Clinical Guidance for physicians regarding patients at risk of NTM infection

This information is intended to provide clinical advice to general practitioners and specialists caring for patients who have undergone open cardiac surgery. There is potential for exposure to nontuberculous Mycobacteria (NTM) *Mycobacterium chimaera* during procedures involving valve replacement / repair or mediastinal vascular graft insertion, between the dates of 1 October 2011 and August 2016.

**Background**

There have been clusters of *Mycobacterium chimaera* infections reported in multiple countries, predominately resulting in prosthetic valve endocarditis (PVE). Disseminated disease without obvious endocarditis may also occur. These infections have been associated with cardiac surgery that has involved the use of heater cooler units (HCUs).

HCUs are used during cardiopulmonary bypass required to perform open heart surgery. HCUs regulate temperature of patients during surgery. While the HCU does not come into contact with the patient, the cause of the infection appears to be linked to biofilm that develops inside the unit, allowing growth of Mycobacteria. The Mycobacterium is subsequently aerosolised into the environment by a unit fan during HCU use. This is due to a combination of issues including some aspects of the design and manufacture of the HCUs.

The initial theory was that the infections were due to cleaning processes which facilitated the growth of biofilm, and the manufacturer subsequently revised the disinfection and maintenance procedure instructions accordingly. A recent article by Haller et al. published in Euro Surveillance on 28 April 2016, is suggesting a possible point source contamination. This would explain why all clinical cases reported to date have involved the single species, *M. chimaera*.

*M. chimaera* is an uncommon cause of NTM infection in Queensland. It is a member of the “MAC” complex organism and not routinely identified to species level.

**Risk**

Recent information indicates that the infections are almost exclusively associated with surgery involving some form of prosthetic implant (e.g. valves or grafts), suggesting that the organism requires a prosthetic surface to adhere to. The time to diagnosis can be several years following exposure to this organism as the incubation period for infection can be up to five years, although median time to symptoms is approximately 18 months.

Without knowing whether a patient was actually exposed to a *M. chimaera*-contaminated HCU, it is difficult to estimate individual risk. Universally the risk is considered very low. Patients who have had cardiopulmonary bypass for coronary bypass grafting, transplantation or other cardiac procedure not involving prosthetic material, appear to be at extremely low risk of any infection.
Initial patient assessment

Every effort should be made by the general practitioner and/or attending specialist to perform an initial patient assessment prior to referral to an infectious disease (ID) physician.

Clinicians should be vigilant for non-specific signs and symptoms of M. chimaera infection which may include one, or a combination of the following, occurring for two weeks or more:

- unexplained fevers
- unexplained weight loss
- increasing shortness of breath
- night sweats
- joint or muscular pain
- nausea, vomiting or abdominal pains
- malaise (note: fevers or night sweats or weight loss should also be present if malaise)
- pain, redness, heat or pus around the surgical site
- failure to gain weight (paediatrics only)

More common causes of the above symptoms should be considered before referral and specialised testing for disseminated Mycobacterial infection is undertaken. However, conventional blood cultures should always be performed early with presentation of the above symptom complex. This should be particularly noted in diagnosing other causes of prosthetic valve endocarditis, which occur at a rate of 1-3% in the first year after surgery and 3-6% after five years.

Patient assessment for Mycobacterial PVE or disseminated disease

Diagnosis of PVE or disseminated infection due to M chimaera is based on:

- detailed patient history
- physical examination – signs of valvular pathology, splenomegaly and signs of retinal involvement should all be clinically reviewed
- routine blood tests: FBE, Biochemistry CRP - Disseminated NTM infections should be considered in the symptomatic patient with unexplained anaemia, thrombocytopenia, pancytopenia, or unexplained elevated liver function tests
- imaging studies based on signs and symptoms
- echocardiography including transoesophageal echocardiography
- biopsy of any tissues as may be implicated with a systemic infection

Specialised testing involving blood culture for NTM (AFB blood culture) and bone marrow culture for NTM should only be ordered by (or on advice from) an infectious diseases physician or consultant microbiologist. When recommended, two MycoF lytic bottles should be collected on separate days to investigate possible PVE or disseminated non-tuberculous Mycobacterial infection including M. chimaera.

Only patients who have signs and symptoms consistent with prosthetic valve endocarditis or a disseminated infection syndrome such as Pyrexia of Unknown Origin (PUO) should be investigated. There is NO indication to investigate asymptomatic patients for possible systemic NTM infection.

There is no recommended screening laboratory test, culture or imaging modality for the asymptomatic patient.

For a symptomatic patient with a prolonged period of unexplained illness of two weeks or more, despite routine work-up, strongly consider referring the patient to their treating cardiologist or cardiac surgeon.
(especially if surgery is recent) and/or an Infectious Diseases Physician. They will be able to perform further investigations.

AFB cultures should not be ordered on asymptomatic patients. Patients should be informed of the risk and limitations of tests in asymptomatic patients.

HCU-associated infections have not included pulmonary infections, and sputum cultures for Mycobacteria are not indicated in the absence of other features of pulmonary disease and unrelated to previous cardiac surgery.

Patient treatment

Treatment for NTM infection requires multiple antibiotic therapy and should be prescribed by an ID specialist.

The optimal duration of therapy is unknown, but 12 months is commonly cited.

In cases reported overseas, revision cardiac valve surgery is commonly required.

There is no antimicrobial prophylaxis treatment for the potentially exposed patient. In this instance, antimicrobial prophylaxis could promote resistance if subclinical disease is already present.

Patient referrals and notification

It is strongly recommended that an infectious diseases physician be consulted prior to requesting specialised tests for Mycobacteria especially as laboratory capacity to provide such testing is very limited. Long term management requires an interdisciplinary approach and is best managed and co-ordinated by an ID physician experienced in the treatment of Mycobacterial diseases.

All patient cases of M. chimaera or other Mycobacteria are Notifiable in Queensland under the Public Health Act 2005.

Queensland Health has commenced sending information to every patient who has had open cardiac surgery involving a heart valve or aortic vascular graft surgery in a public hospital over the past 5 years, and will confirm if recent tests undertaken have identified the bacteria in the heater cooler units. Letters to patients are expected to be received by the end of February 2017.

References that may be of interest


