

Nontuberculous mycobacteria (NTM), also known as environmental mycobacteria, are ubiquitous microorganisms that can inhabit body surfaces and secretions, even in the respiratory tract, without causing disease. For this reason they were considered purely as colonizers until the latter half of the last century. The geographical prevalence of the different mycobacterial species varies widely, and accurate identification is essential, due to differences in their clinical relevance. In countries with low rates of pulmonary tuberculosis (PTB), such as the United States, the incidence of NTM (5 cases per 100 000 and up to 15 per 100 000 in individuals over 50 years of age) is higher than that of PTB (4 per 100 000). Known risk factors for NTM lung disease include cystic fibrosis and other diseases presenting with bronchiectasis, and immunosuppressive states, such as those associated with biological therapy (anti-TNF, rituximab), organ transplantation, and autoimmune deficiency syndrome, although an increasing number of cases of NTM are now detected in patients with no underlying disease. A risk factor which has received less attention is NTM lung disease in silicosis. Although the relationship between silicosis and PTB is well characterized, the role of silicosis as a risk factor for NTM lung disease is less well defined. NTM infection most commonly presents as chronic lung disease. Two radiographic patterns are observed: fibrocavitation in the upper lobes of patients with underlying respiratory disease, such as chronic obstructive pulmonary disease; and bronchiectasis in the right middle lobe or the lingula. For a diagnosis of NTM lung disease, certain clinical, bacteriological and radiological criteria must be met. Radiological criteria in particular are difficult to determine in cases with silicosis, as the pre-existing interstitial-nodular disease makes it difficult to determine if the NTM isolated from the sputum constitutes mycobacterial disease or simply colonization. Accordingly, a detailed evaluation of symptoms and radiological findings is essential. Although the pathogenic potential of NTM is being increasingly recognized, the clinical relevance of NTM has not been determined. The aim of this study was to identify the different species isolated in NTM-infected patients with and without silicosis in our setting, and to describe the clinical characteristics, predisposing factors, and the progress of patients in both groups.

Materials and Methods

We conducted a retrospective observational study of patients with confirmed NTM infection, determined by the Microbiology Laboratory of the Hospital O Meixoeiro (University Hospital Complex, Vigo, Spain) between January 2007 and December 2013.
Results

We reviewed 156 clinical records which contained at least 1 record of a positive NTM microbiological culture in respiratory samples and clinical and radiological data. Most samples were sputum, except for 20 cases of bronchial aspirate or bronchoalveolar lavage (in 10 cases, the culture was from these samples only). In 3 patients, the same NTM was isolated in both a cervical node aspirate and a respiratory sample – in 2 cases Mycobacterium avium complex (M. avium complex) and in 1 case Mycobacterium genavense (M. genavense). Of the 156 patients, 111 (71.2%) were men and 45 were women (28.8%), with a mean age of 62 ± 17 years (range: 26–97). A total of 97 patients (68.2%) had some form of underlying lung disease: silicosis (25.6%), chronic obstructive pulmonary disease (14.1%), previous or active tuberculosis (11%), bronchiectasis (10.3%) and other respiratory diseases (11.5%). Other concomitant diseases included solid tumors (7.6%), HIV infection (3.8%), heart disease (3.8%) and liver disease (3.2%). Twenty-one patients (13.4%) had no underlying disease. The number of mycobacteria identified in our hospital was 7 in 2007, 14 in 2008, 32 in 2009, 41 in 2010, 25 in 2010, 26 in 2011 and 11 in 2013.

The most frequently mycobacteria isolated (Fig. 1) were M. avium complex (100), Mycobacterium gordonae (M. gordonae) (19) and Mycobacterium chelonae (M. chelonae) (13); 23 mycobacteria were unidentified (M. sp.). Fig. 1 also shows the distribution of NTM isolated in the 60 clinically significant cases (≥2 positive cultures). The species most commonly isolated in this group of patients was also M. avium complex, present in 76.7% of cases.

A diagnosis of silicosis was confirmed in 40 (25.6%) patients, compared to 116 (74.4%) without silicosis. All silicosis patients were men, with a mean age of 56.2 years [standard deviation (SD) 13.1; range: 36–85]. The patients without silicosis were significantly older (63.9 years) [SD 17.2; range: 26–94]; 71 (61.2%) were men.

The principal characteristics of both groups are shown in Table 1. The most notable features are the higher rates of smoking, airflow obstruction, and use of inhaled corticosteroids in the silicosis group. Silicosis patients presented airflow obstruction (60.5%) more often than patients without (35.1%), and all (100%) of patients with silicosis and NTM disease had airflow obstruction. Diabetes mellitus, on the other hand, was more common in the group without silicosis. A total of 22 patients (7 with silicosis, and 15 without) had a history of previous PTB; 6 (3 in each group) had active tuberculosis, 5 pulmonary and 1 lymph node tuberculosis, all of whom had concomitant NTB in a single sputum sample, interpreted as NTM colonization. In patients without previous disease, the positive culture was isolated and interpreted as colonization.

Criteria recommended by the American Thoracic Society for the diagnosis of NTM pulmonary disease were met in 34 patients, 21% of all cases, and in 56% of those who met the microbiological criteria (14 with silicosis and 20 without).

The NTM strains isolated in the 14 patients with silicosis who met the microbiological criteria recommended by the American Thoracic Society were (Fig. 2): M. avium complex (n=11; 71.4%), M. genavense (n=2) and Mycobacterium xenopi (M. xenopi) (n=1), and the NTM strains isolated in the 20 non-silicosis patients were: M. avium complex (n=19; 95.0%), M. gordonae (n=1), M. genavense (n=1), Mycobacterium fortuitum (M. fortuitum) (n=1), Mycobacterium abscessus (M. abscessus) (n=1), Mycobacterium malmoense (n=1), M. chelonae (n=1) and Mycobacterium celatum (n=1); 2 mycobacteria were not identified.

The predominant symptom in silicosis patients was dyspnea, detected in 30 (75%); in patients without silicosis, the predominant symptom was cough, seen in 41 (35.3%). Cavitation was observed in 29% of patients with a diagnosis of NTM disease (57% in the silicosis group, and 10% in the non-silicosis group). The most common CT findings in silicosis were nodules and conglomerates (52.5%), and in non-silicosis patients, bronchiectasis (60.0%) (Table 2).

Table 1: Characteristics of Patients In Whom Nontuberculous Mycobacteria Were Isolated.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Silicos N=40</th>
<th>No silicos N=116</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>56.2 ± 13.1</td>
<td>63.9 ± 17.2</td>
<td>.004</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>0 (0%)</td>
<td>45 (38.8%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Men</td>
<td>40 (100%)</td>
<td>71 (61.2%)</td>
<td></td>
</tr>
<tr>
<td>Previous PTB</td>
<td>7 (17.5%)</td>
<td>15 (12.5%)</td>
<td>.650</td>
</tr>
<tr>
<td>Active PTB</td>
<td>3 (7.5%)</td>
<td>3 (2.6%)</td>
<td>.359</td>
</tr>
<tr>
<td>Smoking habit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>14 (35%)</td>
<td>63 (59.4%)</td>
<td>.101</td>
</tr>
<tr>
<td>Former smoker</td>
<td>20 (50%)</td>
<td>26 (24.5%)</td>
<td></td>
</tr>
<tr>
<td>Active smoker</td>
<td>6 (15%)</td>
<td>17 (16%)</td>
<td></td>
</tr>
<tr>
<td>Diabetics</td>
<td>1 (2.5%)</td>
<td>21 (18.1%)</td>
<td>.014</td>
</tr>
<tr>
<td>FEV1/FVC ≤ 70</td>
<td>23 (60.5%)</td>
<td>13 (35.3%)</td>
<td>.028</td>
</tr>
<tr>
<td>Steroid use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>8 (20%)</td>
<td>19 (16.4%)</td>
<td>.602</td>
</tr>
<tr>
<td>Inhaled</td>
<td>24 (60%)</td>
<td>39 (33.6%)</td>
<td>.003</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>0 (0%)</td>
<td>3 (2.6%)</td>
<td>.570</td>
</tr>
</tbody>
</table>

* P<.05. PTB, pulmonary tuberculosis.

Fig. 1. Distribution of all cases (n=156) and significant cases (n=60) in which nontuberculous mycobacteria were isolated. MAC: Mycobacterium avium complex; M.sp.: Mycobacterium species or unidentified mycobacteria.
Discussion

Silicosis is associated with the development of NTM infection and disease, and is the most common predisposing factor for NTM infection in our environment. Prevalence is clearly higher than reported in clinical epidemiological NTM studies performed in Spain, which found silicosis responsible for NTM disease in 0.9%–2.3% of cases.12,13

Recent studies14,15 underline the importance of NTM in silicosis patients. A systematic search by Morita et al.15 reported a positive culture rate of 39% for pathogenic and non-pathogenic NTB species in these patients. The high prevalence of silicosis in Spain—associated with the country’s sizeable granite industry (quarries and workshops)17—may explain the high percentage of silicosis identified as a cause of NTB disease.

NTM lung disease tends to be more often associated with silicosis than with PTB. Publications which included all notifiable cases of PTB in our autonomous community during the same period as our study show a prevalence of silicosis of 0.5%; this is far lower than the 41% prevalence of silicosis we found among our series of patients with NTM lung disease. Corbett et al.14 similarly reported a higher incidence of pneumoconiosis among NTM patients than among those with M. tuberculosis infection. The rising rate of positive NTM cultures does not seem to be exclusively associated with improvements in laboratory methods: other factors may be contributing, such as greater environmental exposure to NTB (exposure to NTM is increasing due to factors such as climate change, earthworks, aerosolized water particles, etc.), underlying host factors (bronchiectasis, chronic aspiration, chronic obstructive pulmonary disease, advancing age, etc.) or innate host characteristics associated with NTM disease (women with slender body habitus, scoliosis, pectus excavatum, and marfanoid habitus).2

In our hospital, a high percentage of patients (61.5%) had only 1 positive culture and were considered colonized. This rate was relatively high compared to that of other authors: Andréjak et al.9 reported 55%, Winthrop et al.10 reported 42% in their review, and Braun et al.19 found only 11.2%. We may have found a higher rate of “colonized” patients because no evidence of subsequent evaluations during the study period was found in the clinical records of many of our patients with 1 positive culture.

The most common colonizing species were M. avium complex, M. gordonae and M. chelonae. The first 2, M. avium complex and M. gordonae, were also reported as the most common in some series conducted in our setting,1 in contrast with other series in which M. gordonae, M. xenopi, M. fortuitum, Mycobacterium terrae,
Our study may have some limitations, primarily its retrospective nature. This prevented us from further investigating any unclear aspects in the patients’ clinical records, which may have led to a more accurate classification of the cases. Moreover, if the treating physicians had conducted a more comprehensive diagnostic process at the time, some patients may have been assigned to a different diagnostic group.

In conclusion, a history of silicosis was related to our setting with a higher incidence of NTM disease. The patient’s underlying disease did not appear to modify the types of species identified, the most common being *M. avium complex* in both silicosis patients and non-silicosis patients. In our study, we found a rate of *M. genavense* that is not echoed in other reviews of NTM. It would be of interest to study the results of cultures taken in coming years, to see if the relevance of this strain is confirmed in our setting. Finally, our cure rates appear to be low. These results suggest that we need to optimize management of these patients and consolidate the diagnostic suspicion of NTM disease in order to improve diagnostic accuracy and cure rates.

**Conflict of Interests**

The authors declare that they have no conflict of interests.

**References**