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Are we missing opportunities to confirm the diagnosis of tuberculosis by microbial culture?

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Summary
Setting: Tuberculosis (TB) incidence is rising globally, with drug resistance becoming increasingly problematic. Microbiological confirmation ensures correct anti-tuberculous chemotherapy.
Objective/design: We retrospectively analysed all TB cases diagnosed in Central Manchester in 2009 investigating how often we are not achieving microbiological diagnosis, factors influencing this and whether opportunities to obtain microbiological samples are missed.
Results: 128/156 (82%) cases had samples sent for microbiology. Factors affecting this included disease site, with ocular disease least likely to be sampled ($p < 0.0001$), and patient age (with children less likely to be sampled $p = 0.002$). Ethnicity did not affect sampling (n.s.). Overall, 92/156 (59%) cases were culture positive. Negative culture was related to specimen type ($p < 0.0001$) and patient age ($p = 0.019$), with children significantly less likely to have a positive culture. Ethnicity and disease site did not affect culture results. There was a trend towards culture positivity being more common in pulmonary (75%) than non-pulmonary (46%) disease (n.s.). In only 7 (4%), could samples have been sent where they were originally absent (3) or further samples obtained where the cultures proved to be negative (4).
Conclusion: Despite an overall culture positive rate of 59%, opportunities to achieve microbiological confirmation are seldom missed. In our centre, which is typical of UK practice, this

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lack of capacity to increase microbiological confirmation, particularly in an era of increasing importance of extra-pulmonary TB, is concerning. Improvements in sample acquisition and laboratory methods are urgently required.

Introduction

Globally the impact of tuberculosis (TB) is vast; in 2011 there were 8.7 million new cases and 1.4 million deaths, with only 66% diagnosed and notified to national programmes [1]. The World Health Organisation (WHO) recommends that guidelines for diagnosis and culture are followed at a national level, according to national TB incidence and prevalence of drug resistance. TB cases in the UK rose from 6724 in 2000—8963 in 2011 [2]. There was an overall culture positive rate of 59%, which was higher in pulmonary (70%) versus non-pulmonary (48%) disease. Currently the National Institute of Clinical Excellence (NICE) guidance recommends that pulmonary disease is diagnosed by the collection of multiple sputum samples (spontaneous or induced) or broncho-alveolar lavage, with treatment commenced soon after samples are taken [3]. NICE also recommend extra-pulmonary TB diagnosis, if suspected, is achieved by sending samples for TB culture. In the UK in 2011 52% of cases had pulmonary disease, a fall from 59% in 2000—2003 [2]. The proportion of extrapulmonary disease is higher in non UK-born cases [2]. TB incidence has risen in Central Manchester between 2000 when there were 114 notifications and 2009 when there were 196 [4].

Drug resistance makes management more complicated and expensive and is an important cause of mortality and morbidity. A gradual rise in some drug resistances is being seen in the UK [2] in 2011 multi-drug resistance or MDR-TB (resistance to at least rifampicin and isoniazid) was seen in 1.6% cases overall and resistance to at least one first line antibiotic was seen in 8.4%. Internationally, the full extent of drug resistance is unknown but China, Russia and India appear to have the highest incidence. Countries in the former Soviet Union have a high incidence of drug resistance, coupled with low rates of sensitivity testing and appropriate treatment [5].

It is therefore vital to obtain samples for microbiological culture and sensitivity to provide absolute confirmation of the diagnosis of tuberculosis and to ensure adequate treatment and prevent spread of drug-resistant disease.

In Central Manchester we have seen an increase in the proportion of cases where samples were sent for microbiological confirmation. 69% had samples sent to microbiology in 2000 and 79% in 2009 [6], but despite this we have been concerned there may have been missed opportunities to obtain proof of the causative organism. We therefore undertook this study to investigate how often we sent samples and how often we achieved microbiological confirmation of TB. We examined what factors affected both sampling and culture results. In addition, we further investigated cases where there were no samples or negative cultures to assess whether there were missed opportunities for microbiological confirmation.

Methods

A retrospective analysis was carried out on all cases (adult and paediatric) diagnosed with TB at Central Manchester NHS Foundation Trust (CMFT) in 2009 identified from our TB database. CMFT is a 1400 bed hospital serving an inner-city population with considerable ethnic diversity, typical of UK cities. The TB unit co-ordinates the treatment of all active TB in this population, regardless of disease site or underlying disease, with treatment adhering to NICE guidance. Around 200 cases per year are seen (accounting for 1/4 cases in Northwest England), of which 50% are pulmonary and 10% have co-existing HIV infection. TB cases in Manchester are similar to those in the rest of the UK, in terms of ethnicity of patient and site of disease [2]. Central Manchester is however under resourced compared to other cities regarding TB nurse to notification ratio and there has recently been a significant increase in clinic numbers compared to other UK cities [4].

TB cases were defined as any subjects who were notified to the HPA as being treated for active TB or any subject restarting TB treatment who had relapsed within 12 months of previous treatment. No cases were retreated in the study period and therefore no cases were counted twice. Demographic details, site of disease, types of specimens and results of TB culture were recorded from computer records, case notes and TB nurse records. Cases were analysed in detail for reasons why specimens were not taken or culture positivity was not confirmed. A judgement was made on whether this was acceptable or non-acceptable management based on the clinical circumstances surrounding the case. Outcome data and relapse rates were also recorded.

Routine investigation of pulmonary TB at CMFT includes obtaining 3 adequate sputum samples or bronchoscopic samples, unless the procedure is contra-indicated. For non-pulmonary disease, Fine needle aspiration (FNA) or biopsy of disease site is routinely performed, except in ocular TB. Clinically acceptable cases were deemed as those in which in the view of the authors and doctors managing the patient an acceptable balance was achieved between the need for invasive procedures, potential harm to the patient and delays in starting treatment, weighed against need to commence treatment in a relatively short time frame.

Culture positivity and whether samples were sent for culture were compared with site of disease, age of patient, ethnic origin and sample type. Statistical analysis was carried out using the software package SPSS. The Chi squared test was used to compare numbers of samples sent for culture and culture positivity with site of disease, age of patient, ethnic origin and sample type.