Mycobacterium abscessus bloodstream infection: unexpected catheter tunnel infection localised by PET/CT

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Abstract
Mycobacterium abscessus is an emerging cause of invasive infection in the immunosuppressed population. We report a case of M. abscessus bloodstream and catheter tunnel infection localised by positron emission tomography/computer tomography (PET/CT) in an allogeneic haematopoietic stem cell transplant recipient. This case highlights the
difficulties in treating invasive *M. abscessus* infection and the potential role of PET/CT in localising infection and guiding therapy in this population.

**Keywords**

*Mycobacterium abscessus*, hematopoietic stem cell transplantation, catheter-related infection, bacteremia.

**Background**

*Mycobacterium abscessus* is a rapidly growing non-tuberculous mycobacterium (RGM) which is ubiquitous in the environment\(^1\)\(^-\)\(^2\). It most commonly causes pulmonary infection and is often resistant to multiple antimicrobials\(^1\)\(^-\)\(^3\). It has been reported to be an emerging cause of invasive infections in the immunosuppressed population\(^4\)\(^-\)\(^6\). We describe a case of *M. abscessus* central line associated bloodstream infection (CLABSI) post allogeneic haematopoietic stem cell transplant (HSCT) complicated by clinically occult catheter tunnel infection which was localised by positron emission tomography/computer tomography (PET/CT). We also present a literature review of RGM catheter tunnel infections in allogeneic HSCT recipients.

**Case presentation**

A 59-year-old lady underwent a matched unrelated donor HSCT for JAK2 positive myelofibrosis which had previously been treated with ruxolitinib. Conditioning consisted of fludarabine, melphalan and thymoglobulin.

A transjugular liver biopsy for progressive liver failure on day 12 was complicated by haemorrhagic shock resulting in oliguric renal failure. A tunnelled dialysis catheter was inserted into the right internal jugular vein on day 26. Blood cultures (BD BACTEC) had previously cultured *Staphylococcus epidermidis* and *Candida glabrata*. Surveillance blood cultures on day 30 from the catheter cultured acid-fast bacilli (AFB) after 3 days. Further blood cultures taken on day 32 were also positive.

The patient had delayed engraftment and was pancytopenic on day 32. Despite multiple blood cultures positive for AFB, she was minimally symptomatic without fever and had no clinical evidence of catheter tunnel infection. Antibiotic therapy was not commenced, the tunnelled catheter was removed on day 42 and a temporary dialysis catheter inserted.

Further blood cultures taken on day 44 after catheter removal remained positive for AFB. The patient was receiving twice weekly haemodialysis and had engrafted by day 40. Empiric
**M. abscessus** catheter infection

treatment was commenced with dialysis adjusted doses of amikacin with monitoring of peak and trough levels (10mg/kg every 96 hours), cefoxitin (2g daily), imipenem (250mg twice daily) and clarithromycin (500mg twice daily) pending susceptibility testing.

The blood culture isolate was identified as *M. abscessus* via sequencing of the internal transcribed spacer (ITS) region within mycobacteria. Subspeciation was not available. Susceptibility testing was performed via sensititre plate microbroth dilution (TREK Diagnostic Systems). *In vitro* susceptibility results are presented in Table 1. Inducible clarithromycin resistance was detected.

Repeat blood cultures were negative from 3 days after commencement of treatment and antibiotic therapy was rationalised to amikacin and cefoxitin. A PET/CT was performed on day 56, 2 weeks after catheter removal, to investigate for metastatic foci of infection. It demonstrated moderate avidity along the catheter tunnel (Figure 1). The catheter tunnel was palpable but had no overt signs of inflammation. The neutrophil count was approximately 1.0 x 10^9/L.

Surgical debridement was discussed but in the setting of high surgical risk post-transplant, it was not pursued. After 6 weeks of therapy (day 90), she developed significant vertigo and remained dialysis dependent. Treatment was ceased.

A repeat PET/CT scan demonstrated persisting moderate uptake along the catheter tunnel. A surgical biopsy was performed and was culture positive for AFB after 5 days and confirmed as *M. abscessus*. Histology demonstrated non-specific fat necrosis.

Treatment was recommenced with tigecycline (50mg twice daily), cefoxitin (2g daily) and clofazimine (100mg daily). An excision of the tunnel was performed on day 112 and treatment continued for 4 weeks after tunnel excision. A repeat PET/CT at the end of treatment on day 140 did not demonstrate any uptake over the former catheter tunnel. Repeat blood cultures after treatment cessation remained negative for AFB and she was weaned off haemodialysis with a degree of renal recovery.

Unfortunately, she developed a recurrence of oliguric renal failure unresponsive to diuretic therapy after ceasing dialysis. She and her family elected not to recommence dialysis and she passed away on day 160 post-transplant.

**Review of literature**

We reviewed publications describing RGM catheter tunnel infections in allogeneic HSCT recipients from PubMed using key words “bone marrow transplant”, “nontuberculous mycobacteria”, “rapidly growing bacteria”, “bacteraemia” and “catheter-related infection”.

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References of articles were screened for further publications. Three case series describing RGM catheter tunnel infections in a total of 11 patients were found. The characteristics of these cases are described in Table 2^{8-10}.

**Discussion**

Infection with *M. abscessus* is difficult to treat and can be associated with significant toxicity. Patients with allogeneic HSCT are especially susceptible due to prolonged neutropenia and impaired cell mediated immunity^{10}. Infections with RGM, including *M. abscessus*, in this population are often in the setting of central venous access devices^{5,8,11,12}. Complications include catheter tunnel infections which can occur late and result in significant morbidity^{10}. We describe a case of clinically occult *M. abscessus* catheter tunnel infection which was localised by PET/CT and confirmed microbiologically on biopsy.

There has been increasing use of PET/CT, particularly in cancer patients, and has been useful in localising causes of neutropenic fever and dissemination of invasive fungal disease^{13}. PET/CT provides functional imaging related to metabolism of glucose by cells and may provide greater sensitivity compared to conventional imaging modalities^{13}. Two cases of *M. abscessus* endovascular infection related to vascular grafts have been reported which were only localised by PET/CT in immunocompetent patients^{14,15}. PET/CT can localise infection even in cases of severe neutropenia due to glucose uptake by other immune cells such as lymphocytes and macrophages and has been used to localise central venous access device related infection post HSCT^{13,16}. PET/CT has also been used to monitor treatment response in invasive fungal disease and in pulmonary NTM infection^{13,17,18}. The PET/CT scan in this case was able to localise a clinically occult site of infection after clearance of bacteraemia and removal of tunnelled intravascular catheter. While the patient later died of unrelated causes, the use of PET/CT facilitated early detection and surgical management of the tunnel infection.

RGM catheter tunnel infections in allogeneic HSCT recipients are uncommonly described in the literature (Table 2). The median time to incidence of NTM bloodstream infection after allogeneic HSCT is approximately 61 days^{8}. RGM, particularly *M. abscessus*, can form biofilms which enhances their ability to cause CLABSI^{11,19}. As such, removal of central venous access devices in *M. abscessus* CLABSI is important for treatment and is associated
M. abscessus catheter infection

with reduced relapse rates. Additionally, soft tissue debridement of infected catheter tunnels is important to achieve cure.

Positive outcomes have been reported with the use of 2 or more antimicrobials for treatment for RGM CLABSI even within an immunosuppressed population. The median duration of treatment for CLABSI is between 4-6 weeks although treatment for tunnel infections may be prolonged to 2 months or longer. M. abscessus is often resistant to multiple antimicrobials with few oral options which may necessitate prolonged intravenous treatment. Most isolates are susceptible to amikacin in vitro but prolonged treatment can cause acute renal impairment, vestibular and ototoxicity. In our patient, underlying renal impairment complicated dosing of amikacin and prolonged treatment resulted in debilitating vertigo. Inducible macrolide resistance mediated by mutations in the erm gene can limit therapeutic options and is commonly present in M. abscessus subsp. abscessus and subsp. bolletii but not in M. abscessus subsp. massiliense. While there are no CLSI breakpoints for tigecycline, it has been used for salvage therapy including a limited number of patients with bloodstream infection and was used in our case after amikacin intolerance.

M. abscessus infection is difficult to treat and bloodstream infection is usually associated with central venous access devices. Removal of the venous access device and surgical debridement of any soft tissue infection are important in treatment. In centres with ready access to PET/CT, it may be useful to detect clinically occult, metastatic foci of infection which could guide surgical treatment and duration of therapy.


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$M. \textit{abscessus}$ catheter infection


\textbf{Author contributions}
OX performed literature review and writing of manuscript
SK assisted with literature review, writing and review of manuscript
MG performed isolate sequencing, susceptibility testing, and assisted with writing and review of manuscript
KL performed isolate sequencing, susceptibility testing, and assisted with writing and review of manuscript
AB assisted with writing of manuscript, review and supervision
MS assisted with writing of manuscript, review and supervision

\textbf{Table 1. In vitro susceptibilities of $M. \textit{abscessus}$ bloodstream isolate}

\textbf{Table 2. Summary of published cases of rapidly growing mycobacterial catheter tunnel infections in allogeneic HSCT}

\textbf{Figure 1.}
PET/CT demonstrating uptake within catheter tunnel
A) At start of treatment
B) After 6 weeks of antimicrobial treatment
C) At end of therapy after surgical debridement and 4 further weeks of antimicrobial treatment

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M. abscessus catheter infection

**Table 1.** In vitro susceptibilities of M. abscessus bloodstream isolate

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>MIC (µg/mL)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>16</td>
<td>Susceptible</td>
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<tr>
<td>Cefoxitin</td>
<td>64</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Imipenem</td>
<td>16</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Trimethoprim/sulfamethoxazole</td>
<td>8/152</td>
<td>Resistant</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>4</td>
<td>Resistant</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>8</td>
<td>Resistant</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>16</td>
<td>Resistant</td>
</tr>
<tr>
<td>Linezolid</td>
<td>32</td>
<td>Resistant</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>-</td>
<td>Inducible resistance detected</td>
</tr>
<tr>
<td>Tigecycline†</td>
<td>0.5</td>
<td>-</td>
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</table>

†No CLSI breakpoint available
Table 2. Summary of published cases of rapidly growing mycobacterial catheter tunnel infections in allogeneic HSCT

<table>
<thead>
<tr>
<th>Study</th>
<th>No cases</th>
<th>Species</th>
<th>Onset</th>
<th>Antimicrobials</th>
<th>Surgery</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>Gaviria JM et al. 2000</td>
<td>7</td>
<td>M. abscessus, M. fortuitum, M. chelonae, M. mucogenicum</td>
<td>Median 61 days following HSCT (3-331 days) †</td>
<td>Average 2 antibiotics (range 1-3) Imipenem or cefoxitin and amikacin for 2-4 weeks followed by 2 of clarithromycin, ciprofloxacin, doxycycline for 4-6 weeks Median 7 weeks total (range 2-12 weeks)</td>
<td>All cases underwent catheter removal and soft tissue debridement</td>
<td>Resolved</td>
</tr>
<tr>
<td>Ward MS et al. 1999¹⁰</td>
<td>1</td>
<td>M. chelonae</td>
<td>3 months before HSCT (1 year after diagnosis and treatment of AML) Worsened 3 months following HSCT</td>
<td>2 antibiotics Amikacin and cefoxitin Duration not specified</td>
<td>Wide surgical excision</td>
<td>Relapse x2 requiring repeat excision and antibiotic therapy at 3 months and 1 year after initial treatment Death 1 year later from GVHD and disseminated M. chelonae infection</td>
</tr>
<tr>
<td>Roy V et al. 1997⁹</td>
<td>3</td>
<td>M. chelonae, M. fortuitum</td>
<td>7-90 days following HSCT</td>
<td>Median 2 antibiotics (range 1-4) Ciprofloxacin, trimethoprim/sulfamethoxazole, clarithromycin, cefoxitin and/or</td>
<td>Line removed Surgery not specified</td>
<td>Resolved</td>
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<tr>
<td></td>
<td></td>
<td>minocycline</td>
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<td>Median 2 months</td>
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<td>(range 1-6 months)</td>
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</table>

†Described as part of cohort of 23 patients with catheter-related infection of which 8 underwent autologous bone marrow transplant – not specified which patients developed tunnel infection

HSCT = hematopoietic stem cell transplant; GVHD = graft versus host disease
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