Non-tuberculous pulmonary infections in Scotland: a cluster in Lothian?

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Abstract

Background - A retrospective study was carried out to confirm the clinical impression that, in Lothian, non-tuberculous mycobacterial infections are as common as pulmonary tuberculosis.

Methods - All pulmonary isolates of Mycobacterium tuberculosis/bovis and non-tuberculous mycobacteria in Scotland from April 1990 to March 1993, and the notes of all patients with M. malmoense isolates in Lothian, were reviewed. Information on mycobacterial culture procedures in Scottish laboratories was obtained as part of an audit project.

Results - Of all pulmonary isolates of mycobacteria in Lothian 53% (108/205) were non-tuberculous strains compared with 18% (140/800) for Scotland outside Lothian. Although comparable in population size and laboratory techniques, Lothian (108) had almost twice as many isolates of non-tuberculous mycobacteria as Glasgow (56), but the proportions of M. malmoense and M. avium intracellularure complex were similar in both areas. Of 41 patients with M. malmoense isolates in Lothian 30 (75%) had clinically significant lung disease; only one was HIV positive.

Conclusions - Non-tuberculous mycobacteria pose an increasing clinical problem in Scotland as a cause of pulmonary disease. There is a cluster of cases with M. malmoense infection in Lothian which cannot be attributed to the high local prevalence of HIV.

Keywords: non-tuberculous mycobacteria, Mycobacterium malmoense, Lothian.
SCOTLAND OUTSIDE LOTHIAN (M TUBERCULOSIS/BOVIS COMPARED WITH NON-TUBERCULOUS MYCOBACTERIA)

There were 800 mycobacterial isolates comprising 644 *M tuberculosis*, 16 *M bovis*, and 140 (18%) non-tuberculous mycobacteria (*M malmoense* 54, *M avium intracellulare* 46, *M xenopi* 11, *M kansasii* 12, and rapid growing mycobacteria 17) in Scotland outside Lothian. The number of patients from whom non-tuberculous mycobacteria were isolated for each health board and the numbers of patients with isolates of *M tuberculosis*, *M bovis*, and non-tuberculous mycobacteria for Lothian and the rest of Scotland are shown in the figure.

LOTHIAN (M MALMOENSE)

There was an even distribution of the 41 Lothian cases with *M malmoense* isolates (24 men, 17 women, median age 58 years) during the three year period (16, 10, and 15 cases).

Thirty one patients had at least two positive cultures and in 20 the first culture positive sample was also film positive. Eleven patients were tested for HIV, 10 had a negative result and one patient had AIDS. Nine patients had their HIV status assessed as part of a research study and none had any risk factors for the virus.

Thirty of the 41 patients (75%) received treatment with varying combinations of antimycobacterial drugs for a median period of 14 months by the end of March 1993. All of these patients fulfilled the diagnostic criteria of non-tuberculous mycobacterial disease as listed by the American Thoracic Society. In all but one patient regimens included at least rifampicin plus ethambutol. Treatment is ongoing in 16 patients and was started in one patient after March 1993.

Ten of the patients treated died and in four (duration of treatment: 3, 13, 21, and 27...
months) necropsy examination revealed that the non-tuberculous infection had contributed to death. Three of these patients had additional infection with *Aspergillus fumigatus*. Identification of the incidence of patients (per 1000 population) with *M. malmoense* isolates in selected postcode districts in Lothian revealed that the majority of them lived in the semi-rural south-east part of the area.

**Mycobacterial Culture Techniques**

Of 20 laboratories which culture mycobacteria routinely 17 (85%) incubated their specimens for at least eight weeks, five followed the practice of the Edinburgh Unit and incubated for 12 weeks, and five extended their incubation periods up to a maximum of 16 weeks for film positive samples.

**Discussion**

*M. malmoense* is characterised by (1) the requirement of prolonged incubation periods of up to 12 weeks although most cultures will be positive at eight weeks; (2) microaerophilia; (3) growth at 25°C and 37°C but not at 45°C; (4) ability to hydrolyse Tween; and (5) a characteristic lipid pattern on thin layer chromatography.

Colonies of the organism on solid media may be small and missed by inexperienced staff. The difference in mycobacterial procedures and lack of experience in detecting the organism might explain some of the geographical variation of *M. malmoense* isolates within Scotland, notably in areas where there were no positive cultures. However, this would not account for the increased number of *M. malmoense* isolates in Lothian compared with Glasgow, as the laboratory techniques were comparable.

Although our data for Scotland refer to pulmonary isolates of *M. malmoense* which, in some cases, might represent casual contamination or colonisation rather than disease, the available literature suggests that about 80% of isolates of *M. malmoense* are clinically significant. This would result in 43 of the 54 cases (80%) in Scotland outside Lothian and a total figure of 73 cases (43 cases in Scotland outside Lothian plus 30 cases in Lothian) for the whole of Scotland from 1990 to 1993, which is more than a threefold rise in incidence compared with that quoted by France et al.

Some clustering of cases was detected within the south-east of Lothian. The gross incidence does not take into account factors such as age distribution and environmental influences, but there was no obvious correlation with deprivation scores or overall mortality.

The natural reservoir for *M. malmoense* is unknown, although the organism has been isolated from fresh water in Finland (personal communication, Katila) and from stools of healthy individuals. All households in Lothian postcode areas receive their water as a mixture from a number of reservoirs which render water contamination as a cause of clustering unlikely.

In summary, this study has revealed that non-tuberculous mycobacteria pose an increasing clinical problem in Scotland, and that there is a cluster of cases with pulmonary *M. malmoense* infections in Lothian which cannot be attributed to the high local prevalence of HIV. Our findings might relate in part to laboratory practice and experience in the Reference Laboratory, though this does not hold true for the comparison of Glasgow and Edinburgh. Epidemiological studies into the possible environmental habitat of *M. malmoense*, documentation and follow up of all patients with *M. malmoense* isolates, and molecular typing of isolates should help to clarify our findings further.

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