Healthcare-associated prosthetic heart valve, aortic vascular graft, and disseminated Mycobacterium chimaera infections subsequent to open heart surgery

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Abstract: Aims We identified 10 patients with disseminated Mycobacterium chimaera infections subsequent to open-heart surgery at three European Hospitals. Infections originated from the heater–cooler unit of the heart–lung machine. Here we describe clinical aspects and treatment course of this novel clinical entity. Methods and results Interdisciplinary care and follow-up of all patients was documented by the study team. Patients’ characteristics, clinical manifestations, microbiological findings, and therapeutic measures including surgical reinterventions were reviewed and treatment outcomes are described. The 10 patients comprise a 1-year-old child and nine adults with a median age of 61 years (range 36–76 years). The median duration from cardiac surgery to diagnosis was 21 (range 5–40) months. All patients had prosthetic material-associated infections with either prosthetic valve endocarditis, aortic graft infection, myocarditis, or infection of the prosthetic material following banding of the pulmonary artery. Extracardiac manifestations preceded cardiovascular disease in some cases. Despite targeted antimicrobial therapy, M. chimaera infection required cardiothoracic reinterventions in eight patients. Six out of 10 patients experienced breakthrough infections, of which four were fatal. Three patients are in a post-treatment monitoring period. Conclusion Healthcare-associated infections due to M. chimaera occurred in patients subsequent to cardiac surgery with extracorporeal circulation and implantation of prosthetic material. Infections became clinically apparent after a time lag of months to years. Mycobacterium chimaera infections are easily missed by routine bacterial diagnostics and outcome is poor despite long-term antymycobacterial therapy, probably because biofilm formation hinders eradication of pathogens.

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Healthcare-associated prosthetic heart valve, aortic vascular graft, and disseminated Mycobacterium chimaera infections subsequent to open heart surgery

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Aims
We identified 10 patients with disseminated Mycobacterium chimaera infections subsequent to open-heart surgery at three European Hospitals. Infections originated from the heater—cooler unit of the heart—lung machine. Here we describe clinical aspects and treatment course of this novel clinical entity.

Methods and results
Interdisciplinary care and follow-up of all patients was documented by the study team. Patients’ characteristics, clinical manifestations, microbiological findings, and therapeutic measures including surgical reinterventions were reviewed and treatment outcomes are described. The 10 patients comprise a 1-year-old child and nine adults with a median age of 61 years (range 36–76 years). The median duration from cardiac surgery to diagnosis was 21 (range 5–40) months. All patients had prosthetic material-associated infections with either prosthetic valve endocarditis, aortic graft infection, myocarditis, or infection of the prosthetic material following banding of the pulmonary artery. Extracardiac manifestations preceded cardiovascular disease in some cases. Despite targeted antimicrobial therapy, M. chimaera infection required cardiac surgical reinterventions in eight patients. Six out of 10 patients experienced breakthrough infections, of which four were fatal. Three patients are in a post-treatment monitoring period.

Conclusion
Healthcare-associated infections due to M. chimaera occurred in patients subsequent to cardiac surgery with extracorporeal circulation and implantation of prosthetic material. Infections became clinically apparent after a time lag of months to years. Mycobacterium chimaera infections are easily missed by routine bacterial diagnostics and outcome is...
poor despite long-term antimycobacterial therapy, probably because biofilm formation hinders eradication of pathogens.

**Keywords**  
*Mycobacterium chimaera* • Cardiac surgery • Prosthetic valve endocarditis • Aortic graft infection • Myocarditis • Health-care associated infection

### Introduction

Non-tuberculous mycobacteria (NTM) can cause pulmonary disease, particularly in patients with pre-disposing structural lung disease, skin, soft tissue and bone infections, endocarditis, and disseminated infections in immunocompromised hosts. Signs and symptoms are variable and often non-specific. Also, a growing number of case reports of cardiosurgical site infections due to NTM have been reported in recent years.1–5 Thus far, only rapid-growing NTM have been found to be associated with prosthetic valve endocarditis (PVE).1–4,6 Recently, we published two cases of PVE and bloodstream infection due to *Mycobacterium chimaera*,7 a slow-growing NTM and member of the *M. avium* complex (MAC)8 that has previously been cultured from tapwater in patients’ households.9

Cardiosurgical outbreaks of NTM infections have been associated with contaminated water used for the cardioplegia solution,4 contamination during the manufacturing process9 or use of a contaminated patch for septum defect repair,3 but source identification often failed.7,10 In the course of an outbreak at the Zurich Heart Center, *M. chimaera* was cultured from air sampling in the operating theatre and from water tanks of heater–cooler units (HCUs) serving the heart–lung machine. Identical randomly amplified polymorphic DNA–polymerase chain reaction (RAPD-PCR) results indicated that patients were infected by intraoperative contamination of the surgical site due to airborne transmission of microorganisms sprayed from the ventilation outlet of HCUs into the operating theatre.11,12 As of February 2015 a total of six cases were identified in Zurich (Switzerland). Another four patients were detected in parallel in Freiburg, Zwolle and Rotterdam, where the notification of respective HCUs pointing to a similar transmission route. On 30 April 2015, an alert was published by the European Centre for Disease Prevention and Control, warning healthcare providers in care of patients who have undergone open-heart surgery to be vigilant for cases of endocarditis or other cardiovascular infections of unknown origin and consider testing mycobacteria.13,14 Here we aim to give a comprehensive description of the clinical manifestations and outcome of this novel disease entity. In addition, we provide exposure criteria and a case definition to facilitate the detection of potential cases on a global level.

### Methods

**Exposure criteria**

A former open-heart surgery and implantation of a cardiovascular implant were our exposure criteria.

**Case definition**

Our clinical criteria were: PVE, prosthetic vascular graft infection (PVGI), or disseminated infection including embolic and immunologic manifestations.

**Confirmed cases**

Confirmed cases were defined as cases meeting the clinical and exposure criteria and *M. chimaera* proven by culture or polymerase chain reaction (PCR) identification from an invasive sample from the cardiac surgery site.

**Probable cases**

Probable cases were defined as cases meeting the clinical and exposure criteria and detection of *M. chimaera* or *M. avium* complex in blood and/or extracardiac tissue cultures.

**Case finding**

Mycobacterial cultures are not part of the routine microbiological workup in the case of cardiovascular infections. The first patient was detected by a thorough histopathological analysis of cardiac tissue, which triggered a PCR for non-tuberculous mycobacteria yielding the diagnosis.13 The remaining patients were detected based on direct 16S rRNA gene-sequencing results of cardiac tissue or bone or on positive mycobacterial blood cultures.

**Microbiology of Mycobacterium chimaera**

Standard methods were used to culture mycobacteria, using the MGIT 960 system (Becton Dickinson Microbiology Systems, Sparks, MD, USA) and Middlebrook 7H11 agar plates incubated at 37°C for 7 weeks or until positive. In Zurich, 16S rRNA gene sequencing was performed as described before.15 Antimicrobial susceptibility testing was performed in the MGIT 960 system equipped with the TB Exist module for rifampin, rifabutin, amikacin, ofloxacin, moxifloxacin, clarithromycin, and ethambutol.16 The German strain was identified by sequencing of the 16S rRNA gene and the 16S-26S rRNA Gene Internal Transcribed Spacer, the Dutch strains were identified by the Inno-LiPA Mycobacteria v2 line probe assay, which features a specific probe for *M. chimaera*. The MICs of the German and Dutch strains were determined by broth microdilution in cation-adjusted Mueller Hinton Broth, as recommended by CLSI (document M24-A2, 2011).17

**Clinical investigations**

We obtained patient informed consent to publish their clinical data. Co-morbidities were quantified using the Charlson comorbidity index.18 The information on index surgery included American Society of Anaesthesiologists (ASA) score,19 type of operation, timing of operation, and the extracorporeal circulation time. All patients were assessed according to the modified Duke criteria.20 We collected treatment information and, if available, results of therapeutic drug monitoring. In all patients, transthoracic (TTE) and transoesophageal echocardiography (TEE) was performed. Histopathological features of infected tissue before or
after initiation of antimicrobial treatment were collected. In Zurich, pa-
tients were screened for ophthalmologic manifestations of the disease, includ-
ing fundoscopy and multimodal imaging.

We assumed treatment failure if the patient died due to uncontrolled infec-
tion or if a patient showed a positive culture for *M. chimaera* despite anti-
microbial therapy for at least 3 months.

**Results**

**Population at risk and prevalence**

In Zurich, Switzerland, cases were associated with procedures be-
tween 13 August 2008 and 30 May 2012. During this period a total of
3706 cardiosurgical procedures with extracorporeal circulation
were conducted. We identified six disseminated *M. chimaera* cases,
corresponding to a cross-sectional prevalence of 0.16%. Other pa-
tients with *M. chimaera* cardiac infection were not detected despite
extensive case finding strategies. 11

After the detection of the first case at the Freiburg University
Hospital, Germany, a national alert was issued. In the Netherlands,
the second case was identified after publication of the first case in a
national newsletter. Review of charts of patients with positive
*M. chimaera* cultures yielded one paediatric case in Rotterdam.
A case finding protocol has now been implemented in Germany
and the Netherlands nationwide.

**Patient characteristics**

Overall, nine confirmed cases including eight adults and one
child, and one probable case are described. For the adult patients
the median age and median BMI were 61 years (range, 36–76)
and 24.9 kg/m² (23.4–35.7), respectively. Details on the index car-
diac surgery are shown in Table 1. The median extracorporeal circu-
tation time was 191 min (range, 123–294). Two patients had
diabetes mellitus, one patient received azathioprine and salazopyr-
ine for Crohn’s disease, and one patient had lymphocytopenia of
unknown origin. After the index surgery, two patients received
corticosteroid treatment for presumptive sarcoidosis and one pa-
tient received repetitive intra-articular methotrexate for suspected
rheumatologic disease. All patients were HIV negative.

The child with a congenital cardiac anomaly was in neonatal age
when he received a correction of the aortic anomalies and banding of
the pulmonary artery.

**Manifestations of disease**

The most common initial complaints in adults were fever, shortness
of breath, fatigue, and weight loss. Physical findings were non-
specific with the exception of splenomegaly. All patients had an-
aemia, pronounced lymphocytopenia, and thrombocytopenia.
C-reactive protein, lactate dehydrogenase, transaminases, and cre-
tinine levels were elevated in all subjects. In the infant, clinical sus-
picion arose due to fever episodes and failure to thrive. A summary
of the presenting clinical signs and laboratory analyses are shown in
Supplementary material online, Table S1, which occurred after a me-
dian incubation time of 18 (range, 11–40) months. Details on the
microbiological and histopathological findings are summarized in
Supplementary material online, Table S2.

**Confirmed cases**

**Cardiac manifestations**

Five of the nine patients with confirmed diagnosis presented with
PVE, two with PVGI and one with myocarditis. The child presented
with infection of the prosthetic band and a mycotic aneurysm of the
pulmonary artery. All diagnoses were made upon cardiosurgical re-
intervention with cultures or PCR from cardiac tissue being positive
for *M. chimaera*. No other microorganisms were detected in the
blood, and there was no serological evidence of a culture-negative
endocarditis of other cause (i.e. *Bartonella* spp., *Brucella* spp., *Coxiella
burnetii*, *Treponema whippelii*). Diagnosis was delayed with a median
duration between index surgery and culture confirmed diagnosis of
almost 2 years (21 months; range, 5–40). AFFECTED patients pre-

tened with prevailing cardiac complications like severe valve insuf-

ciency and subsequent reduction in ejection fraction, paravalvular
abscess, or pseudoaneurysm formation (Figure 1). The TEE showed
paravalvular regurgitation or leakage, anteroseptal pseudoaneurysm
as well as a paravalvular abscess with extension into the interatrial
septum (Figure 1A). Additionally, vegetations or multiple short,
thin and sparse filaments on the ventricular side were detected
(Figure 18).

**Extracardiac manifestations**

In six of nine patients with confirmed diagnosis extracardiac manifes-
tations preceded cardiac disease. Among the first disease manifesta-
tions were bone infections (osteoarthritis, spondylodiscitis, or sternal
wound infection together with a large retrosternal abscess forma-
tion), cholestatic hepatitis, nephritis, or blood stream infection. Myco-
bacterial blood cultures were positive a priori in four patients. At the
time of diagnosis, most patients had splenomegaly. In the course of
the disease, patients developed bi- or even pancytopenia, panuveitis,
or multifocal chorioretinitis (Figure 1H), pneumonitis (Figure 1E)
or cerebral vasculitis. One patient developed a surgical site infection
with *M. chimaera* at the removal site of the saphenal vein.

**Probable case**

The probable case (Table 1, Patient 9) presented with fever of un-
known origin subsequent to open heart surgery. He had been treated
for presumptive sarcoidosis due to granulomatous hepatitis, but per-
sistent fever prompted new diagnostic procedures including a PET/CT
scan. Diagnosis of *M. chimaera* infection was ascertained after bi-
opsy of the right sternoclavicular joint, bone marrow, liver, and blood
cultures. However, TEE did not reveal any signs of endocarditis.

**Antimicrobial therapy**

The detailed time course of events and treatment information is de-
picted in Figure 2. Targeted antimicrobial therapy consisted of cla-
rithromycin or azithromycin, rifabutin or rifampicin, ethambutol,
plus/minus amikacin, or moxifloxacin. The number of available ana-
lyses, mean drug doses, serum maximum observed concentration
levels, and the percentage of analyses revealing subtherapeutic
drug concentrations are recorded in Supplementary material online,
Table S3. In more than half of the cases the recommended macrolide
drug levels were not reached. The same holds true for rifabutin, eth-
ambutol, moxifloxacin, and amikacin. Antimicrobial drugs, tested
drug concentrations, and phenotypic drug susceptibilities of patient
<table>
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<th>3a</th>
<th>4a</th>
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<th>8a</th>
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<td>Male</td>
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<td>Female</td>
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<td>64</td>
<td>49</td>
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<td>63</td>
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<td>No</td>
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<td>COPD</td>
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<td>Severe renal insufficiency</td>
<td>Hypertension</td>
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<td>Mitral insufficiency</td>
<td>Aortic valve stenosis</td>
<td>Aneurysma spurium of descending aorta</td>
<td>Aortic valve dissection</td>
<td>Aortic valve stenosis CHD</td>
<td>Mitral valve insufficiency</td>
<td>Aortic valve stenosis CHD</td>
<td>Congenital cardiac anomaly</td>
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<td>CHD</td>
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<td>Composite graft replacement</td>
<td>Mitral valve reconstruction</td>
<td>Aortic valve replacement</td>
<td>Aortic valve replacement</td>
<td>Aortic root and arch replacement</td>
<td>Aortic valve replacement</td>
<td>Aortic valve replacement</td>
<td>Aortic valve replacement combined with CABG</td>
<td>Aortic arch reconstruction Coarctectomy Ductal closure Allograft patch enlargement of the arch Banding of the pulmonary artery</td>
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<td>3</td>
<td>4</td>
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<td>4</td>
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<td>No</td>
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<td><strong>ECC time</strong></td>
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<td>150</td>
<td>210</td>
<td>166</td>
<td>235</td>
<td>272</td>
<td>123</td>
<td>294</td>
<td>158</td>
<td>na</td>
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</table>

CHD, coronary heart disease; CABP, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; BMI, body mass index; HIV, human immunodeficiency virus; IFNγ, interferon gamma; ASA, American Society of Anesthesiology; ECC, extracorporeal circulation time; na, not available

*Patients 1–6.*

b Alcohol use: severe (female subjects, 140 g/day; male subjects, 160 g/day) or moderate (female subjects, 20–40 g/day; male subjects, 40–60 g/day).

cDiagnosis or treatment initiation after index surgery.

dInvestigation done after manifestation of the disease.

eImplants differed in types of material and manufacturers.
isolates are provided in Table 2. Drug susceptibility testing of breakthrough isolates was unchanged.

**Outcome**

At least eight patients experienced therapy failure according to our definition. Five patients died, four of them due to uncontrolled *M. chimaera* infection despite being under targeted combination therapy for 15, 31, 270, and 375 days, respectively. Tissue cultures from Patient 3 (bone and annuloplasty ring (Figure 1G)), Patient 4 (sternoclavicular mass, epicardial pacemaker wire), Patient 8 (annuloplasty ring) and blood cultures from Patients 6 and 9 became positive for *M. chimaera* despite prolonged antimicrobial therapy.
Persistent signs of infection (Patients 4 and 5, Figure 1C and D) and progressive chorioretinal lesions (Patient 5, Figure 1H) represented an indication for immediate cardiosurgical reintervention. Of note, all these patients were previously considered inoperable due to presumptively high perioperative mortality, but the risk to benefit assessment changed in the light of uncontrolled *M. chimaera* infection. Currently, three patients are in a post-treatment monitoring period.

**Discussion**

As of February 2015, 10 heart surgery patients from four hospitals in three different European countries have been diagnosed with disseminated *M. chimaera* infection. Airborne contamination of the operation region and/or prosthetic material with *M. chimaera* during cardiac surgery is the most likely source of infection. This new clinical entity may manifest itself after an incubation time of several months or even years after surgery. The patients present with non-specific clinical signs and symptoms and a variety of local or disseminated infection sites, which may hamper the diagnosis. Furthermore, diagnosis of mycobacterial infection is delayed as culture for mycobacteria is not part of the routine diagnostic work-up. Despite surgical reintervention and long-term antimicrobial therapy, the outcome is mostly poor.

Based on the disease prevalence in the four affected centres, we estimate a minimum of one to two *M. chimaera* infections per 1000 patients undergoing open-heart surgery. In total, 8 out of 16 tested Swiss hospitals, one out of one tested German hospital, eight out of eight tested Dutch hospitals performing cardio-surgical procedures have detected *M. chimaera* in the water system of their HCUs, and in some hospitals also in air cultures of the operating theatre, suggesting a high significance of our findings. In addition, a recent investigation from England reported that *M. chimaera* was found in the water within HCUs (air investigation ongoing). Of note, until now cases were only detected in hospitals where the HCUs are placed inside the operating theatre, hence some public health authorities now recommend to put HCUs outside the operating theatre. However, these epidemiological findings need to be extended. Ongoing whole-genome sequencing efforts indicate a match between patient isolates and air samples from the proximity of the heat cooler units.

In our patients, mycobacterial infection occurred in the absence of severe immunodeficiency. Apart from infection of the cardiac prosthetic material, disease manifestations were similar to what has been described for other disseminated NTM disease. This involves constitutional symptoms such as fever, night sweats and
Healthcare-associated prosthetic heart valve, aortic vascular graft, and disseminated *Mycobacterium chimaera* infections

**Table 2. Phenotypic drug susceptibility testing of 15 *M. chimaera* isolates of the 10 study patients.**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Sample date</th>
<th>Material</th>
<th>MIC (mg/L)</th>
</tr>
</thead>
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<tr>
<td></td>
<td></td>
<td>Mitral ring</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bone marrow</td>
<td>Moxifloxacin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wrist</td>
<td>Lincomycin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardiac tissue</td>
<td>Amikacin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bone</td>
<td>Rifampicin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardiac tissue</td>
<td>Rifabutin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pocket</td>
<td>Ethambutol</td>
</tr>
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</table>

Data are minimum inhibitory concentrations, in mg/L. ND, not done. Minimum inhibitory concentrations, MICs, MGIT method applied in Patients 1–6; the broth dilution method has been applied in Patients 7–10.

As in all foreign body infections, a removal of the prosthetic material and a surgical debridement have to be thoroughly discussed with the cardiovascular surgeon in the case of invasive infection with *M. chimaera*. Excisional surgery without antimicrobial therapy is not advisable, but the most appropriate timing of surgery is unknown. If the diagnosis is made prior to surgical intervention, it is prudent to wait for antimicrobial therapy in an attempt to sterilize/decrease the bacterial load at the site where prosthetic valves have to be reinserted.

*Mycobacterium chimaera* strains were uniformly susceptible to clarithromycin (MIC < 8 mg/L).

As for severe pulmonary *M. chimaera* disease, it appears prudent to add amikacin during the first 3 months of treatment, akin to staphylococcal and streptococcal endocarditis.

No statement can be made regarding the duration of treatment since there are no data regarding cardiac implants infected with NTM. According to ATS/IDSA guidelines, a minimum of 12 months of therapy after immune restoration is indicated for non-HIV patients with disseminated MAC disease. Despite our attempts to optimize therapy with therapeutic drug monitoring, breakthrough infection occurred in most of patients. Low drug concentrations of macrolides, rifabutin, and moxifloxacin due to drug–drug interactions were recorded. The relevance of these findings remains unknown.

Macrolides have a strong tissue penetration and hence, serum concentration is much lower than the concentration at the surgical site. A beneficial role of therapeutic drug monitoring has not yet been proved in NTM diseases. Most anti-mycobacterial agents are associated with a high rate of side effects and increased macrolide or rifabutin doses were not tolerated due to QT-interval prolongation and liver or bone marrow toxicity. The in vitro activity against an organism may not necessarily translate to the in vivo situation, especially in the context of potential biofilm formation, where the interpretation of traditional in vitro susceptibility testing is problematic.

Our findings have important implications. First, infections with *M. chimaera* and other NTM have to be considered in the differential diagnosis of cardiac infections. Second, in the context of potential biofilm formation, where the interpretation of traditional in vitro susceptibility testing is problematic.

**Table 2.** Phenotypic drug susceptibility testing of 15 *M. chimaera* isolates of the 10 study patients.
Table 3  Recommendations for future case detection

<table>
<thead>
<tr>
<th>Exposure criteria</th>
<th>Clinical criteria</th>
<th>Microbiology</th>
<th>Histopathology</th>
<th>Additional criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>A patient having undergone surgery requiring cardiopulmonary bypass prior to symptoms of infection</td>
<td>Prosthetic valve endocarditis</td>
<td>Positive heparin blood cultures for <em>M. chimaera</em></td>
<td>Detection of non-caseating granuloma and foamy/swollen macrophages with/without acid fast bacilli in cardiac tissue in the proximity of the prosthetic material</td>
<td>Negative conventional blood cultures</td>
</tr>
<tr>
<td></td>
<td>Prosthetic vascular graft infection</td>
<td>Detection of <em>M. chimaera</em> by culture or PCR in cardiac tissue in the proximity of the prosthetic material</td>
<td></td>
<td>Serologic exclusion of <em>Coxiella</em>, <em>Bartonella</em>, <em>Brucella</em>, <em>Tropheryma whippelii</em>, <em>Legionella</em>, <em>Mycoplasma</em>, <em>Chlamydia</em></td>
</tr>
<tr>
<td></td>
<td>Sternotomy wound infection</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Mediastinitis</td>
<td>Histopathology</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fever of unknown origin</td>
<td></td>
<td>Detection of non-caseating granuloma and foamy/swollen macrophages with acid fast bacilli in cardiac tissue in the proximity of the prosthetic material</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Disseminated infection including embolic and immunologic manifestations (e.g. splenomegaly, arthritis, osteomyelitis, bone marrow involvement with cytopenia, chorioretinitis, cerebral vasculitis, pneumonitis, myocarditis, hepatitis, nephritis)</td>
<td></td>
<td>Additional criteria</td>
<td></td>
</tr>
</tbody>
</table>

Confirmed cases

Meet clinical and exposure criteria

AND

*M. chimaera* is detected by culture and polymerase chain reaction (PCR) identification from invasive sample (blood, pus, biopsy or prosthetic material).

Probable cases

Meet clinical and exposure criteria

AND

*M. chimaera* is detected by polymerase chain reaction (PCR) identification from invasive sample (blood, pus, biopsy or prosthetic material) operating theatre.

M. avium complex (MAC) is detected by culture and polymerase chain reaction (PCR) identification from invasive sample (blood, pus, biopsy or prosthetic material) operating theatre.

Detection of non-caseating granuloma and foamy/swollen macrophages with acid fast bacilli in cardiac tissue in the proximity of the prosthetic material or in specimen from sternotomy wound.

EU protocol for case detection, laboratory diagnosis and environmental testing of *Mycobacterium chimaera* infections potentially associated with heater-cooler units (available to the member states through the EPIS AMR-HAI platform).

Diagnosis of patients with previous cardiac surgery and extracorporeal circulation, even in the absence of severe immuno-suppression. A few more case patients are already identified in Europe and more cases are likely to be found in the future when clinicians are alerted and, as a consequence of active case finding (recommendation for case detection, Table 3). Second, HCU as potential source of *M. chimaera* and other waterborne microorganisms in the operating theatre have to be identified and avoided by either placing HCU's outside of the operating theatre with independent air flow control, by making the water reservoir and piping air-tight or by reliable disinfection of the water circuits and reservoirs. Recommendations for the prevention of these waterborne, aerogenic infections in cardiac surgery are strongly warranted. Third, these infections are recalcitrant to classic antimycobacterial therapy, because of intrinsic antibiotic resilience, notoriously challenging infection sites such as bone tissue, and biofilm formation on the cardiovascular implant. More studies are needed with regard to the clinical phenotype of disseminated *M. chimaera* infection, its epidemiology, virulence mechanisms, and susceptibility to antibiotics.

Supplementary material

Supplementary Material is available at European Heart Journal online.

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Authors’ contributions


References


