Comparison of characteristics of patients and treatment outcome for pulmonary non-tuberculous mycobacterial infection and pulmonary tuberculosis

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Abstract

Background **– Patients with non-tuberculous mycobacteria are usually started on conventional antituberculous triple therapy once acid fast bacilli are detected, before the exact type of mycobacteria has been identified. The ability to identify the characteristics of patients with tuberculous and non-tuberculous mycobacteria may be helpful in identifying before treatment those patients more likely to have non-tuberculous infection.**

Methods **– A retrospective study was conducted of all patients in one unit in whom non-tuberculous mycobacteria were identified in sputum or bronchoalveolar washings in the period 1987–93. The pattern of drug resistance was determined from laboratory records, and all case notes and chest radiographs were reviewed to identify the underlying disease and treatment outcome. All cases were compared with a matched control group of patients with culture positive *Mycobacterium tuberculosis* diagnosed during the same period.**

Results **– In the period studied there were 70 non-tuberculous and 221 tuberculous isolates. The non-tuberculous bacteria were typed as follows: *M xenopi* 23 (33%), *M kansasii* 19 (27%), *M fortuitum* 14 (20%), others 14 (20%). Of those with non-tuberculous mycobacteria, 83% were white subjects compared with 47% for tuberculosis. Patients with non-tuberculous mycobacteria were older than those with tuberculosis. Pre-existing lung disease or AIDS was present in 81% of patients with non-tuberculous mycobacteria and in 17% of patients with tuberculosis. Sensitivity to rifampicin and ethambutol was seen in 95% of *M xenopi* and 96% of *M kansasii* isolates. Relapse occurred in 60% of cases infected with *M xenopi*, 20% infected with *M kansasii*, and in 7% of cases with tuberculosis.**

Conclusions **– In the population studied non-tuberculous mycobacteria occurred most frequently in elderly white subjects with pre-existing lung disease. If mycobacteria are detected in this group, consideration should be given to the possibility of non-tuberculous infection before embarking on treatment. A combination containing rifampicin and ethambutol is effective. The relapse rate for infection with *M xenopi* is high and prospective studies of the effect of the above combination of antituberculosis drugs are needed.**

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Keywords: tuberculosis, non-tuberculous mycobacterial infection, characteristics.

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Non-tuberculous mycobacteria (also called atypical mycobacteria, mycobacteria other than tuberculosis, environmental mycobacteria, opportunistic mycobacteria) are ubiquitous pathogens and have been found in soil, domestic tap water, and in animals.[1 2] Although exposure to non-tuberculous mycobacteria often occurs without any clinical manifestation, there are differences in the virulence of these mycobacteria and clinical manifestations may range from no symptoms or signs to destructive or even fatal disease. When symptoms and signs occur they are often indistinguishable both clinically and radiographically from those caused by *Mycobacterium tuberculosis*.

The bacterial components, pattern of resistance, and outcome of treatment of non-tuberculous mycobacteria are significantly different from those for tuberculosis, resulting in different implications for public health. The disease is not notifiable and contact tracing is not necessary. It is acknowledged that laboratory resistance and clinical resistance to non-tuberculous mycobacteria cannot always be equated.[1 2]

The laboratory report of growth of non-tuberculous mycobacteria is often a cause of anxiety to the patient and a problem to the clinician, as the significance of infection is often difficult to determine in patients with chronic pre-existing lung disease. Most patients with non-tuberculous mycobacteria are initially treated with the conventional combination of isoniazid, rifampicin, and pyrazinamide before the results of culture to identify the bacteria as non-tuberculous are available, resulting in a period of time in which patients are treated with drugs to which the bacteria are frequently resistant.[3] Identification of patients at risk of infection with non-tuberculous mycobacteria, the pattern of drug resistance, and the outcome of treatment are thus important in the provision of appropriate treatment at an early stage.

Table 1 Demographic data

	Non-tuberculous mycobacteria (n=70)	*Mycobacterium tuberculosis (n=221)*
Median (range) age (years)	58 (28–83)	45 (12–91)*
Sex (male/female)	52/18	151/70
Ethnic group (white/non-white)	58/12	104/117**

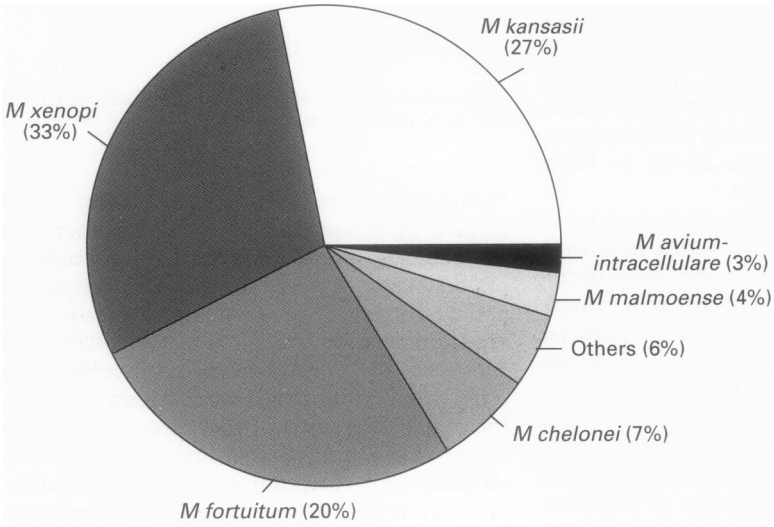
* p<0·0001.
** Odds ratio 4·13, confidence interval 2·11 to 8·14, χ^2 21·3, p<0·0001.

Methods

Microbiological results from the London Chest Hospital and the Royal London Hospital for the seven years from January 1987 to December 1993 were reviewed and all patients with mycobacterial growth were subsequently identified. Patients with non-tuberculous mycobacterial infection were included in the study if at least three colonies were isolated from two samples.

The case notes and chest radiographs of all patients with non-tuberculous mycobacteria were reviewed. Data regarding age, sex, ethnic origin, underlying lung disease or AIDS, pattern of resistance to first line drugs, and outcome of treatment were collected. Patients were considered to have chronic airflow limitation when there was a clear history, radiographic evidence, and respiratory function data to suggest chronic asthma or chronic obstructive pulmonary disease. Patients were considered to have been treated if they received at least six months of therapy. Relapse was considered to have occurred when the same type of mycobacterium was isolated from sputum after cessation of treatment, with or without radiographic changes. Data on relapse were collected for all patients diagnosed between January 1987 and December 1991.

Patients with culture positive *M tuberculosis* diagnosed within the same period were used as a control group.



Types of non-tuberculous mycobacteria included in the study.

Table 2 Pre-existing lung disease and patterns of drug resistance in patients with non-tuberculous mycobacteria

	M xenopi	*M kansasii*	*M fortuitum*	*Others*
Pre-existing lung disease				
Data available	20	16	14	12
CAL	5	9	3	2
Previous tuberculosis	7	2	1	1
Lung cancer	7	0	1	4
AIDS*	0	2	1	2
Others	0	1	3	0
No disease	1	2	5	3
Resistance				
Data available	20	19	10	13
To none of the drugs	6	0	0	0
Isoniazid alone	5	10	0	0
Isoniazid + pyrazinamide	5	1	0	1
Rifampicin + ethambutol	1	0	0	0
To combinations containing streptomycin	1	7	7	4
Other combinations	2	1	3	8

CAL=chronic airflow limitation.
*Although AIDS was included as a pre-existing lung disease, infection with non-tuberculous mycobacteria was the only respiratory manifestation of AIDS in all five patients.

Table 3 Outcome of treatment in patients with non-tuberculous mycobacteria

	M xenopi	*M kansasii*	*M fortuitum*	*Others*
Data available	19	14	13	9
Indicated	12	9	2	6
Clinical improvement + sputum clearance	6	4	0	2
Clinical improvement + persistent positive sputum	2	5	0	1
Died	4	0	2	3

DATA ANALYSIS

Frequency of factors seen in tuberculosis and non-tuberculous mycobacteria were compared using the χ^2 test. Age was compared using the two tailed *t* test.

Results

Over the seven year study period non-tuberculous mycobacteria and *M tuberculosis* were cultured from sputum or bronchoalveolar lavage fluid in 70 and 221 patients, respectively. Non-tuberculous mycobacteria were typed as follows: *M xenopi* 23 cases (33%), *M kansasii* 19 (27%), *M fortuitum* 14 (20%), *M chelonae* 5 (7%), *M malmoense* 3 (4%), *M gordonae* 2 (3%), *M avium intracellulare* 2 (3%), *M scrufulacium* 1 (1·5%), and *M bovis* 1 (1·5%) (figure).

Patients with non-tuberculous mycobacteria were older than those with tuberculosis, and most were white subjects (table 1). Data on patterns of drug resistance were available in 64 (91%) patients with non-tuberculous mycobacteria and on clinical presentation and outcome of the treatment in 57 (81%), and for all patients with tuberculosis.

Data on pre-existing lung disease or AIDS and pattern of drug resistance were available in 62 (89%) of cases of non-tuberculous bacterial infection. Pre-existing lung disease or AIDS was seen in 46 (74%) cases of non-tuberculous mycobacteria and in 37 (16·7%) cases of tuberculosis (odds ratio 14·3, confidence interval 7 to 29·6, p<0·001). None of the patients with tuberculosis was HIV positive. The range of pre-existing lung disease or AIDS in cases of non-tuberculous mycobacteria infection is shown in table 2. Resistance to one or more first line drugs was detected in 56 (90%) cases of non-tuberculous mycobacteria and in seven (3·2%) cases of tuberculosis (table 2). In six patients with *M xenopi* infection the organism was fully sensitive to all antituberculous drugs.

All isolates of *M kansasii* and all but one of *M xenopi* were susceptible to rifampicin and ethambutol.

Sensitivity to streptomycin was seen in all but one isolate of *M xenopi* (95%) and in 13 cases (68%) of *M kansasii*. *M fortuitum* was highly resistant to most first line drugs. In seven cases of tuberculosis the organism was resistant to one (four patients) or more than one (three patients) first line drugs.

All patients with tuberculosis were treated. Treatment was felt to be appropriate in most of the patients with *M xenopi* and *M kansasii* (71% and 64%, respectively). The duration of treatment ranged from six to 28 months (median 15 months), and the outcome is shown in table 3. The major reasons for non-treatment were lack of symptoms and/or radiographic signs, or the presence of advanced underlying lung disease. Spontaneous sputum clearance was seen in one case of *M xenopi* and in seven cases of *M fortuitum*, but in no cases of *M kansasii*.

For patients diagnosed before January 1991 and in whom reliable data were available, relapse occurred in six of 10 patients with *M xenopi*, one of five with *M kansasii*, and in 11 of 157 with tuberculosis.

Discussion

In this study non-tuberculous mycobacteria were isolated mainly from older white patients, whereas culture positive tuberculosis affected a younger population of both white patients and those from the ethnic minorities. *M xenopi* and *M kansasii* were most frequently detected, reflecting the distribution of mycobacteria found in south east England.[4]

As in previous studies,[5–7] the types of lung disease most frequently associated with non-tuberculous mycobacterial infection were chronic obstructive airway disease, lung cancer, and previous tuberculosis.

All isolates of *M kansasii* were sensitive to rifampicin and ethambutol. This is consistent with previous studies.[8–10] For *M xenopi* more than 25% of isolates were fully sensitive and all but one were susceptible to rifampicin and ethambutol. These findings are in contrast with a previous study by Banks *et al* which reported that only 16 of 47 (34%) cases were susceptible to rifampicin.[5] Sensitivity to streptomycin was frequently seen in patients with *M kansasii* and *M xenopi*. This suggests that a combination of rifampicin, streptomycin, and ethambutol may be used when non-tuberculous mycobacteria are suspected pending the results of culture and sensitivity.

The relapse rate was high in patients with *M xenopi*, reaching 60%. In a previous study Banks reported relapse in 26% of patients with *M xenopi* after sufficient treatment with a combination containing isoniazid, rifampicin, ethambutol, and streptomycin. As *M xenopi* is widespread in the environment, reinfection is also possible no matter what treatment regimen has been used. For *M kansasii* relapse occurred in one of the five patients (20%) who had a sufficiently long follow up period. In previous retrospective studies[5 6 9] relapse rates of 0–34% have been described. In the prospective study conducted by the British Thoracic Society the relapse rate for *M kansasii* was 9·7%.[10]

Treatment was started on clinical grounds in two cases of *M fortuitum*; however, both patients subsequently died of their underlying disease (lung cancer and AIDS).

Establishing the relationship between non-tuberculous mycobacteria and the lungs is often difficult, but three types of relationship have been proposed.[8] The first is colonisation, defined as isolation of mycobacteria without conversion of the skin test and with no clinical or radiographic signs of infection; the second is subclinical infection where the skin test becomes positive without any clinical or radiographic signs; and the third is clinical disease with symptoms and signs of infection. Skin tests were not performed in any of the patients in our study. The spontaneous clearance of *M fortuitum* in over half of the cases, however, suggests colonisation or subclinical infection rather than clinical disease.

Our retrospective study suggests that, when mycobacteria are isolated from an older white population with pre-existing lung disease, consideration should be given as to whether this is a non-tuberculous infection. A combination containing rifampicin and ethambutol is suggested when infection with non-tuberculous mycobacteria is suspected. The relapse rate for *M xenopi* is high, and a prospective study of the effect of the above combination of treatment is needed.

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