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Non-tuberculous mycobacteria in patients with bronchiectasis

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Abstract

Background

Non-tuberculous mycobacteria (NTM) are ubiquitous environmental organisms. Patients with pre-existing lung damage are susceptible to NTM but their prevalence in bronchiectasis is unknown. Distinguishing between lung colonisation and disease can be difficult.

Methods

A prospective study of 100 bronchiectasis patients to evaluate sputum NTM prevalence, and a retrospective analysis over 11 years of clinical, microbiological, lung function and radiology data of our clinic patients with NTM sputum isolates, was performed.

Results

NTM prevalence in this population of bronchiectatics was 2%. Patients in the retrospective study were defined as bronchiectasis and multiple NTM isolates (n=25), bronchiectasis and single isolates (n=23) and non-bronchiectasis and multiple isolates (n=22). *Mycobacterium avium complex* (*MAC*) species predominated in bronchiectasis compared to non-bronchiectasis lung disease (72% vs. 9% p<0.0001). Single isolates were also frequently *MAC* (45.5%). Multiple isolates in bronchiectasis were more often smear positive on first sample than single isolates (p<0.0001). NTM were identified on routine screening samples or because of suggestive radiology. No particular bronchiectasis aetiology was associated with a NTM. *Pseudomonas aeruginosa* and *Staphylococcus aureus* were frequently co-cultured. Six (25%) of multiple NTM patients had cavities of which five were due to *MAC.* Half of patients with multiple isolates were treated, mostly due to progressive radiology.

Conclusions.

NTM are uncommon in non-cystic fibrosis bronchiectasis. Routine screening identifies otherwise unsuspected patients. MAC is the most frequent NTM isolated. Half of patients with multiple isolates were treated, based on progressive radiology.

Introduction

Non-tuberculous mycobacteria (NTM) are ubiquitous environmental organisms that sometimes cause respiratory disease, usually in patients with pre-existing damage. Patients with bronchiectasis, as with other chronic lung diseases, are predisposed to infection with NTM (1, 2). The symptom profile of NTM pulmonary infection, such as increased sputum production, cough, breathlessness and haemoptysis is similar to bronchiectasis, making differentiation of active infection from colonisation difficult. Furthermore, some NTM infections cause bronchiectasis (3), thus making the radiological diagnosis of NTM infection difficult to make in the presence of underlying disease. Similarly, primary infections that have caused bronchiectasis may be impossible to differentiate from secondary infections of bronchiectasis due to another cause.

NTM are inhaled as aerosol droplets so may be cultured if a sputum sample is obtained soon after environmental exposure. This probably accounts for most of the single isolates found (4). However, because single isolates could reflect a low level of infection, which may increase, careful follow up with repeated sampling is required.
Multiple isolates, with clinical evidence of disease, should be obtained before prolonged treatments that are sometimes poorly tolerated are commenced (5-7).

Few studies have undertaken any detailed analysis of NTM in the context of bronchiectasis. The prevalence of NTM in bronchiectasis may be higher than anticipated because of the non-specific symptoms and because routine screening is not usually undertaken. In one study, three cases of NTM were detected over 6 years in 91 patients with bronchiectasis (8). In another, NTM were found in 6% of bronchiectatic patients(9). No mycobacteria were isolated in a study of 150 patients over 3 years (10), but in this study sputum was sent only if no response to standard treatment occurred.

We have investigated the prevalence of NTM prospectively in two groups of bronchiectasis patients: a) newly referred patients to our unit in whom NTM were unsuspected b) patients being followed up in our unit who had a previous negative sputum examination for acid-fast bacilli (AFB) At the time of this study, it was not our practice to routinely screen for AFB. In a retrospective study, over eleven years, we identified patients with and without bronchiectasis with NTM isolates who were seen in our clinic. We also studied different NTM species in the retrospective study with respect to high resolution computerised tomography (HRCT) features, lung function and co-existent sputum pathogens. Lastly we investigated how many patients were judged to require treatment for NTM infection and why.

Methods

Prospective study population

A prospective analysis of the prevalence of NTM isolates in sputum from 50 consecutive newly referred bronchiectasis patients who were admitted to our minimal dependency unit for investigation which is our usual practice for new patients; and 50 follow up bronchiectasis patients recruited from outpatient clinics because their condition was stable and they had a previous negative sputum examination for AFB. Patients referred because of known mycobacterial infection, and those with a positive sweat test indicative of cystic fibrosis were excluded. Sputum was sent for smear and culture examination on three separate occasions (0, 6, and 12 months) were recorded. At the time of this study, it was not our practice to screen routinely for NTM except during the patient's initial investigations in our unit.

Retrospective study population

A retrospective analysis over 11 years, from 1991 to 2001, of Host Defence Unit patients with a positive NTM sputum culture was performed using the Royal Brompton Hospital Department of Microbiology database. Case notes were reviewed and patients allocated to the following groups; patients with bronchiectasis and a single NTM isolate, patients with bronchiectasis and multiple NTM isolates, and patients with non-bronchiectasis lung disease and multiple NTM isolates.

All patients had daily sputum production and a history of recurrent infective exacerbations. The diagnosis of bronchiectasis was made by high resolution computerised tomography (HRCT) (2). Patients with bronchiectasis and multiple isolates were analysed for: age, sex, aetiology of bronchiectasis, whether the NTM infection was primary or secondary, past medical history, drug history, sputum microbiology, HRCT appearance, lung function and drug treatment.

Microbiology

Samples were processed for mycobacteria using the modified Petroff's 4% sodium hydroxide method (11). The processed samples were then inoculated onto two Lowerstein-Jensen slopes (one with pyruvate and one with glycerol). AFB positive smear samples were also inoculated into Middlebrook >H12 Bactec vials. Positive cultures were identified by biochemical and temperature tests and where appropriate Accuprobe (12). The criterion for multiple isolates were two isolates that were cultured greater than one week apart (5). Single isolates were a single positive NTM culture listed in the microbiology database. The presence of negative cultures before and after the single isolate was confirmed. The presence or absence of smear positivity was documented. Sputum was sent at the same time as AFB examination for routine bacteriology. Pathogens cultured within one week of

the first or single NTM isolate were documented and described as a co-cultured pathogen. These were described as chronic isolates if grown on more than two successive occasions.

Lung function

Lung function parameters of airflow obstruction, gas trapping and gas transfer were used since these are usually impaired in bronchiectasis (13). Forced expiratory flow in one second (FEV_1), maximum expiratory flow with 50% of vital capacity remaining in lung (MEF_{50}), residual volume (RV) and diffusing capacity of carbon monoxide (TLCO) were measured. Lung function nearest the time of the first isolate was compared to the most recent set of lung function recorded.

Radiology

All HRCT was performed at the Royal Brompton Hospital. The timing of the first HRCT with respect to the first NTM isolate was calculated. The predominant location of bronchiectasis, severity, presence or absence of nodules, mucus plugging, cavitation, consolidation, infiltrates and dyshomogeneity (air trapping) was assessed (13,14).

Statistical analysis

Group comparisons were made using chi-squared or Fisher's exact test as appropriate. Lung function data was analysed using paired t tests. A p value of less than 0.05 was regarded as statistically significant.

Results

Prospective study of NTM in sputum from bronchiectatic patients

Of the 50 newly referred bronchiectatic patients, one had multiple *MAC* isolates. This was a 52-year-old lady referred because of poor symptom control and chronic *Staphylococcus*

aureus infection. Investigation showed idiopathic bronchiectasis and an HRCT which had an unusual pattern of bronchiectasis involving the anterior segment of the right upper lobe and right middle lobe with marked dyshomogeneity suggesting small airways disease. Sputum had not been investigated for mycobacteria previously. Another patient had a single *M. chelonae* isolate that was never repeated.

Of the 50 bronchiectatic patients who were follow-ups, one patient had multiple *MAC* isolates. This 64 year old lady had a ten year history of allergic broncho-pulmonary aspergillosis and seropositive rheumatoid arthritis. During initial assessment she was smear and culture negative for mycobacteria and had widespread severe bronchiectasis with a left apical cavity and mycetoma. She was stable over the next eight years after which she was enrolled into the study and her sputum sent for this purpose was smear and culture positive for *MAC* on all three occasions.

The prevalence of NTM in this bronchiectatic population of our Host Defence Unit was therefore 2% over 1 year. The two patients were regarded as colonisation in that their condition was well controlled with general treatment. The first patient improved with broad spectrum antibiotics and teaching of physiotherapy; the second patient remained stable for several years but then became more symptomatic and a new CT demonstrated several cavitatory nodules. Treatment was commenced at that time.

Patient demographic data from retrospective study

Seventy one patients with NTM isolates were identified over 11 years: 23 with bronchiectasis and single NTM isolates (single NTMB group), 25 with bronchiectasis and multiple NTM isolates (multiple NTMB group), 22 with multiple NTM isolates and non-bronchiectatic lung disease.

There was a female preponderance in both the single (9 male, 14 female) and multiple NTMB groups (9 male, 16 female). The mean age at identification of first isolate in

the multiple NTMB group was 62.2yrs (62.5yrs, range 26-78yrs for males, and 62.1yrs, range 43-85 yrs for females). In contrast, we found the single NTMB group to be younger (mean age 55.1years, 50.5yrs males, 58.1yrs females) as were those with non-bronchiectasis lung disease and multiple isolates (mean age 47.2 years).

In the multiple NTMB group 52% were non-smokers and 40% ex smokers. Only 8% of bronchiectatics were current smokers compared to 27% current smokers in patients with non-bronchiectasis lung disease. 24% of the multiple NTMB group were on oral steroids at the time of the first isolate, and 16% had a history of lobectomy. There was one patient of non-Caucasian origin in each group.

Sputum samples were sent at the time of first isolate for a variety of reasons: 32% were referred to our unit with known NTM, 28% were sent during routine surveillance, 16% due to suggestive CT changes, 16% due to suggestive symptoms (cough, weight loss, fever, increased sputum, malaise, breathlessness) and only 8% because of failure to respond to usual bronchiectasis therapy.

Comparison of NTM species in the three patient groups from the retrospective study (Table 1)

MAC was by far the commonest species identified in the multiple and single NTMB groups. In the non-bronchiectasis group *M. kansasii* and *M. xenopi* predominated.

Causes of bronchiectasis in the multiple NTMB group were: 24% idiopathic, 24% post-tuberculous (all *MAC*), 12% rheumatoid arthritis (all *MAC*), 8% each for post childhood infections, post adult infections, primary ciliary dyskinesia (PCD). There was one each of pulmonary lymphangioleiomyomatosis, pulmonary sarcoidosis, allergic broncho-pulmonary aspergillosis and a compound heterozygote for cystic fibrosis with normal sweat test (*M. chelonae)*. Patients were not tested for HIV, but none were in high risk groups for this condition, nor had lymphopaenia.

In six patients (28%), all who cultured *MAC,* the bronchiectasis was considered to be a consequence of primary NTM infection. In these cases, the possibility of pre-existing bronchiectasis prior to NTM infection could not be excluded. However, the NTM infection was judged to have either led to marked progression of disease on the HRCT scan or have been the sole cause of the bronchiectasis. Three of these patients also had rheumatoid arthritis, and one case was a middle aged lady with a persistent dry cough whose bronchiectasis was present in the middle lobes, a pattern which has been described as Lady Windermere syndrome (15).

Table 1

	Bronchiectasis multiple isolates N=25	Bronchiectasis single isolates N=23	Non-bronchiectasis multiple isolates N=22
M. avium complex	18 (72)	10 (43.5)	2 (9.0)
M. kansasii	1 (4)	5 (21.5)	9 (40.9)
M. chelonae	2 (8)	4 (17.4)	0
M. fortuitum	2 (8)	1 (4.4)	1 (4.5)
M. malmoense	2 (8)	2 (8.7)	3 (13.6)
M. xenopi	0	1 (4.4)	7 (31.8)

Table 1. Comparison of species isolated in the retrospective study: bronchiectasis with single non-tuberculous mycobacteria (NTM) isolates, bronchiectasis with multiple NTM isolates and non-bronchiectasis with multiple NTM isolates. Data shown is number of patients with percentage of total shown in parentheses**.**

Microbiology of the retrospective study

Patients in the single NTMB group were more likely to be smear negative (83.3%) compared to the multiple NTMB group (15.7%) ($p<0.0001$). Within the multiple NTMB group, 84% of smear positive sputums grew *MAC* in first isolates compared to 33.3% of smear negatives. All of the three plus smear positive sputums grew *MAC*. By comparison, non- *MAC* species were much less likely to be smear positive (15.7%).

Pseudomonas aeruginosa was a co-pathogen at the time of first isolation of NTM in 52% of the multiple NTMB group, but isolation of *P. aeruginosa* in these patients was chronic in only 16%. 61% of patients with multiple *MAC* isolates cultured *P. aeruginosa* compared to 28% of patients with non-*MAC* isolates. S. *aureus* was co-cultured frequently in the multiple NTMB group (28% (7/25)).The single NTMB group had co-culture of *P. aeruginosa* and *S. aureus* less often (39% and 21.7% respectively) than in the multiple NTMB group. Rarer co-pathogens in the multiple NTMB group included *Haemophilus influenza*e (12%), *Aspergillus fumigatus* (4%), *Candida albicans* (8%), *Stenotrophomonas maltophilia* (4%).

HRCT chest at time of first isolate in the retrospective study

In the multiple NTMB group, 24/25 underwent HRCT (one patient had severe bronchiectasis previously shown by bronchography). 20 HRCT were performed within 6 months of first NTM isolate identification (17 of these were performed within one month of the first isolate). Two HRCT were performed 9 months before, and one 7 months and one 11 months after first NTM isolate.

The majority of patients had widespread bronchiectasis (see table 2). Because of numbers of patients comparisons were made between *MAC* and non-*MAC* species.

Nodules, mucus plugging and dyshomogeneity were common features, and a quarter had cavities. *MAC* accounted for 5 (83.3%) of the 6 patients with cavities and consolidation and for 78.6% of nodules and mucus plugging compared to non- *MAC* species. Dyshomogeneity was a feature with similar prevalence in both groups.

Patients requiring treatment showed more cavities (33.3% vs. 9.1%), consolidation (41.6% vs. 9.1%), and had more severe (58.3% vs. 18.2%) and widespread (75% vs. 45.4%) bronchiectasis than those who did not.

Table 2

	All isolates N=24	*M. avium complex* N=17	Non- *M. avium complex* N=7
Bronchiectasis distribution			
Widespread	15 (62.5)		
Lower & middle lobes	4 (16.6)		
Lower lobes	3 (12.5)		
Upper & middle lobes	2 (8.3)		
Lower& upper lobes	2 (8.3)		
Localised	3 (12.5)		
Middle lobe & lingula	2 (8.3)		
Upper lobe	1 (4.2)		
Specific HRCT features			
Nodules & mucus plugging	14 (58.3)	11	3
Dishomogeneity	11 (45.8)	6	5
Cavities	6 (25)	5	1
Consolidation	6 (25)	5	1
Infiltrates	1 (4.2)	1	

Table 2. High resolution computerised tomography appearances in patients with bronchiectasis and multiple non-tuberculous mycobacteria isolates in the retrospective study. Data shown is number of patients with percentage of total shown in parentheses.

Lung function in the retrospective study

Lung function data was analysed for 22 patients in the multiple NTMB group (two patients had incomplete lung function data, one patient underwent surgery for NTM and was excluded). These were analysed as follows: those considered not to require treatment (N=11), those who had completed anti-mycobacterial treatment (N=5) and those continuing on anti-mycobacterial treatment (N=6) For each patient group lung function data nearest to the time of first NTM isolate was taken (median time –2 days before NTM isolate, range –8 months to + 11 months). This was compared to the latest lung function data available.

In colonised patients mean FEV_1 was 60.7 ± 4.1% compared to 55.0 ± 8.9% in drug treated patients at first isolate (non-significant) (Figure 1). Patients untreated with NTM showed stable lung function, although there was a trend for increasing FEV_1 and MEF_{50} and decreasing RV over time (non-significant). This might be due to general measures such as physiotherapy taken to improve the control of their bronchiectasis. Patients who had completed anti-mycobacterial treatment also showed stable lung function (Figure 2). Patients still taking anti-mycobacterial treatment showed a rise in RV over time (133% that rose to 150%,) and a fall in MEF_{50} ($p<0.05$) (Figure 3).

Management in the retrospective study

Of the 25 patients, 11 were considered not to require antibiotic treatment. Reasons for deciding to monitor rather than treat included having a stable clinical condition with routine management and no HRCT evidence of active NTM disease. There was no species difference between the monitored and the treated group: 64.3% *MAC* in treated group vs. 72.7% *MAC* in the monitored group.

Of the remaining 14 patients, one underwent surgical resection of a cavity having previously completed one year of anti-mycobacterial therapy at the referring hospital, and 13 were prescribed anti-mycobacterial drugs. Reasons for initiating treatment were multifactorial, but HRCT changes influenced the decision in 11/13 (84.6%). These were: progressive bronchiectasis (36.4%), new nodules 3 (27.3%), new/progression of cavities (36.4%) and consolidation (18.1%). Failure of symptoms to respond to usual treatment was a reason in 27.3%. Common symptoms in this regard were cough (45.4%) and weight loss (36.4%).

Discussion

Patients are admitted to our minimal dependency unit for planned investigations (2) at a time that their condition is stable, but they have usually been referred to our unit which is in a tertiary centre because their condition is causing concern. Similarly patients followed up regularly in our clinics are usually more complicated than a population that would be seen in a general respiratory clinic.

The prevalence of NTM in our bronchiectatic population was 2%. Previous studies have found similar low prevalence, so it is likely that the prevalence of NTM in an unselected bronchiectasis population would be even lower than our study. (8-10).

This is the first study to demonstrate that *MAC* is the predominant NTM species isolated from sputum of patients with non-cystic fibrosis bronchiectasis, both in single (45.5%) and multiple isolates (72%). This suggests that patients with bronchiectasis are susceptible to contracting *MAC* and in some of these cases long term colonisation or infection is established. In contrast, in our series and others (16), the species profile of NTM in patients without bronchiectasis is very different, with *M. kansasii* and *M. xenopi* predominating, and *MAC* present in less than 10% of cases (16,17). *M. xenopi* was found in only one single isolate and in no multiple isolates in patients with bronchiectasis. Single isolates are usually thought to represent environmental exposure just before the sample is taken. However the predominance of *MAC* in single as well as multiple isolates suggests that in bronchiectasis single isolates might represent temporary colonisation, and the difference in species profile compared to non-bronchiectasis is probably due to unidentified factors causing a predisposition to infection. Since no particular cause of bronchiectasis was associated with NTM or *MAC* infection, this is likely to be due to the local environment of the bronchiectatic airway.

Pulmonary *MAC* disease is reported to present in two ways (18,19). The first is a classical presentation of fibro-cavitatory lung disease in patients with either smoking related COPD, previous tuberculosis, bronchiectasis or cystic fibrosis. The smoking related group are predominantly male between the ages 50-70 years (1). A second form of *MAC* infection has been increasingly recognised occurring in apparently immunocompetent individuals with no pre-existing lung disease(18,19). This group is most commonly non-smoking females aged 40-80 years. These patients have no known pre-existing lung disease but HRCT demonstrates the presence of small nodules most commonly involving the middle lobe and mild cylindrical bronchiectasis (3,20). This presentation has been described as the Lady Windermere syndrome because habitual voluntary cough suppression is postulated to account for retained secretions and focal disease in the lingula and middle lobe (15,21). After careful examination of the evidence available we considered 6 of the 25 multiple NTMB cases to be primary infections. This was based on HRCT appearances (19,20,22) no other cause of bronchiectasis identified (2), and patient history including lack of chronic rhinosinusitis and profound tiredness which is present in most cases of idiopathic bronchiectasis. All 6 were primary infections with *MAC*. In primary infections it is usually impossible to be certain whether silent bronchiectasis predisposes to the *MAC* infection, or the primary MAC infection itself causes the bronchiectasis in individuals who may have a genetic predisposition (22). Recently abnormalities in the gamma interferon pathway have been identified (23). HRCT studies of patients with MAC infection have shown small peripheral nodules which may coalesce and ectatic changes which develop in draining bronchi (14). Destruction of bronchial wall structure due to extensive granuloma formation in *MAC* lung infection has also recently been demonstrated (24).

In our study, the patients with bronchiectasis and multiple NTM isolates were predominantly female which is also true of bronchiectasis in general (2). However, other features of the group were different than those reported in other bronchiectasis series. The

mean age of the group, 62.2yrs, is higher than in other studies of bronchiectasis, e.g. 50.4 years (8), 52.7 years (10), and 41.6 years (25). The single NTMB group in our paper were younger, which suggests that bronchiectatic patients may be less able to clear NTM to which they are exposed as they get older. Previous studies of bronchiectasis have suggested a negative smoking history with only 1% current smokers (25). The multiple NTMB group contained 40% ex-smokers and 8% current smokers. This association with cigarette smoking has also been noted with primary MAC infections in which 38% were ex-smokers (18). Treatment with regular oral corticosteroids and a history of previous lobectomy was also commoner than is usual in a general bronchiectasis population (2,25)

No particular aetiology of bronchiectasis was associated with NTM isolation. The prevalence of tuberculosis as a cause of bronchiectasis has been found to be 19% or less (8,26) , and as low as 2% (10). We found tuberculosis related bronchiectasis in patients with multiple NTM isolates to be more common (24%), which suggests a possible increased general susceptibility to mycobacterial infection (27,28). Similarly the frequency of rheumatoid arthritis was higher than other studies (10), either suggesting an immune mechanism for increased susceptibility to NTM, or that rheumatoid associated small airways disease predisposes to NTM colonisation (29).

Symptoms of cough, sputum production and breathlessness are common in bronchiectasis. Hence a high index of clinical suspicion is required to identify NTM. A high number of NTM isolates were detected by routine surveillance (28%), and it is now our practice to screen our patients routinely once a year. Radiology suggestive of NTM also accounted for a high proportion of NTM isolates reflecting increased knowledge of the HRCT features of NTM lung disease (20).

P. aeruginosa was a frequent co-pathogen with *MAC* in patients with bronchiectasis and multiple NTM isolates (52%) compared to other studies of bronchiectasis that have reported positive cultures in 20%(9), 26%(30) and 31%(10) of patients. However only a

quarter of these were persistent isolates. Patients with bronchiectasis and single isolates also frequently co-cultured *P. aeruginosa* (39%) with *MAC*. *P. aeruginosa* infection is associated with greater extent of disease and worse lung function and may be a marker of patients whose lung function is declining (13,31). Therefore co-culture of *P. aeruginosa* and *MAC* may simply reflect worse bronchiectasis and therefore increased susceptibility to NTM. *S. aureus* is an uncommon pathogen in bronchiectasis and is associated with allergic broncho-pulmonary aspergillosis (ABPA) and atypical variants of cystic fibrosis (32), both diseases which usually manifest as upper lobe disease. However *S. aureus* was more frequently isolated in bronchiectasis and NTM (28%) than in other published studies (9,10,30). This suggests that repeated isolation of *S. aureus* in bronchiectasis should prompt a search for NTM as well as testing for ABPA and atypical cystic fibrosis.

In a comparative study of CT appearances of patients infected with NTM species *MAC* was found to have higher numbers of nodules and bronchiectasis, which was more severe than other NTM species (20). No differences were found in frequency of cavitation, consolidation or “tree in bud” pattern between *MAC* and non- *MAC* species. Although the frequency of cavitation in our study was similar to that in a mixed lung disease population (20), we found that *MAC* accounted for the majority of cavities in bronchiectasis. This suggests that, in bronchiectasis, *MAC* behaves in a more aggressive fashion compared to non- *MAC* species, causing greater destruction of lung parenchyma and cavity formation.

Only just over half of patients with bronchiectasis and multiple isolates were judged to require treatment (5,7). The rest were considered to be colonised but careful monitoring was continued, and our results show that lung function and radiology remained stable. Patients who required treatment had more severe impairment of lung function and this got worse if patients remained on treatment usually due to failure of eradication. A key factor in the decision to treat was evidence of changes on HRCT, especially progression of bronchiectasis and appearance of new cavities. A higher proportion of patients who went on

to have treatment had cavities (33.3% vs. 9.1%), consolidation (58.3% vs. 9.1%), or had more widespread and severe bronchiectasis (75% vs. 45.4%).

In summary, we have demonstrated that although NTM are uncommon in bronchiectasis, infection can lead to worsening of the condition. A significant number of cases were detected by routine surveillance. MAC is the predominant species whatever the underlying aetiology, and is responsible for most of the cavitatory disease. Patients with bronchiectasis may be more susceptible to *MAC*. However, pulmonary MAC infection might progress early bronchiectasis into more severe disease in genetically susceptible individuals such as those with rheumatoid arthritis. A proportion of patients presenting with symptoms of bronchiectasis are probably due to primary MAC infections in previously normal lungs. HRCT is very important in aiding the decision about when to commence treatment.

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Figure 1

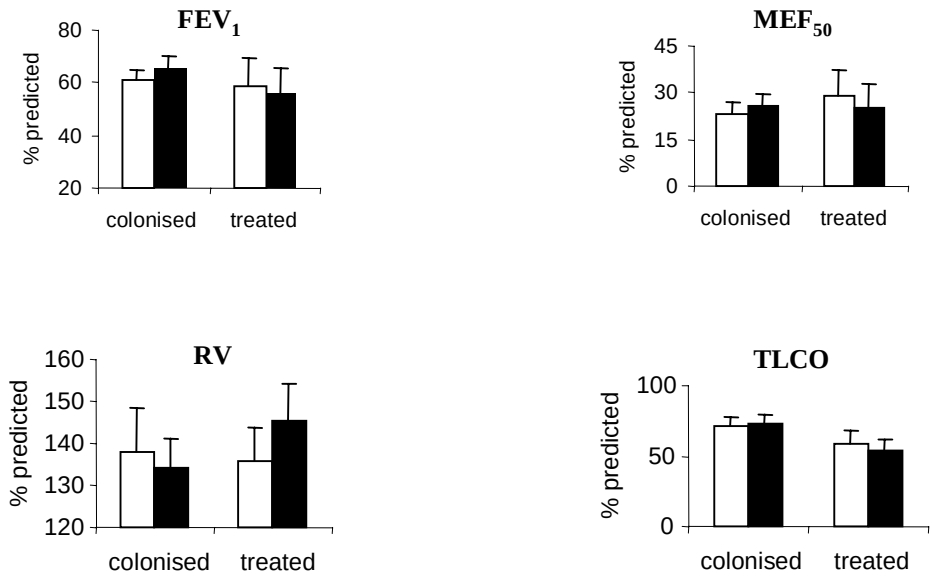

Figure 1. Lung function data in the bronchiectasis and multiple non-tuberculous mycobacteria isolates (NTMB) group. Lung function measured near the time of first NTM isolate (open bars) was compared to latest available lung function (solid bars) for two groups of patients :(a) colonised group (mean 22.18 months post NTM isolation) (b) drug treated group (mean 34.9 months post NTM isolation). Values are % predicted (mean + SEM).

Figure 2

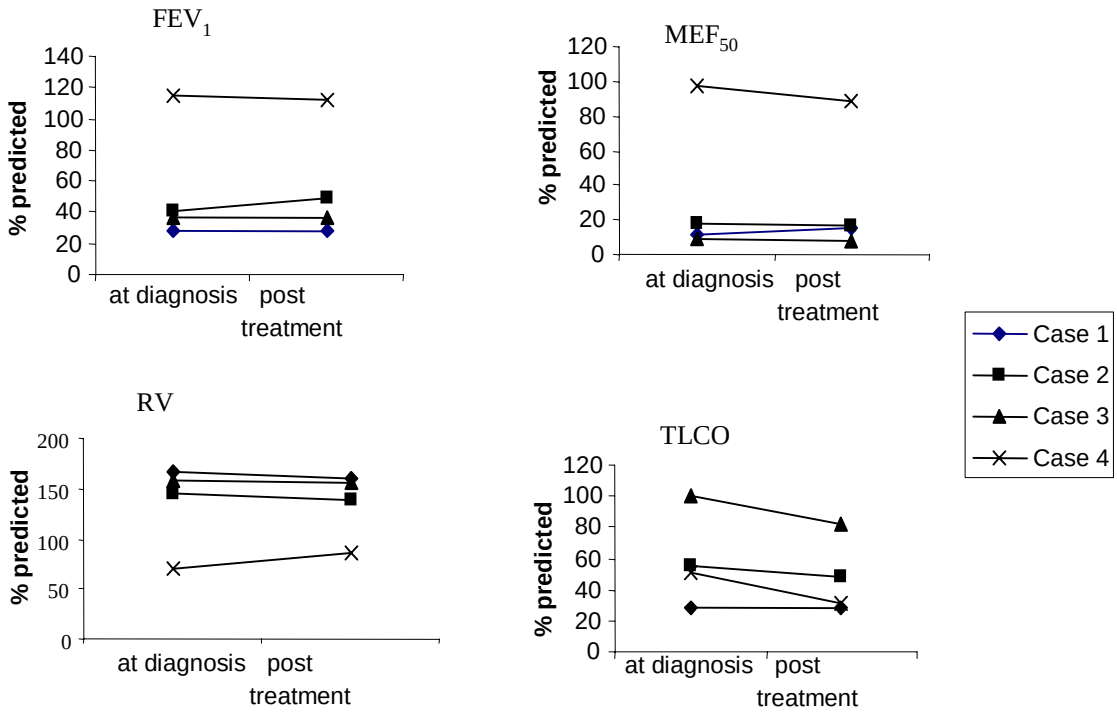

Figure 2. Lung function data in the bronchiectasis and multiple non-tuberculous mycobacteria isolates (NTMB) group who had finished treatment and were sputum negative for NTM (N=4) post treatment. Each patient is represented as Case 1 to 4 in the figure legend. Mean duration of treatment 16.7 months. Lung function measured near the time of first NTM isolate (diagnosis) was compared to latest available lung function (mean 60 months later).Values are % predicted.

Mean values as % predicted ± SEM, at diagnosis and later are FEV_1 54±20 vs 56±18, MEF_{50} 33±21 vs 31± 18, RV 135±21 vs 135±17 and TLCO 58±15 vs 47±12.

Figure 3

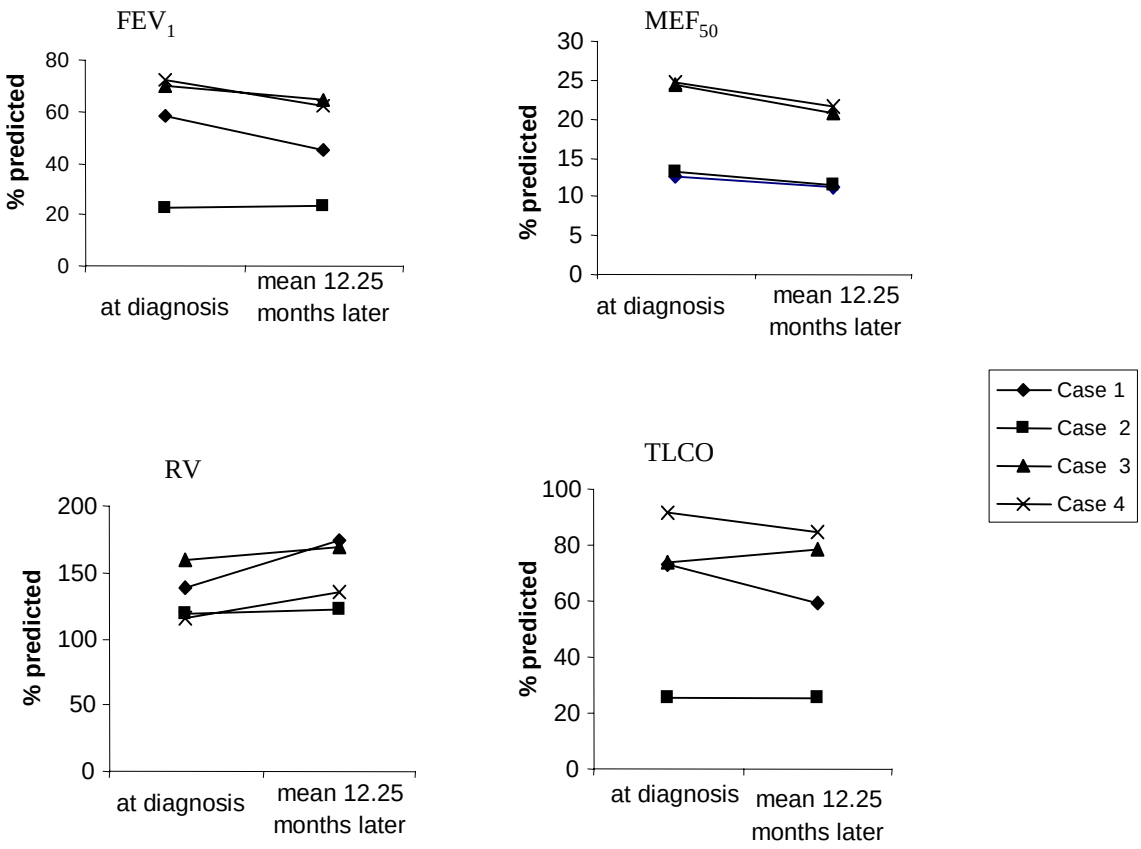

Figure 3. Lung function data in the bronchiectasis and multiple non-tuberculous mycobacteria isolates (NTMB) group who were still on treatment and were sputum positive for NTM despite treatment (mean time on treatment 13.7 months) (N=4). Each patient is represented as Case 1 to 4 in the figure legend. Lung function measured near the time of first NTM isolate (diagnosis) was compared to latest available lung function (mean 12.25 months later).Values are % predicted.

Mean values as % predicted ± SEM, at diagnosis and later are FEV_1 56±11 vs 49±9, MEF_{50} 18±3 vs 16±3 $p<0.05$, RV 133±10 vs 150±12 and TLCO 66±14 vs 62±13.