Pulmonary Non-Tuberculous Mycobacteria in a General Respiratory Population

Abstract:

The prevalence of non-tuberculous mycobacterium (NTM) appears to be increasing. Much of the experience in the literature about this emerging organism comes from specialised units or populations such as cystic fibrosis patients. We, therefore, aim to evaluate the experience in a general respiratory population of dealing with patients with positive culture of NTM. We did a retrospective review of medical notes of general respiratory patients from whom NTM were isolated from July 2007 to July 2012. Cystic fibrosis patients were excluded. We reviewed 37 patients (19 males, 18 females) medical records. A total of 73 positive cultures were reviewed. 28 isolates were from sputum samples alone, 34 isolates were from bronchoalveolar lavage alone and 11 isolates were from a combination of sputum and bronchoalveolar lavage (11 isolates). We found that Mycobacterium avium was the most frequently isolated Mycobacterium in our laboratory with 22 (60%) patients had Mycobacterium avium in their pulmonary cultures. Interestingly, Mycobacterium gordonae was isolated from microbronchiectasis patients were the second commonest mycobacterium (4, 11%) cultured. We noted 2 (5%), cases of Mycobacterium szulgai, 2 (5%) cases of Mycobacterium chelonae and 2 (5%) cases of Mycobacterium abscessus. There was a female predominance among the patients in our microorganism profile (15 females, 12 males). Our patients had a median age of 46 years. All except 6 patients had underlying respiratory disease; the most common were bronchiectasis (14, 37%) and COPD (10, 27%). Of the 37 patients, only 6 (16%) received treatment. However, 2 patients stopped their treatment due to treatment toxicity. We concluded that the isolation of NTM is not uncommon. Defining NTM disease is difficult and deciding which patient to be treated needs careful evaluation as treatment can potentially be very toxic.

Introduction

The past twenty years have seen an increased recognition of the role of non-tuberculous mycobacteria (NTM) in respiratory disease. This growing awareness may be attributed both to increasing prevalence of infection and a more widespread acknowledgement of a pathogenic role for NTM. Studies from Europe and North America have demonstrated that isolation of NTM is not uncommon. Some of this increase in the number of NTM isolates may be due to improvement in the microbiological culture methods, increasing awareness of NTM infections, aging and increasing numbers of immunosuppressed populations. There are conflicting data between North American and European studies on incidence and other epidemiological features with variations in the prevalence of specific mycobacteria even within countries, the presence of underlying disease and differences in gender prevalence in patients with the disease. Whilst some NTMs may not be pathogenic, they have been associated with a wide variety of lung diseases including cavitory disease, bronchiectasis and hypersensitivity pneumonitis. Because environmental NTMs are capable of contaminating clinical specimens or acting merely as commensals, correlation with clinical and radiological findings is required to define the presence of the disease.

Discussion

One of the 2 patients who stopped treatment died due to pulmonary NTM disease. The remaining 3 (8%) was unknown. Of the 37 patients, only 6 (16%) received treatment. However, 2 patients stopped their treatment due to treatment toxicity. We concluded that the isolation of NTM is not uncommon. Defining NTM disease is difficult and deciding which patient to be treated needs careful evaluation as treatment can potentially be very toxic.

Published criteria include the presence of pulmonary symptoms, together with radiographic opacities on plain radiographs or computed tomography (CT) scans; radiographic changes need to be persistent on follow-up results from patients specimens. Despite increasing awareness of the role of NTMs in respiratory disease, most published data comes from individual case reports, epidemiological studies, or reports from specialised institutions or specific populations such as cystic fibrosis patients. The implication of these studies for the individual practicing clinician is not clear. We therefore reviewed the cases of all non-cystic fibrosis patients who had positive respiratory cultures for NTM over a five year period in our institution, a tertiary care university teaching hospital, examining the relationship of NTM culture and disease with underlying demographic and clinical variables.

Methods

The laboratory records in the department of Microbiology were used to identify all isolates of NTM from January 2007 to July 2012. The medical records of patients from whom NTM were isolated were reviewed and patients with cystic fibrosis or non-pulmonary isolates were excluded.

Results

A total of 57 patients from whom NTM were isolated were identified. Of these, 20 were excluded from further analysis as 16 patients had cystic fibrosis and 4 had non-pulmonary isolates of non-tuberculous mycobacteria (Figure 1). The medical records of 37 patients (13 male and 24 female) with a total of 73 positive cultures were reviewed. The 73 respiratory tract isolates were from sputum samples alone (28 isolates), bronchoalveolar lavage alone (34 isolates) and combinations of sputum and bronchoalveolar lavage (11 isolates). The NTM most frequently isolated in our institution was Mycobacterium avium (n=22) (Figure 2).

Mycobacterium gordonae and Mycobacterium intracellulare were each isolated from 4 patients. 2 patients had Mycobacterium szulgai, 2 had Mycobacterium chelonae and 2 had Mycobacterium abscessus. 1 patient had Mycobacterium malmoense. Our study population consisted of 19 male and 18 female patients. The mean age of our patients was 64.8±14.6 years. All except 6 patients had underlying respiratory disease; the most common were bronchiectasis (14, 37%) and COPD (10, 27%). Of our patients characteristics are shown in Table 1. There was a significant female predominance among subjects with bronchiectasis (77%), while those with underlying chronic obstructive pulmonary disease (COPD) were more likely to be male (89%) (Figure 3). Of our COPD patients, 6 were on inhaled corticosteroids for their bronchiectasis or asthma. Symptoms such as fever, weight loss, night sweats and loss of appetite occurred in 7 patients in our population.

Seven patients presented with recurrent lower respiratory tract infections, 3 presented with persistent productive cough and 3 had a history of haemoptysis. Two patients were asymptomatic at diagnosis but had chest x-ray changes that were consistent with mycobacterial infections. 9 (24%) patients were smokers, 11 (30%) were ex-smokers, 14 (38%) were non-smokers and the smoking status of the remaining 3 (8%) was unknown. Most of our patients remained well despite having NTM positive cultures. We utilised the American Thoracic Society/Infectious Disease Society of America (ATS/IDSA) formulation of guidelines for the identification and management of patients with NTM. These guidelines suggest that patients suspected of having NTM disease must have persistent symptoms compatible with NTM infection, radiologic changes and the finding of at least two sputum samples or one bronchial wash or lavage positive for NTM. Follow-up of patients whose...
Our data confirm the findings of Winthrop et al. that men with NTM were more likely to have COPD and women were more likely to have bronchiectasis. The reason for this is unknown. An association of pulmonary NTM with pectus excavatum and a history of childhood asthma was also suggested. In the latter, smoking was noted to lower the FEF25-75 after ex vivo nicotine stimulation, and altered serum adipokine levels normalized for body fat. Thus this phenotype may be associated with an underlying immunological or mucociliary clearance defect. The severity of any immune dysfunction has also been postulated to contribute both to the severity of the structural lung disease and NTM disease. Inhaled corticosteroids may impair airway inflammatory responses and predispose to respiratory infections in COPD. NTM appears to have a predilection for patients with COPD who use inhaled corticosteroids, with an adjusted odds ratio of 29.1 in a recent study. In our study, 60% of COPD patients had been on inhaled steroids. The precise mechanism underlying an increased risk of NTM infection in patients on inhaled corticosteroids remains unclear. As expected, the majority of the NTM cultured in our laboratory were Mycobacterium avium complex, in keeping with the majority of previous studies. Interestingly, Mycobacterium gordonae, a mycobacterium with very low pathogenicity, was the second commonest organism found, in 10% of samples in our series.

This is in contrast to the study done by Kennedy et al on the incidence of NTM in southwestern Ireland from 1987 to 2000 who found that the commonest NTM isolated in decreasing order are MAC, malmoense, marinum and kansaii. Although low in pathogenicity, Mycobacterium gordonae has been reported to cause disease even in immunocompetent patients requiring treatment. In our series there were also two cases of Mycobacterium szulgai, which is rare occurrence in most international series. A previous case report by Sanchez-Alarcos stated that there had only been 35 cases previously described in the English language literature. However a single case has recently been reported by another institution in Ireland.

These differences in findings probably reflect geographical variation in the prevalence of NTM species between and within countries and emphasize the need to be aware of the occurrence of unusual NTM locally. As smoking is a risk factor for underlying lung disease, it might be assumed that the prevalence of smoking in patients with NTM would be very high. However, in our series, 42% of all patients, who had an extensive amount of background lung disease, had a current smoking habit. It can be argued that cigarette smoking depends on ethnicity, sex and duration of the smoking habit. Another possible hypothesis is that smoking produces significant levels of oxygen radicals that destroy NTM and thus helps to protect against NTM disease. As our results show, not all patients will benefit from treatment for NTM disease. 33% of the treated patients in our population did not tolerate the medications well.

Treatment guidelines for NTM disease issued by ATS were followed in the management of these cases. Treatment consisted of a multidrug regimen, which may be complicated by potential toxicity, interactions with other concomitant medications and a prolonged requirement for treatment. The multidrug regimen prescribed to patients with NTM disease depends on the particular NTM species isolated. Treatment is recommended to guide therapy and close liaison with a local clinical microbiologist is advised. Expertise from an experienced respiratory physician in NTM disease should be sought and patients diagnosed with NTM disease need to be regularly monitored for clinical improvement and toxicity. It is important to note that failure rates are high, treatment might be prolonged, nearly always in excess of twelve months and relapses despite initial successful therapy can occur.

In conclusion, this series suggests that the isolation of NTM is not uncommon in a general respiratory practice. Physicians should be aware of any unusual local epidemiology of NTMs. A diagnosis of NTM disease can be difficult to make and not all patients with positive NTM respiratory culture requirement treated. Treatment should be tailored individually as treatment is often poorly tolerated.

References