Mycobacterium smegmatis bacteremia in an immunocompetent host

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\textbf{ABSTRACT}

Non-tuberculous mycobacteria can cause catheter associated blood stream infections. The causative agents are generally rapid growers that belong to the Mycobacterium fortuitum and Mycobacterium mucogenicum groups. A 65 year hospitalized patient with temporary central venous catheter who developed Mycobacterium smegmatis bacteremia. Bacteremia cleared after removal of the catheter. Patient was treated initially with 4 weeks of intravenous amikacin, intravenous meropenem, oral doxycycline and oral etambutol and then deescalated to oral doxycycline and oral ciprofloxacin for 8 weeks. He improved clinically and remained stable. A literature search identified total of 22 articles that reported 47 unique cases of Mycobacterium smegmatis infection. To our knowledge, this is the first case of Mycobacterium smegmatis central venous catheter associated bacteremia in an immunocompetent host.

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**Introduction**

Non-tuberculous mycobacterial (NTM) human infections are gaining clinical recognition due to modern molecular techniques. NTM can cause skin and soft tissue infection, lymphadenitis, pulmonary infection, bone and joint infection, catheter related bacteremia and disseminated infection. Sporadic cases of health care associated infections are reported. These cases include infections due to peritoneal catheter; intravenous indwelling catheters, injection related abscesses, surgical site wounds and infections post plastic surgery procedures [1].

NTMs are classified, in part, classified based on their growth rate. Rapidly growing mycobacteria (RGM) produce mature growth on media plates within 7 days. There are currently six groups based on pigmentation and genetic relatedness. One group within RGM is the Mycobacterium smegmatis group consisting of two late pigmenting species: Mycobacterium smegmatis and Mycobacterium goodii. Mycobacterium smegmatis is resistant to anti tuberculous agents except for ethambutol. Generally, it has an erm gene, which induces macrolide resistance. Monotherapy with quinolones is avoided due to high risk of mutational resistance to these agents [1].

Currently, catheter related infections are the most common health care associated NTM infections encountered. These Infections are seen most often with long-term central venous catheters but may also occur with peritoneal or shunt catheters. The causative RGMs usually belong to the Mycobacterium fortuitum and Mycobacterium mucogenicum groups. Treatment involves removal of the catheter and long-term antibiotics for 6–12 weeks [1]. We present the first case of Mycobacterium smegmatis catheter associated bloodstream infection in an immunocompetent patient.

**Case report**

A 64 year old Caucasian male with recent history of constractive pericarditis and 4.7 cm ascending aortic aneurysm was admitted to the hospital for an elective surgery. He underwent repair of his ascending aortic aneurysm and pericardiectomy on day 1 of admission. During his hospital stay, he had a cardiac arrest with ventricular fibrillation and underwent pacemaker placement (day 7). He also developed acute kidney injury and underwent tunneled central venous catheter (CVC) placement for hemodialysis (day 10).

He was transferred to the intensive care unit (ICU) with hypotension and fever, and blood cultures were drawn (day 20). Microbiology laboratory reported blood cultures positive for RGM, possibly mycobacterium smegmatis based on in-house MALDI-TOF (matrix-assisted laser desorption ionization time-of-flight mass spectrometry) (day 24). Mycobacterium tuberculosis PCR was negative. Infectious diseases team was consulted and CVC was removed per their advice (day 26). Repeat blood cultures drawn on day 24 and day 26 were reported positive for RGM. The patient was started on empiric intravenous (IV) amikacin 15 mg/kg every 24 h, IV meropenem 1 g every 8 h, oral (PO) etambutol 1200 mg daily.

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and PO doxycycline 100 mg daily (day 26). The CVC tip was positive for *Mycobacterium smegmatis* (day 28). Post catheter removal, he improved clinically and his repeat blood cultures obtained on day 28 were negative. *Mycobacterium smegmatis* isolate was sent to National Jewish Medical Center for susceptibility testing (day 35). The isolate was resistant to ceftriaxone, cefotaxime and cefepime; intermediate to clarithromycin, cefoxitin and amoxicillin/clavulanate; and susceptible to aminoglycosides, trimethoprim/sulfamethoxazole, tetracyclines, imipenem, fluoroquinolones, linezolid, and clofazamine based on RPOB (β subunit of bacterial RNA polymerase) gene sequencing (day 48). The patient received 28 days of empiric IV amikacin 15 mg/kg every 24 h, IV meropenem 1 g every 8 h, PO ethambutol 1200 mg daily and PO doxycycline 100 mg daily and once susceptibilities were available, he was deescalated to PO doxycycline 100 mg daily and PO ciprofloxacin 500 mg twice a day for 8 weeks. Patient was followed at the infectious diseases outpatient clinic at the end of treatment and was still clinically stable by week 12.

Table 1
*Mycobacterium smegmatis* infections (Literature review).

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Number</th>
<th>Risk factors</th>
<th>Infection type</th>
<th>Bacteremia</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vonmoos [2] 1986</td>
<td>Switzerland</td>
<td>1</td>
<td>Laryngeal cancer</td>
<td>PNA</td>
<td>no</td>
<td>NA</td>
<td>Resolved</td>
</tr>
<tr>
<td>Plaus [4] 1991</td>
<td>USA</td>
<td>2</td>
<td>veterinary grade steroid injection trauma</td>
<td>SSTI</td>
<td>No</td>
<td>Erythromycin + amikacin x 2wks f/u cipro x 6 wks plus I&amp;D Cefoxitin, doxy, TMP/SMX plus I&amp;D</td>
<td>Resolved</td>
</tr>
<tr>
<td>Roger [5] 1991</td>
<td>France</td>
<td>1</td>
<td>Puncture injury to ankle while gardening</td>
<td>SSTI</td>
<td>No</td>
<td>NA</td>
<td>Resolved</td>
</tr>
<tr>
<td>Newton [6] 1993</td>
<td>USA</td>
<td>2</td>
<td>s/p keratotomy</td>
<td>Sebaceous cyst</td>
<td>No</td>
<td>1) cefoxitin + amikacin f/u TMP/SMX x8 wks plus I&amp;D 2) doxy + cipro Amikacin + kanamycin f/u amikacin + ofloxacin optic</td>
<td>Resolved</td>
</tr>
<tr>
<td>Lin [7] 1994</td>
<td>China</td>
<td>1</td>
<td>Mineral oil for constipation</td>
<td>PNA</td>
<td>No</td>
<td>Resolved</td>
<td></td>
</tr>
<tr>
<td>Cox [8] 1994</td>
<td>USA</td>
<td>1</td>
<td>Term infant</td>
<td>PNA</td>
<td>No</td>
<td>NA</td>
<td>Death</td>
</tr>
<tr>
<td>Kumar [9] 1995</td>
<td>India</td>
<td>1</td>
<td>Interferon gamma deficiency</td>
<td>Disseminated</td>
<td>Yes</td>
<td>Streptomycin+ sulphonamides + ofloxacin</td>
<td>Death</td>
</tr>
<tr>
<td>Pierre-Audiger [10] 1997</td>
<td>France</td>
<td>1</td>
<td>facelift</td>
<td>SSTI</td>
<td>No</td>
<td>Cipro + doxy+ amikacin I&amp;D</td>
<td>Resolved</td>
</tr>
<tr>
<td>Pennekamp [11] 1997</td>
<td>USA</td>
<td>1</td>
<td>catheter</td>
<td>CVC BSI</td>
<td>Yes</td>
<td>Rifabutin + ETA + clarithro + ofloxacin</td>
<td>Resolved</td>
</tr>
<tr>
<td>Schreiber [12] 1998</td>
<td>Germany</td>
<td>1</td>
<td>Gastrectomy, splenectomy</td>
<td>PNA</td>
<td>No</td>
<td>Resolved</td>
<td></td>
</tr>
<tr>
<td>Ergan [13] 2004</td>
<td>Turkey</td>
<td>1</td>
<td>smoker</td>
<td>PNA</td>
<td>No</td>
<td>Doxy + cipro x 3 mo</td>
<td>Resolved</td>
</tr>
<tr>
<td>Eid [14] 2007</td>
<td>USA</td>
<td>1</td>
<td>Knee prothesis</td>
<td>PJI</td>
<td>No</td>
<td>Doxy + amikacin x 2 wks f/u cipro + TMP/SMX x16wks; MRP + Cipro x4 wks &amp; post implantation cipro x 6 wks</td>
<td>Resolved</td>
</tr>
<tr>
<td>Chang [15] 2009</td>
<td>Taiwan</td>
<td>3</td>
<td>CVC</td>
<td>CVC BSI</td>
<td>Yes</td>
<td>NA</td>
<td>Resolved</td>
</tr>
<tr>
<td>Corliss [16] 2009</td>
<td>USA</td>
<td>1</td>
<td>none</td>
<td>SSTI</td>
<td>No</td>
<td>Cipro + Doxy x 10 wks I&amp;D x2</td>
<td>Resolved</td>
</tr>
<tr>
<td>Redelman-Sidi [17] 2010</td>
<td>USA</td>
<td>2</td>
<td>chemo</td>
<td>1 BSI 1 SSTI</td>
<td>1 yes 1 No</td>
<td>Resolved</td>
<td></td>
</tr>
<tr>
<td>Driks [18] 2011</td>
<td>USA</td>
<td>1</td>
<td>gastrectomy</td>
<td>PNA</td>
<td>No</td>
<td>Doxy + cipro f/u TMP/SMX+ cipro x 14 mo</td>
<td>Resolved</td>
</tr>
<tr>
<td>Jiang [19] 2011</td>
<td>USA</td>
<td>1</td>
<td>PD</td>
<td>peritonitis</td>
<td>No</td>
<td>Cipro +TMP/SMX x 6 mo</td>
<td>Resolved</td>
</tr>
<tr>
<td>Zinna [20] 2011</td>
<td>USA</td>
<td>1</td>
<td>Lumbar spine hardware</td>
<td>Vertebral OM</td>
<td>No</td>
<td>Amikacin + ETA + TMP/SMX + clarithro x 12 wks plus I&amp;D but Retained hardware cefazolin x 5 days</td>
<td>Resolved</td>
</tr>
<tr>
<td>Shimizu [21] 2012</td>
<td>USA</td>
<td>1</td>
<td>trauma</td>
<td>SSTI</td>
<td>No</td>
<td>Resolved</td>
<td></td>
</tr>
<tr>
<td>Saffo [22] 2016</td>
<td>USA</td>
<td>1</td>
<td>Stitch abscess</td>
<td>PJI</td>
<td>No</td>
<td>Levo + amp/sulbactam, removal of hardware f/u doxy + levo x 10 months</td>
<td>Resolved</td>
</tr>
</tbody>
</table>

Abbreviations: PNA (pneumonia); NA (not available); OM (osteomyelitis); IE (infectious endocarditis); SSTI (skin and soft tissue infection); surg (surgery); CVC (central venous catheter); I&D (incision and drainage); abx (antibiotic); doxy (doxycycline); TMP/SMX (trimethoprim/sulfamethoxazole); tobra (tobramycin); wks (weeks); cipro (ciprofloxacin); MVA (motor vehicle accident); f/u (follow up); BSI (blood stream infection); ETA (ethambutol); clarithro (clarithromycin); PJI (prosthetic joint infection); MRP (meropenem); IC (immunocompromised); chemo (chemotherapy); PD (peritoneal dialysis); levo (levofloxacin).
Methods

The PubMed database and Google scholar were used to search the medical literature to identify all reported cases of Mycobacterium smegmatis infections. A secondary search was performed using references in the articles identified in the initial search. We identified total of 22 articles that reported 47 unique cases of Mycobacterium smegmatis infection (Table 1).

Discussion

Literature review of all reported cases of Mycobacterium smegmatis revealed 21 cases of skin and soft tissue infections [3, 6, 11, 17, 18, 22], 8 cases each of pneumonia [2, 3, 8, 9, 13, 14, 19], and joint infections [3, 15, 21, 23], 1 case each of endocarditis [3], corneal ulcer [7] and disseminated infection (10) and 6 cases of catheter-associated bacteremia [3, 12, 16, 18], Table 1. Various rapidly growing mycobacteria (RGM) species has been associated with catheter-associated infections. These infections are seen with long term central venous catheter, peritoneal or shunt catheters. Most common causative species are members of the Mycobacterium fortuitum and Mycobacterium mucogenenium groups. These infections generally present with fever, local catheter site drainage, lung infiltrates or bacteremia [1]. Mycobacterium smegmatis bacteremia has been reported in CV associated infections in immunocompromised hosts. Wallace [3], Skiest [12], and Redelman-Sidi [18] have described one case each in cancer patients and Chang [16] described 3 cases of Mycobacterium smegmatis catheter-associated bacteremia in immunocompromised patients.

We present the first case of Mycobacterium smegmatis central venous catheter-associated bacteremia in an immunocompetent host. The patient developed bacteremia 10 days post CV placement. Blood cultures were obtained due to hypotension and fever. He had no catheter site inflammation or drainage. No abnormalities were seen on chest x-ray. Infection control was notified and they labeled it as an isolated case of infection. Catheter was removed for source control as bacteremia can relapse in patients with delayed catheter removal. The catheter tip was sent for culture, which did grow Mycobacterium smegmatis. Bacteremia cleared post catheter removal. Initially, the patient was empirically treated with amikacin, meropenem, ethambutol and doxycycline. The empiric antimicrobial agents were chosen based on known Mycobacterium smegmatis in-vitro susceptibility to sulfonamides, doxycycline, imipenem and amikacin. Cephalosporins and macrolides were avoided due to resistance. Our patient’s isolate was sent to National Jewish Medical Center for susceptibility testing and antimicrobial agents were later narrowed to doxycycline and ciprofloxacin based on these results.

Mycobacterium smegmatis can rarely cause catheter-associated bacteremia in any patient with an indwelling catheter regardless of their immune status so it should be considered as part of the differential. Management includes source control, susceptibility testing, and appropriate antimicrobial agents.

Conflict of interest

None.

CRediT authorship contribution statement

Saira Butt: Data curation, Methodology, Writing - original draft.
Amir Tirmizi: Writing - review & editing.

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References