Public Health England

Protecting and improving the nation's health

Mycobacterium chimaera Infections Associated with Cardiopulmonary Bypass

Clinical guidance for secondary care

Version 1

A resource produced by Public Health England and partners

About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-class science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health, and are a distinct delivery organisation with operational autonomy to advise and support government, local authorities and the NHS in a professionally independent manner.

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Summary

Mycobacterium chimaera, an environmental non-tuberculous mycobacteria, has been newly recognised as a cause of severe infections in patients who have undergone cardiothoracic surgery. Evidence indicates this is likely to be transmitted from part of the cardiopulmonary bypass equipment.

M. chimaera is now understood to be a cause of endocarditis, severe disseminated infection and chronic sternal wound infection, which may manifest many years after surgery on bypass. *M. chimaera* infection has an insidious and non-specific presentation, is not always identified through conventional microbiology, and requires specific treatment. It has a high mortality.

In addition to the usual investigations, specific *M. chimaera* microbiological investigations must be undertaken in patients who have been on cardiopulmonary bypass and who present with endocarditis, symptoms of chronic systemic infection, or chronic sternal wound infection.

Background

M. chimaera is a non tuberculous mycobacterium which is a member of the *Mycobacterium avium* complex, most similar to *Mycobacterium intracellulare*. It was relatively recently described and would have been identified previously as *M. intracellulare*. This type of mycobacterium is widespread in the environment, including tapwater, and is usually associated clinically with respiratory disease or with disseminated disease in the immunocompromised patient.

It is now recognised that *M. chimaera* has caused severe infections in a small proportion of patients who have had cardiac surgery. UK and international investigations have implicated contaminated heater cooler units used for cardiopulmonary bypass, transmitting infection from their water tanks via generation of a contaminated aerosol with particles reaching the operative field.

The risk remains low, for example <1 case per 100,000 coronary artery bypass graft procedures. The highest risk group is patients who have undergone valve replacement or repair, whose risk is currently estimated at 1 case per 5000 procedures. However, *M. chimaera* infection can be difficult to diagnose, requires specific treatment, and has a high mortality.

This guidance for use in secondary care provides information on:

- recognising and diagnosing cases of *M. chimaera* infection
- where to access expert advice on diagnosis and treatment
- reporting requirements

For more information about the risk and the UK investigation, please see the guidance at www.gov.uk/government/collections/mycobacterial-infections-associated-with-heater-cooler-units

Recognising *M. chimaera* infections associated with cardiopulmonary bypass: features of UK cases

Clinical data in this section is based on the **first 25 UK cases**. Clinical understanding of this infection continues to evolve. Increasing awareness among patients and clinicians means that patients now may be investigated earlier with less developed disease.

Please continue to check the webpage for updates:
www.gov.uk/government/collections/mycobacterial-infections-associated-with-heater-cooler-units

Incubation period

M. chimaera infections following cardiothoracic surgery can have long latency periods. The time between surgery and development of symptoms ranged from 2-58 months. The upper limit is unknown.

Risk factors

The possibility of *M. chimaera* infection should be considered in any patient who has had surgery on cardiopulmonary bypass, who has been on ECMO or who has been otherwise exposed to a running heater cooler unit at any time.

The highest risk procedures in the UK are valve replacement or repair, with one case following CABG. Internationally *M. chimaera* infection has also been reported after CABG, vascular grafts, LVAD insertion and heart/lung transplant.

The most common comorbidities identified were ischaemic heart disease (7/25) and diabetes mellitus (6/25). Only one patient was reported as being immunosuppressed (due to haematological malignancy); no patients were identified as infected with HIV.

Clinical and laboratory features at presentation

Four of the 25 UK cases presented with chronic sternal wound infection, 8 with prosthetic valve endocarditis or vascular graft infection and 13 with disseminated infection. Sites of infection in disseminated disease included liver, bone marrow, bone (especially spine), lungs, lymph nodes, skin, brain and eyes.

Common clinical and laboratory features at presentation (>50% of cases) were:

- reported fever (though only half of patients were objectively febrile at presentation)
- malaise
- weight loss
- cough or shortness of breath
- lymphocytes <1.0 x 10^9/l
- albumin <30 g/L
- alkaline phosphatase >150 IU/l
- CRP <50 mg/L

Notable but less common features in the UK patient group at presentation included:

- splenomegaly
- eye involvement (eg choroidoretinitis)
- total white blood cell count <3.5 x 10^9/l
- platelets <150 x 10^9/l

The presentation and laboratory features of the disease **can be very similar to sarcoidosis**. *M. chimaera* investigations should be undertaken in anyone in whom a diagnosis of sarcoidosis is being considered and who has an appropriate history of cardiothoracic surgery.

Patients with *M. chimaera* infected wounds presented with chronic non healing sternal wounds not responding to conventional antibiotic therapy. Three of four sternal wound infection cases went on to be diagnosed with deep (aortic graft) infections.

Imaging

Echocardiography (including transoesophageal) was normal in some patients at presentation who later went on to be diagnosed with prosthetic valve endocarditis, disseminated disease or aortic graft infection. Although echocardiography is an important part of the assessment and contributed to some diagnoses, a normal echocardiogram alone cannot be used to exclude current or developing infection.

Microbiology

Mycobacterial blood cultures were positive in the majority of cases where they were performed. Mycobacteria were grown from cardiac samples in all cases where mycobacterial culture was performed, although this was undertaken in only five cases. 16S rRNA gene sequencing also detected mycobacteria in cardiac tissue, although it is a suboptimal test if used in isolation as it does not provide antimicrobial susceptibility data.

Histopathology

8 of 14 UK cases who had biopsies of affected sites had granulomatous pathology described.

Outcome

As of January 2017, 15 of the 25 patients with *M. chimaera* infection have died (of whom 10 died despite treatment for *M. chimaera*). Four have completed treatment and are well, and six continue on treatment.

Investigating patients for *M. chimaera* infection associated with cardiopulmonary bypass

1. Discuss all suspected cases with cardiology and infectious diseases specialists.

2. Patients should be investigated as appropriate for the clinical presentation, following national guidelines (eg for endocarditis) and including appropriate imaging and microbiology for the common causes of the syndrome. *M. chimaera* remains a rare cause of post surgical infection.

3. In addition, all patients who have had exposure to heater cooler units and who present with the relevant clinical syndromes should have microbiological investigations specifically directed towards *M. chimaera*.

4. Patients with suspected or confirmed *M. chimaera* sternal wound infection patients should have imaging to assess whether there is underlying deep infection

Microbiological investigation

Mycobacterial culture is the essential investigation for all sample types. It allows full characterization and antimicrobial susceptibility testing. 16S rRNA gene sequencing may be used as a supplementary test, but a negative result does not rule out infection. Microbiology results should be considered alongside histopathology findings

It is essential to inform the testing laboratory of the possibility of *M. chimaera* infection to ensure correct processing and also to ensure samples are taken into the correct containers.

- **Endocarditis**: Take three sets of mycobacterial blood cultures (on different days if feasible).Obtain correct containers from your local laboratory. It is preferable to take these whilst the patient is off antibiotics which may be active against mycobacteria such as quinolones or macrolides, however if not possible the blood cultures should still be taken. Any non-repeatable samples (eg valve tissue) should be tested by mycobacterial culture (**essential**) and 16S rRNA gene sequencing in addition to the usual investigations

- **Wound infection**: Mycobacteria cannot be cultured from swabs; send a tissue, bone or pus sample, specifically requesting mycobacterial culture

- **Patients with possible disseminated disease:** Take three sets of mycobacterial blood cultures and early morning urine for mycobacterial culture. Obtain correct containers from your local laboratory. It is preferable to take these while the patient is off antibiotics which may be active against mycobacteria such as quinolones or macrolides, however if not possible the blood cultures should still be taken. Consider obtaining appropriate tissue samples depending on the distribution of disease, for example liver biopsy, bone marrow. All tissue samples should be sent for mycobacterial culture (essential) +/- 16S rRNA gene sequencing, as well as conventional microbiology and histopathology

- **Patients with pulmonary infiltrates**: In addition to three sets of mycobacterial blood cultures, consider sending bronchoalveolar lavage +/- relevant biopsies for mycobacterial culture (essential) and 16S rRNA gene sequencing

Other infections potentially acquired from heater cooler units

Other organisms have been detected in heater cooler units and may pose a theoretical risk of transmission to patients and in some cases staff. These include *Legionella* spp and other bacteria found in water environments such as *Stenotrophomonas maltophilia*. A further discussion of this is available in the infection control guidance: www.gov.uk/government/publications/infections-associated-with-heater-cooler-units-used-in-cardiopulmonary-bypass-and-ecmo

Clinical management

In the first instance, clinical advice should be obtained from the local infection team. Infection teams requiring specialist advice should contact the nearest reference service:

England (National Mycobacterial Reference Service South, London)
Dr Eliza Alexander 020 8327 6957
eliza.alexander@phe.gov.uk, copying nmrl@phe.gov.uk

England (National Mycobacterial Reference Service Central/North, Birmingham)
Dr Grace Smith 0121 424 3247 or 0121 424 2500
grace.smith@phe.gov.uk, copying esther.robinson@phe.gov.uk

Wales (PHW Mycobacterial Reference laboratory, Cardiff)
Dr Matt Backx 029 20744515
matthijs.backx2@wales.nhs.uk

Scotland (Scottish Mycobacteria Reference Laboratory)
Dr Ian Laurenson 0131 242 6016 and 0131 242 6022/6033
lothian.smrl@nhs.net

NI (Royal Victoria Hospital)
Regional Infectious Disease Service 028 90329241

Deaths

Doctors responsible for the care of patients who die of known or suspected *M. chimaera* infection as a result of medical intervention are reminded that this may be considered an unnatural death and as such should be reported to the Coroner for the area (or in Scotland, the Scottish Fatalities Investigation Unit of the Crown Office and Procurator Fiscal Service).

Reporting requirements

The following arrangements cover cases identified in **England**. For arrangements for Wales, Scotland and Northern Ireland, please refer to local guidance.

Infection specialists should report to their local health protection team (HPT) any cases of non tuberculous mycobacterial infection in patients who have had cardiothoracic surgery or ECMO, and also of any cases of other infections, including Legionella, which are strongly believed to be linked to HCUs.

The HPT will request information for a short case report form, which will be submitted to the relevant national surveillance team. National aggregate data will be shared at: www.gov.uk/government/collections/mycobacterial-infections-associated-with- heater-cooler-units