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

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Received 27 May 2015; revised 30 June 2015; accepted 1 July 2015; online publish-ahead-of-print 17 July 2015

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 cardiosurgical 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

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doi:10.1093/eurheartj/ehv342
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 cardio-surgical 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,7 contamination during the manufacturing process9 or use of a contaminated patch for septum defect repair,7 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 from 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 national public health authorities led to thorough investigation of the 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. 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-23S 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 (TEE) and transoesophageal echocardiography (TEE) was performed. Histopathological features of infected tissue before or
after initiation of antimicrobial treatment were collected. In Zurich, patients were screened for ophthalmologic manifestations of the disease, including fundoscopy and multimodal imaging.

We assumed treatment failure if the patient died due to uncontrolled infection or if a patient showed a positive culture for M. chimaera despite antimicrobial therapy for at least 3 months.

Results

Population at risk and prevalence

In Zurich, Switzerland, cases were associated with procedures between 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 patients 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 cardiac surgery are shown in Table 1. The median extracorporeal circulation time was 191 min (range, 123–294). Two patients had diabetes mellitus, one patient received azathioprine and salazopyrine 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 patient had lymphocytopenia of unknown origin. After the index surgery, two patients received corticosteroid treatment for presumptive sarcoidosis and one patient 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 anaemia, pronounced lymphocytopenia, and thrombocytopenia. C-reactive protein, lactate dehydrogenase, transaminases, and creatinine levels were elevated in all subjects. In the infant, clinical suspicion arose due to fever episodes and failure to thrive. A summary of the presentling clinical signs and laboratory analyses are shown in Supplementary material online, Table S1, which occurred after a median 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., Caxiella burnetti, Tropheryma 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 presented with prevailing cardiac complications like severe valve insuﬃciency 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 1B).

Extracardiac manifestations

In six of nine patients with conﬁrmed diagnosis extracardiac manifestations preceded cardiac disease. Among the ﬁrst disease manifestations were bone infections (osteoarthritis, spondylodiscitis, or sternal wound infection together with a large retrosternal abscess forma tion), cholestatic hepatitis, nephritis, or blood stream infection. Mycobacterial 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 saphenous vein.

Probable case

The probable case (Table 1, Patient 9) presented with fever of unknown origin subsequent to open heart surgery. He had been treated for presumptive sarcoidosis due to granulomatous hepatitis, but persistent fever prompted new diagnostic procedures including a PET/CT scan. Diagnosis of M. chimaera infection was ascertained after biopsy 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 depicted in Figure 2. Targeted antimicrobial therapy consisted of clarithromycin or azithromycin, rifabutin or rifampicin, ethambutol, plus/minus amikacin, or moxifloxacin. The number of available analyses, 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, ethambutol, moxifloxacin, and amikacin. Antimicrobial drugs, tested drug concentrations, and phenotypic drug susceptibilities of patient
# Table I  Baseline characteristics of patients with invasive infection due to M. chimaera at time of the index cardiac surgery

<table>
<thead>
<tr>
<th>Patient no.</th>
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<th>4</th>
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<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Male</td>
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<td>51</td>
<td>64</td>
<td>49</td>
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<td>76</td>
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<td>23.4</td>
<td>29.4</td>
<td>30.6</td>
<td>24.9</td>
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<td>35.7</td>
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<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<td>No</td>
<td>Yes</td>
<td>No</td>
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<td>No</td>
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<tr>
<td>Comorbidities</td>
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<td>Diabetes mellitus</td>
<td>Sarcoidosis</td>
<td>Crohn's disease</td>
<td>COPD</td>
<td>None</td>
<td>Severe renal insufficiency</td>
<td>Hypertension</td>
<td>Cardiomyopathy</td>
<td>Diabetes mellitus</td>
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<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6</td>
<td>0</td>
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<tr>
<td>Immune status</td>
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<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>HIV serology</td>
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<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
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<td>Lymphocytes, G/L</td>
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<td>2.11</td>
<td>1.66</td>
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<td>1.37</td>
<td>0.75</td>
<td>1.0</td>
<td>0.46</td>
<td>0.66</td>
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<td>Immunosuppression</td>
<td>Steroids</td>
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<td>Methotrexate</td>
<td>Azathioprine</td>
<td>Sulfasalazine</td>
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<td></td>
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<td>Cardiac surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Reason for surgery</td>
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<td>Aortic dissection</td>
<td>Mitral insufficiency</td>
<td>Aortic valve stenosis</td>
<td>Aneurysma spurious of descending aorta</td>
<td>Aortic valve dissection</td>
<td>Aortic valve stenosis CHD</td>
<td>Aortic valve insufficiency Dilated cardiomyopathy</td>
<td>Aortic valve stenosis CHD</td>
<td>Aortic valve replacement combined with CABG</td>
</tr>
<tr>
<td>Type of surgery</td>
<td>Mitral valve reconstruction</td>
<td>Composite graft replacement</td>
<td>Mitral valve reconstruction</td>
<td>Aortic valve replacement</td>
<td>Aortic root and arch replacement</td>
<td>Aortic root and arch replacement</td>
<td>Aortic valve replacement</td>
<td>Aortic valve replacement</td>
<td>Aortic root reconstruction</td>
<td>Aortic arch reconstruction</td>
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<td>ASA score</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>3</td>
<td>4</td>
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<td>No</td>
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<td>ECC time</td>
<td>191</td>
<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; CABG, 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, 11

*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).

*Diagnosis or treatment initiation after index surgery.

*Investigation done after manifestation of the disease.

*Implants 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.
(median 8 months, range 0.5–12). 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 HCU’s, 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 HCU’s (air investigation ongoing). Of note, until now cases were only detected in hospitals where the HCU’s are placed inside the operating theatre, hence some public health authorities now recommend to put HCU’s 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...
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>Cardiac pocket</th>
<th>Cardiac valve</th>
<th>Mitral ring</th>
<th>Bone marrow</th>
<th>Wrist tissue</th>
<th>Urine</th>
<th>Blood culture</th>
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<td>1</td>
<td>06.06.11</td>
<td>Mitral</td>
<td>2.5</td>
<td>2.5</td>
<td>25</td>
<td>ND</td>
<td>0.4</td>
<td>2</td>
<td>0.5</td>
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<tr>
<td>2</td>
<td>27.05.11</td>
<td>Bone</td>
<td>2.5</td>
<td>2.5</td>
<td>25</td>
<td>25</td>
<td>25</td>
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<td>2</td>
</tr>
<tr>
<td>3</td>
<td>10.05.12</td>
<td>Urine</td>
<td>2.5</td>
<td>2.5</td>
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<td>4</td>
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<tr>
<td>6</td>
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<td>7</td>
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<td>8</td>
<td>12.06.13</td>
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MIC (mg/L)

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<td>≤ 4</td>
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<td>≤ 4</td>
<td>≤ 4</td>
<td>≤ 4</td>
<td>≤ 4</td>
<td>≤ 4</td>
<td>≤ 4</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>≤ 1</td>
<td>≤ 1</td>
<td>≤ 1</td>
<td>≤ 1</td>
<td>≤ 1</td>
<td>≤ 1</td>
<td>≤ 1</td>
<td>≤ 1</td>
<td>≤ 1</td>
<td>≤ 1</td>
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<tr>
<td>Clarithromycin</td>
<td>≤ 2</td>
<td>≤ 2</td>
<td>≤ 2</td>
<td>≤ 2</td>
<td>≤ 2</td>
<td>≤ 2</td>
<td>≤ 2</td>
<td>≤ 2</td>
<td>≤ 2</td>
<td>≤ 2</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>≤ 0.1</td>
<td>≤ 0.1</td>
<td>≤ 0.1</td>
<td>≤ 0.1</td>
<td>≤ 0.1</td>
<td>≤ 0.1</td>
<td>≤ 0.1</td>
<td>≤ 0.1</td>
<td>≤ 0.1</td>
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<tr>
<td>Ethambutol</td>
<td>≤ 0.25</td>
<td>≤ 0.25</td>
<td>≤ 0.25</td>
<td>≤ 0.25</td>
<td>≤ 0.25</td>
<td>≤ 0.25</td>
<td>≤ 0.25</td>
<td>≤ 0.25</td>
<td>≤ 0.25</td>
<td>≤ 0.25</td>
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</tbody>
</table>

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

Mycobacterium chimaera strains were uniformly susceptible to clarithromycin (MIC < 8 mg/L). We used the combination of clarithromycin, rifabutin, and ethambutol as the basis of treatment regimens. 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...
Table 3 Recommendations for future case detection

<table>
<thead>
<tr>
<th>Exposure criteria</th>
<th>Clinical criteria</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>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></td>
<td>Serologic exclusion of Coxiella, Bartonella, Brucella, Tropheryma whippelii, Legionella, Mycoplasma, Chlamydia</td>
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<tr>
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<td>Sternotomy wound infection</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Mediastinitis</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Fever of unknown origin</td>
<td></td>
<td></td>
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<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></td>
</tr>
</tbody>
</table>

Microbiology
- Positive heparin blood cultures for M. chimaera
- Detection of M. chimaera by culture or PCR in cardiac tissue in the proximity of the prosthetic material

Histopathology
- Detection of non-caseating granuloma and foamy/swollen macrophages with/without acid fast bacilli in cardiac tissue in the proximity of the prosthetic material

Additional criteria
- Negative conventional blood cultures
- Serologic exclusion of Coxiella, Bartonella, Brucella, Tropheryma whippelii, Legionella, Mycoplasma, Chlamydia

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 or PCR in cardiac tissue in the proximity of the 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).

Supplementary material
Supplementary Material is available at European Heart Journal online.

Acknowledgements
We are grateful to our patients for their informed consent to publish their case. Patients 5 and 6 are participants of VASGRA, an observational cohort located at the University Hospital Zurich studying the epidemiology and best treatment options of prosthetic vascular graft infection, supported by the Swiss National Science Foundation (grant # 320030_144277/1). We would like to thank J. Hasse, U. Karrer, and R. Speck for helpful discussions. We thank M. Flepp, P. Vogt, A. von Braun, A. Wolfensberger, Ch. Ruegg, P. Paioni, and M. Hoffmann for excellent patient care.

Conflict of interest: none declared.

Authors’ contributions

References


