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Cluster of non-tuberculous mycobacteraemia associated with water supply in a haemato-oncology unit

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SUMMARY

Non-tuberculous mycobacteria (NTM) are ubiquitous environmental organisms but rarely cause infections. Clinical, microbiological and epidemiological investigations and subsequent management of a cluster of NTM bacteraemia on a haemato-oncology unit are reported. From October 2007 to July 2008, five patients being managed for haematological malignancies developed pyrexia and general malaise. *Mycobacterium mucogenicum* (four patients) and *Mycobacterium neoaurum* (one patient) were identified from their blood cultures. The environment, in particular the water system, was investigated to identify the source of the infection and multiple water samples were cultured according to established criteria. NTM were also isolated from the hospital water system. Central venous catheters (CVCs) were removed and the patients were successfully treated with antibiotics. Environmental measures and changes in CVC care were introduced to prevent further episodes of NTM bacteraemia in these patients. Despite these measures, NTM continued to be present in the water system, but new clinical cases were not identified. NTM are common environmental organisms and are recognized as being difficult to remove from water systems. CVCs were presumed to be the portal of entry in this cluster of NTM bacteraemia, and the implementation of changes to CVC care protocols was successful in preventing further infections in this immunocompromised patient group.

Introduction

Central venous catheters (CVCs) are essential for the delivery of chemotherapeutic agents, administration of blood products and total parenteral nutrition (TPN), and the management of infections in patients with haematological malignancies, especially those undergoing intensive therapy such as haematopoietic stem cell transplantation. The risk of CVC-associated bacteraemia is increased in this patient population as a result of a number of factors including prolonged neutropenia, allografting and the administration of TPN. Environmental organisms have been increasingly reported as a cause of bacteraemia in this patient group.

Overall, CVC-associated mycobacterial infections are uncommon but clusters of cases of bloodstream infections caused by non-tuberculous mycobacteria (NTM) secondary to water contamination are known to occur. Species such as *Mycobacterium mucogenicum*, *Mycobacterium phocaicum* and *Mycobacterium chelonae* have been reported.[1–5] NTM are environmental organisms, commonly found in domestic water supplies, and complete eradication from hospital water supplies is difficult. Misinterpretation of the initial microbiological findings may lead to delays in diagnosis.[4] Potential clinical complications of infection include bacteraemia, septic emboli, lung colonization and soft tissue and bone infections. The prompt identification and investigation of clusters of cases is of prime importance in prevention and control by appropriate corrective measures.

In this report, a cluster of five cases of CVC-associated NTM bacteraemia over a 10-month period in a haemato-oncology unit are described. The investigations undertaken to identify clinical

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cases and sources of infection along with the prevention and control measures are discussed.

Methods

Hospital setting

The Western General Hospital in Edinburgh is a tertiary care teaching hospital in central Scotland. The haemato-oncology unit has 24 inpatient beds; 10 of these are on the transplant unit (all single room accommodation with en-suite showers and toilets) where patients undergoing intensive therapy, including haematopoietic stem cell transplants (HSCTs), are treated within protective isolation. The other 14 inpatient beds are located in an adjacent ward, which has a mixture of single-, two-, and four-bedded rooms and communal showers. The day-patient unit is housed on the same site but in a separate building. The unit performs around 10 sibling allografts and 25 autografts per year.

Description of incident

The first patient (A), who was post-autologous peripheral blood stem cell transplant for relapsed follicular non-Hodgkin lymphoma (NHL), presented with general malaise and high temperature in October 2007. A Gram-positive bacillus was cultured from blood taken from the Hickman line but was initially misidentified as a coryneform bacterium. When a repeat culture was positive, further tests identified it as an atypical mycobacterium. Subsequently, four similar cases were identified between June and July 2008.

Epidemiology

Clinical data on the patients involved were obtained from the case notes and the laboratory information management system.

A case was defined as any patient on the unit with pyrexia and with NTM bacteraemia who had been admitted to the haematology transplant unit between October 2007 and October 2008.

Microbiological methods

Culture and identification

Blood cultures were taken from each lumen of the Hickman line of patients with fever and other evidence of infection and, where possible, samples for blood culture were also obtained from a peripheral vein (BacT/Alert® 3D, bioMérieux, Hazelwood, MO, USA). On removal of colonized Hickman lines the catheter tips were sent for microbiological investigation and were processed by semiquantitative culture.[6]

Positive blood culture bottles were subcultured on to non-selective media and the NTM isolates were identified by Ziehl Neelsen (ZN) stain and cultural characteristics, in accordance with accepted protocols.[7] The NTM were confirmed by the Scottish Mycobacteria Reference Laboratory (SMRL) with a commercial kit combining polymerase chain reaction and hybridization (GenoType Mycobacterium CM kit; Hain Lifescience GmbH, Nehren, Germany). Sequencing of the 65 kDa heat shock protein gene (*hsp* 65) followed by comparison of the sequence data from the online database (GenBank) was used to identify isolates not confirmed by this method. Determination of sensitivity to co-amoxiclav, carbapenems, clarithromycin, amikacin, ciprofloxacin, cotrimoxazole, vancomycin, tetracycline, tigecycline and linezolid was performed using E-tests (AB Biodisk, Solna, Sweden).

In response to the NTM cluster, surveillance blood cultures were performed to detect mycobacterial colonization of Hickman lines from patients admitted to the haemato-oncology unit during the period of the cluster. For this purpose weekly Hickman line blood cultures were taken from all inpatients and those who had been recently discharged, over a four-week period. These were additional to the blood cultures performed for clinical indications.

Environmental samples

Water sampling was commenced in July 2008 and repeat water testing was done at regular intervals. Water was collected from all hot and cold showers, sinks, and baths on the haemato-oncology unit before and after running the water for 2 minutes. The water in the mains tank inlets and other areas thought to be a potential source of biofilm was also sampled. Water samples were tested by pour plate method using yeast extract agar to determine aerobic colony counts.[8] Counts >300 cfu/mL were determined using suitable dilutions. For detection of NTM, a 100 mL water sample was drawn through a 47 mm diameter hydrophilic membrane under negative pressure. The membrane was then placed on tryptone soy agar and blood agar with GC (gonococcal) supplement and incubated at 35 °C for 48–72 h and 30 °C for one week respectively.[9] Growth on the membrane was screened for the presence of NTM by the ZN stain, and positive samples were sent to the SMRL for identification. At SMRL, 5×20 mL aliquots of the water were centrifuged and the deposit pooled together, plated on to LJ slopes and inoculated into Bactec MGIT 960 (Becton Dickinson, Oxford, UK) bottles. Isolate identification was confirmed as outlined in the previous section.

Environmental investigations

An investigation of the water system was carried out by the Estates Department to identify potential contributing factors.

Results

Epidemiology

NTM bacteraemia was identified in five patients. The patient clinical characteristics are summarized in Table I. All five patients presented with pyrexia. They all had Hickman lines, had been inpatients on the transplant unit and had also attended the day-patient unit. Three patients were undergoing intensive treatment for acute myeloid leukaemia, one patient was <100 days from autologous HSCT for follicular lymphoma and one patient was receiving intensive therapy for transformed follicular lymphoma. The clinical outcomes for the patients are summarized in Table I. The Hickman lines were presumed to be the portal of entry of NTM and were removed or replaced when NTM were identified in blood cultures. Initial antibiotic therapy was continued in patients with resolving pyrexia; otherwise the patients' antibiotics were changed to clarithromycin and meropenem as per antibiotic sensitivities. One patient (A) died of post-transplant complications not directly related to the infection, four weeks after diagnosis of NTM bacteraemia. The other patients had no long-term consequences of the infection.

Microbiological results

Clinical samples

In total, 14 blood culture bottles were positive for NTM (all aerobic), from five clinically infected patients. All patients had multiple blood cultures taken and all had more than one blood culture bottle positive with mycobacteria. Three patients had positive peripheral blood cultures in addition to positive Hickman line