

# A totally implantable venous access port associated with bloodstream infection caused by *Mycobacterium fortuitum*

## A case report

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### Abstract

**Rationale:** Rapidly growing mycobacteria (RGM) are well-known causative agents of human infections, particularly in immunocompromised hosts. However, *Mycobacterium fortuitum*, a predominant organism, in catheter-associated infections, has rarely been documented in totally implantable venous access port (TVIAP)-associated bloodstream infections.

**Patient concerns:** A 25-year-old woman with breast cancer presented to hospital with repeated fever for several days. The patient first refused to remove the TVIAP in her body, and had a relapse of *M. fortuitum* bacteraemia four months later.

**Diagnoses:** Bacteria isolated from patient's blood and TVIAP were identified as *M. fortuitum* by Matrix-assisted laser desorption/ionization-time of flight spectrometry and bacterial 16s rDNA sequencing. The patient was diagnosed as a TVIAP-associated bloodstream infection.

**Interventions:** The TVIAP was eventually surgically removed, and *M. fortuitum* was found to have localized on the tip of the catheter. The patient was treated by anti-infection therapy.

**Outcomes:** The patient was treated with 4 weeks of intravenous amikacin and levofloxacin followed by 4 weeks of oral levofloxacin. No episodes of fever occurred during the follow-up to date.

**Lessons:** RGM infections remain a challenging issue for TIVAPs. Accurate species identification, timely intravascular catheter removal and appropriate antibiotic therapy are recommended to ensure successful outcomes.

**Abbreviations:** BLAST = Basic local alignment search tool, MALDI-TOF MS = matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, RGM = rapidly growing mycobacteria, TVIAP = totally implantable venous access port.

**Keywords:** antibiotic schedule, bloodstream infection, *Mycobacterium fortuitum*, rapidly growing mycobacteria, totally implantable venous access port

## 1. Introduction

*Mycobacterium fortuitum*, which is classified as one of several rapidly growing mycobacteria (RGM), is ubiquitously distrib-

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HY and JZ contributed equally to this work.

Written informed consent was obtained from the patient for publication of this report.

All data are available in the patient's admission record to the hospital.

The authors declare that they have no competing interests.

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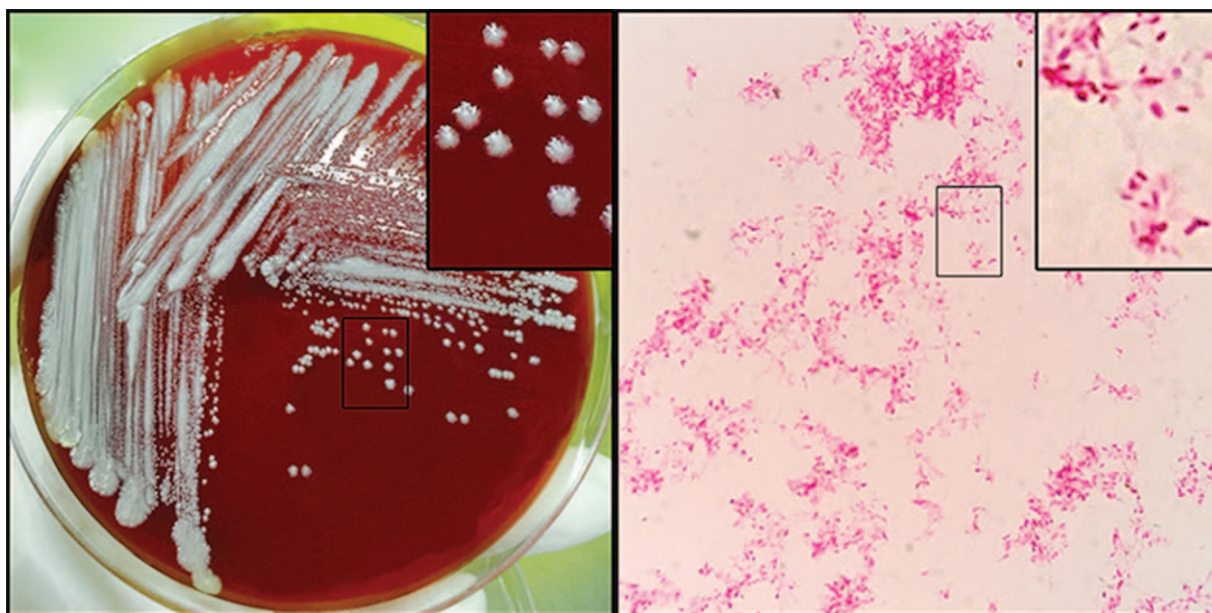
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ed in nature. As an environmental organism, *M. fortuitum* is regarded as an opportunistic pathogen.<sup>[1]</sup> *M. fortuitum* infections have been increasing in frequency with the wide application of immunosuppressants. *M. fortuitum* infections are characterized by pulmonary diseases, lymphadenitis, cutaneous manifestations, and disseminated diseases.<sup>[2]</sup> Invasive bloodstream infections caused by *M. fortuitum* have been associated with indwelling intravenous catheters in patients with underlying immunocompromising conditions.<sup>[1]</sup> Totally implantable venous access ports (TVIAPs) are regarded as the most secure method for intermittent central venous access; however, far too little attention has been paid to the relationship between TVIAP-related bloodstream infections and RGM. Here, we present a TVIAP-associated bloodstream infection caused by *M. fortuitum* in a breast cancer patient.

## 2. Case report

On July 7, 2017, a 25-year-old woman with breast cancer was admitted to our hospital for repeated fever lasting several days. In December 2016, she was diagnosed with breast cancer. A lumpectomy surgery was subsequently performed, and a TVIAP was inserted into her right subclavian vein for chemotherapy. She had just completed her last cycle of chemotherapy and commenced the first cycle of radiotherapy 3 days before the onset of fever.



**Figure 1.** Left: The sixth day *M. fortuitum* grew on blood plate; Right: Optical microscope image of the *M. fortuitum* strain with acid-fast stain, under a 1000× magnification.

The physical examination of the patient demonstrated her temperature was 39.7°C, with chills. Physical examinations of the other organs showed no abnormality. Initial laboratory results revealed a total leukocyte count of  $12.2 \times 10^9/L$  (normal:  $6\text{--}10 \times 10^9/L$ ) and neutrophil count of  $10.5 \times 10^9/L$ , which were highly elevated compared with the total leukocyte count of  $2.6 \times 10^9/L$  and neutrophil count of  $1.4 \times 10^9/L$  3 days before presentation. The serum procalcitonin (PCT) level was 0.15 mg/L (normal: 0–0.05 mg/L). These results suggested the patient had an infectious process. Paired blood cultures were drawn from the venous port and peripheral vein and cultured in an incubator BacT/ALERT3DTM (Biomérieux, Paris, France). On day 5 of incubation, both sets of blood cultures became positive, and they were transferred to sheep blood agar on which the same colonies of gram-positive bacilli with a beaded appearance and positive anti-fast staining were shown. *M. fortuitum* was subsequently identified by matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS; Biomerieux, France). To further validate the identification of the strain, bacterial 16s rDNA sequencing was carried out using a method described previously.<sup>[31]</sup> Briefly, genome DNA was extracted and subjected to amplification by PCR for a 1493-bp gene fragment using the following primers. Forward primer sequences: 5'-CAGAGTTTGATCCTGGCT-3' and reverse primer sequences: 5'-AGGAGGTGATCCAGCCGCA-3', were used for amplification. The amplicon was sequenced by 2 sets of primers using the dye terminator method in an ABI 3730XL (Applied Biosystems). The BLAST online search tool was used to analyze the sequencing results, and the highest hit showed 99.8% identity to *M. fortuitum*.

These findings indicated that the central port might have a strong association with the invasive infection. Port removal as well as intravenous amikacin and levofloxacin were recommended. The patient's fever was resolved, and the temperature returned to normal on the second day after receiving antibiotic treatment. However, the patient refused to remove the TVIAP

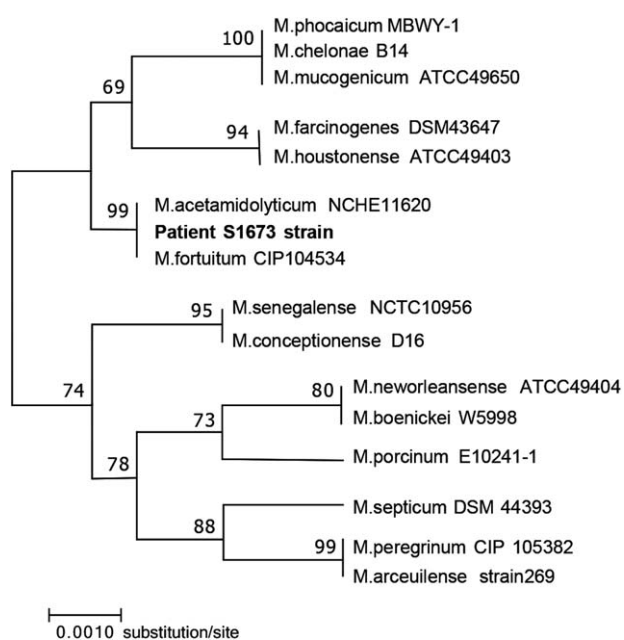
from her body, the main reason being that she felt herself to be clinically well, without infection, and that her medical insurance would not cover the cost of TVIAP and related surgery. Moreover, it would be difficult for the patient to receive subsequent treatment without the port. The antibiotic therapy lasted for 4 weeks, and the patient was discharged.

Four months later, on November 6, the patient was readmitted for persistent fever, with chills; the highest temperature was 39.8°C. *M. fortuitum* was isolated again from culture of her peripheral blood, and the patient finally agreed to remove the port. The TVIAP was surgically removed on the second day of hospitalization. The same organism was also isolated from the tip of the removed catheter (850 colonies from a 5-mL sonicate solution of the tip), indicating its colonization of the catheter without clearance by the antibiotics. The antimicrobial regimens included 4 weeks of intravenous amikacin and levofloxacin followed by 4 weeks of oral levofloxacin, which was consistent with the antibiotic susceptibility test. Repeat blood cultures, which were collected on day 3 and day 6 after receiving antibiotic treatment, showed negative results. No episodes of fever occurred during the follow-up to date (Figs. 1 and 2).

### 3. Discussion

*M. fortuitum* is one of the most frequent RGMs, causing catheter-related infections, with an estimated incidence of 1%. The prevalence of *M. fortuitum* is increasing due to increased recognition of this organism and to advances in identification techniques, as well as the continuously decreasing costs of phenotypic and molecular diagnostic technology.<sup>[41]</sup> In addition, the increased prevalence of immunocompromised hosts has contributed to the increasing incidence of RGMs.

To the best of our knowledge, TVIAP-associated bloodstream infection caused by *M. fortuitum* is rare, that is, partly because of the view that TVIAPs are the most secure approach for long-term intermittent central venous access and the relatively low incidence



**Figure 2.** Polygenetic tree (neighbor-joining method, 1000 bootstrap replicates) of the 16s rDNA sequence from the patient's blood sample and other *Mycobacterium* spp. was built using Mega 7.026.

of RGMs in bloodstream infections and the delayed recognition of these infections. As an environmental organism, *M. fortuitum* can be resistant to commonly used disinfectants, which facilitates its role in nosocomial infection.<sup>[3]</sup> In addition, the ability to form biofilm can increase its pathogenicity and enhance its ability to cause bloodstream infection.<sup>[4]</sup> Prior studies<sup>[1,3,4,6]</sup> have established that RGM bloodstream infections most commonly occur in patients with cancer, with most being catheter associated. The incidence of *M. fortuitum* bloodstream infection is likely related to the duration of catheter placement as well as the location site and type of catheter.<sup>[5]</sup> Our patient had several risk factors, including cancer, immunocompromising conditions, and central port placement. Previous evidence<sup>[6]</sup> has suggested that specific diseases such as breast cancer might be an independent predisposing factor for catheter-related RGM invasive infection. Raad et al<sup>[6]</sup> reported that 4 of 15 patients with catheter-related RGM bacteremia had breast cancer as the primary disease. However, the mechanism remains unclear, and further studies and experimentation regarding the role of breast cancer would be interesting.

The rapid and accurate identification of RGM species plays an important role in the diagnosis of *M. fortuitum* bacteremia. Traditional biochemical tests have proven inefficiently sensitive for distinguishing among species of RGM<sup>[4]</sup>; thus, most laboratories in developing countries must use a reference laboratory to identify RGM, which can take much more time. Furthermore, delay in organism identification may have a potential influence on the treatment effect because the optimal antibiotic regimens differ among species. Advanced microbiologic techniques, such as sequencing and MALDI-TOF MS, may allow rapid identification of pathogens. However, the real difficulties in diagnosing catheter-related invasive infection caused by RGM lies in their relatively low growth. Therefore, it is difficult to cultivate these bacteria within 72 hours, and catheter segments with no organism growth within 48 to 72 hours

are usually considered negative and discarded.<sup>[4]</sup> Early recognition of RGM catheter-related bloodstream infection is challenging, and clinicians and laboratories must maintain a high index for these pathogens.<sup>[7]</sup>

The final management of TVIAP-related bloodstream infection in our case included port removal and appropriate antimicrobial treatment. The relapse of *M. fortuitum* bacteremia in our case emphasizes the key role of port removal in successful intervention. An early example of this issue was carried out by Raad et al<sup>[6]</sup>: all patients whose catheters were properly removed completely recovered, whereas those whose catheters stayed in place either failed treatment or had a relapse of bacteria infection. EI Helou et al<sup>[8]</sup> also showed a decreased relapse rate if the catheter was removed. A common feature of RGMs is their resistance to first-line anti-tuberculosis antimicrobials. However, there is no evidence-based consensus to guide RGM infection treatments. A recently published literature review<sup>[1]</sup> concluded that *Mycobacterium mucogenicum* and *M. fortuitum* tend to have a more favorable antibiotic susceptibility profile, whereby they are typically susceptible to amikacin, ciprofloxacin, imipenem, and co-trimoxazole. Amikacin shows excellent activity against *M. fortuitum* and other RGM. Some studies have shown that inducible erythromycin methylase genes (*erm* gene) are present in *M. fortuitum* and related species, which can confer resistance to macrolides.<sup>[4]</sup> Therefore, the use of macrolides or clarithromycin to treat infections caused by these isolates should be executed with caution, especially when given as monotherapy. The duration of antibiotic therapy for the treatment of RGM invasive infections differs among studies. Researchers<sup>[4]</sup> believe that at least 4 weeks of a combination of antimicrobial regimen can resolve progression and lead to better outcomes. Compared with other bacterial invasive bacteremia, the RGM-associated bloodstream infections usually have a low mortality.<sup>[4]</sup>

#### 4. Conclusion

RGM infection is associated with increased mobility in immunocompromised patients and remains a challenging issue for long-term intravenous catheter use, which highlights the need for rapid and accurate species identification and susceptibility testing. Initiation of appropriate antimicrobial treatment and timely intravenous catheter removal are recommended to guarantee fruitful results.

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#### Author contributions

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