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Catheter-related bloodstream infection caused by *Mycobacterium mucogenicum* in an immunocompromised patient

Sepsis asociada a catéter causada por *Mycobacterium mucogenicum* en un paciente inmunodeprimido

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Abstract

We report a case of *Mycobacterium mucogenicum* catheter-related sepsis in a patient with recurring plasmablastic lymphoma. The patient was being treated via a totally implantable central venous device (Port-a-Cath). Appropriate treatment consisted of antibiotic therapy and catheter removal. Recognizing rapidly growing mycobacteria (RGM) is essential for diagnosis and appropriate therapy.

Key words: *Mycobacterium mucogenicum*, catheter-related sepsis, immunocompromised patient, lymphoma.

Resumen

Describimos un caso de sepsis asociada a catéter por *Mycobacterium mucogenicum* en un paciente con linfoma plasmablástico recurrente. El paciente estaba siendo tratado a través de un reservorio subcutáneo implantable (Port-a-cath®). El tratamiento adecuado consistió en antibioterapia y retirada del catéter. En nuestro caso no se pudo demostrar la fuente de la infección. La identificación correcta de las micobacterias de crecimiento rápido es importante para el diagnóstico de la infección y su correcto tratamiento.

Palabras clave: *Mycobacterium mucogenicum*, sepsis asociada a catéter, inmunodepresión, linfoma.

Introduction

Mycobacterium mucogenicum is a rapidly growing mycobacterium (RGM) responsible for a wide range of diseases, including skin and blood stream infections.^(1,2) Most reports refer to immunocompromised patients with long term indwelling catheters, with diseases which include hematologic cancers.⁽²⁻⁴⁾ Despite the rising number of cases described, the diagnosis of catheter-related sepsis by RGM is still challenging, due to the risk of misidentification of significant isolates.

We describe a case of catheter-related sepsis secondary to *M. mucogenicum* in a patient with fever and a recurring plasmablastic lymphoma, pointing out the importance of suspecting that RGM are responsible for catheter-related sepsis in immunocompromised patients with lymphoproliferative disorders.

Case report

A 68 year-old man who suffered from recurring plasmoblastic lymphoma was admitted to the Emergency Unit with fever and shivers. His medical record showed tuberculosis and lymphoma, which had been diagnosed three years prior to this episode. After complete remission on chemotherapy, he had had a relapse three months earlier and was currently on chemo-immunotherapy (Rituximab-ESHAP) via a totally implanted central venous device (TID) (Port-a-Cath®; Smiths Medical, St. Paul, USA) inserted 40 days before.

Physical examination revealed a disoriented patient with pale skin and mucosa, a fever of 38°C with no signs of focal infection and shivers. Systemic examination was essentially normal. The TID site was not inflamed. Counts were as follows: white blood cells, $0.5 \times 10^9/L$ (absolute neutrophil count of $0.1 \times 10^9/L$); platelets, $55 \times 10^9/L$; hemoglobin, 8.6 g/dL.

First impression at the emergency room was that of a grade IV febrile neutropenia with no focal sign and pancytopenia post-chemotherapy, suggesting a possible opportunistic infection. After admission, blood from the TID catheter and a peripheral vein was collected and cultured in BACTEC 9240 aerobic and anaerobic bottles (Becton Dickinson, Sparks, MD, USA). The patient was empirically treated with ceftadizime and amikacin. The fever went down within three days. On day four after admission, he was asymptomatic and his white cell count had recovered. Although blood culture results were not yet available, the patient was discharged on a new treatment with cefuroxime-axetil and trimethoprim-sulfamethoxazole for one week. Five days later, he was admitted for a new chemotherapy cycle, and referred repeated chills and slight fever for the past two days. Physical examination was normal. Laboratory tests showed a white blood cell count of $14 \times 10^9/L$, neutrophils 83%, and a hemoglobin count of 9.7/g/dL. The previous blood culture, now available, yielded positive results for the TID within 72 h, showing a gram-positive bacillus, initially reported as a "diphtheroid" species. The bacillus was later identified as an acid-fast bacillus by carbol fuchsin staining. Subcultures from the blood bottles to blood and chocolate agar at 35°C showed smooth and mucoid colonies of gram-positive bacilli after 2 days of incubation. The peripheral blood culture was positive within 77 hours with the same organism. The diagnosis of a catheter-related infection was based on the time to positivity of the peripheral and catheter drawn blood cultures, according to published guidelines.⁽⁵⁾ The organism was sent to the Centro Nacional de Microbiología (Majadahonda, Spain), where it was definitely identified as *M. mucogenicum* through sequencing analysis of the 16S rRNA gene⁽⁶⁾ and PCR restriction enzyme analysis (PRA) of the *hsp65* gene.⁽⁷⁾

Antimicrobial agent susceptibility of the organism was

tested in-vitro using the E-test method (Biodisk, Solna, Sweden) and the results were interpreted according to the criteria established by the Clinical Laboratory Standards Institute.⁽⁸⁾ The strain proved to be susceptible to amoxicillin-clavulanic acid, amikacin, ciprofloxacin, clarithromycin, minocycline, trimethoprim-sulfamethoxazole, ceftoxitin, cefuroxime, imipenem and linezolid, intermediate to tobramycin, and resistant to vancomycin.

Treatment on amoxicillin-clavulanic acid via a venous device was initiated and the reservoir of the catheter was sealed with amikacin. On day five after admission, he was discharged on cefuroxime-axetil and trimethoprim-sulfamethoxazole for four days. Thirteen days after sealing, the patient was admitted again with fever of 37.5 – 38°C for two days, shivers and no focal sign. Physical exploration was normal. Counts were as follows: white blood cells, $1.3 \times 10^9/L$; neutrophils, $0.5 \times 10^9/L$; platelets, $34 \times 10^9/L$; hemoglobin, 7.9 g/dL. Performed tests were normal. Peripheral and site blood cultures were performed, subsequently yielding negative results, and treatment on piperacillin-tazobactam was started. During admission, the patient had no fever and recovered white cell count. On day four after admission he was discharged on trimethoprim-sulfamethoxazole. Ten days after discharge, and with no fever, the TID was removed but the catheter was not sent for microbiological studies.

Discussion

RGM have emerged as a frequent cause of infection in healthy and immunocompromised patients, including pulmonary and skin infections, catheter related bacteremia and some less common infections.^(2,4)

The number of RGM species associated with various indwelling devices has also increased, being *M. fortuitum*, *M. chelonae* and *M. mucogenicum* the most frequently isolated species.^(2,4) *M. mucogenicum* is an opportunistic pathogen responsible for several clinical pictures, although it commonly causes posttraumatic skin infections and catheter-related sepsis.^(2-4,9)

M. mucogenicum grows aerobically in solid media producing non-pigmented mucoid and non-mucoid colonies in 2 to 4 days. The Gram staining shows curved gram-positive bacilli, which can be misidentified as a "diphtheroid" species and thus as a contaminant. The RGM are environmental organisms which behave as a contaminant or as a pathogen. *M. mucogenicum* is widely spread and can be isolated from several water sources, including tap water in hospital water systems, a fact that may suggest its ubiquity and potential role as an opportunistic pathogen.^(10,11) In our patient, the source of the infection is uncertain as no environmental investigation was carried in the hospital. However, acquisition is likely to have occurred through contact with a contaminated environmental water source, in or outside the hospital.

In patients with malignancies, totally implanted intravascular devices (TID) are commonly used for chemotherapy. Although the number of RGM infections associated to these devices is low,^(12,13) the most frequent disease associated with *M. mucogenicum* is bloodstream and long term indwelling catheter infection.^(2-4,14) The highest incidence of catheter-related sepsis by *M. mucogenicum* occurs in immunocompromised hosts, many of whom suffer from leukemia or other neoplasm.^(2,4) In our case, *M. mucogenicum* caused TID-related sepsis in a neutropenic patient who suffered from a recurring plasmablastic lymphoma and had a Port-a-Cath device placed for 40 days.

In a recently published study on 115 patients with a primary diagnosis of cancer, RGM were isolated from blood or the catheter tip in 46, and *M. mucogenicum* accounted for 52% of the isolates (24 cases), followed by *M. abscessus* (6 cases) and *M. fortuitum* (6 cases).⁽²⁾ Other species were isolated, but accounted for lower percentages. Most of the patients (96%) suffered from underlying malignancy, and almost half presented with hematologic cancers. Our patient was immunocompromised due to a recurring plasmablastic lymphoma and subsequent chemotherapy.

The optimal therapy for *M. mucogenicum* has not been established. Susceptibility to amikacin, cefoxitin, clarithromycin, imipenem, trimethoprim-sulfamethoxazole and ciprofloxacin is common among *M. mucogenicum*, but other RGM have different antimicrobial susceptibility patterns.

Exclusive antibiotic therapy has proved to be insufficient and catheter removal is recommended to avoid reinfections.^(2,12) Our patient presented with recurrent fever despite systemic and local (sealing of catheter) antibiotic treatment. Eventually the infection was successfully controlled by removal of the TID and appropriate antimicrobial therapy.

M. mucogenicum is increasingly recognized as an opportunistic pathogen causing bloodstream and catheter-related infections. An accurate identification of RGM is important for the diagnosis and appropriate treatment of the infection, the latter consisting of antibiotic therapy and catheter removal. It should be considered as a possible cause of infection when isolated in the setting of implantable devices and lymphoproliferative disorders.

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