Tsukamurella catheter-related bloodstream infection in a pediatric patient with pulmonary hypertension

Kristen A. Wendorf,1 Claudia M. Espinosa,2 William D. LeBar,3 Jason B. Weinberg4
1University of Michigan Medical School; 2Department of Pediatrics and Communicable Diseases; 3Department of Pathology; and 4Department of Microbiology and Immunology, University of Michigan, Ann Arbor, Michigan, USA

Abstract

Catheter-related bloodstream infections (CR-BSI) are important complications in patients with long-term indwelling central venous catheters. In this report, we present the case of a 14-year-old male with pulmonary hypertension treated with continuous treprostinil infusion, who presented with a CR-BSI caused by a Tsukamurella species. This case highlights the potential for this unusual organism to cause infection in immunocompetent patients.

Introduction

Intravascular catheters have become an integral component of contemporary medical treatment for various diseases, and they are used commonly for infusions of chemotherapeutics and antibiotics. Complications including catheter-related bloodstream infections (CR-BSI) can be a significant source of morbidity and mortality for patients with indwelling central venous catheters.1 Patients with pulmonary hypertension require long-term central venous catheters for the continuous infusion of prostanoids, which help to reduce pulmonary artery pressure.2 Therefore, these patients are at risk for CR-BSI. While CR-BSI are frequently caused by Staphylococcus species,3 many other pathogens have been identified as causes of CR-BSI. In this report, we describe a pediatric patient with pulmonary hypertension who had a CR-BSI caused by a Tsukamurella species, which is an unusual pathogen to cause infection in an otherwise immunocompetent patient.

Case Report

A 14-year-old male with a history of idiopathic pulmonary hypertension treated with intravenous treprostinil presented to the emergency room with a three-day history of fever to 103.2°F along with leakage from his Broviac central venous catheter. The catheter, which had been in place for three years, was found to have an external break and subsequently was repaired. There was no evidence of infection at the insertion site. Blood cultures obtained from the catheter grew catalase-negative staphylococci and a gram-positive bacillus. The patient was admitted to the hospital and treated with intravenous vancomycin run through the catheter. Vancomycin locks were used in the catheter between antibiotic doses.

The patient remained afebrile after admission, but a second blood culture obtained on hospital day number 2 (to determine whether the line had been sterilized) again grew a gram-positive bacillus. Catalase-positive, beaded gram-positive bacilli were isolated from subcultures to solid media. Based on these initial characteristics, a preliminary identification of a possible rapid-growing mycobacterium was considered. The patient’s antibiotic regimen was changed to a combination of amikacin, clarithromycin, and linezolid on hospital day number 6. Line removal was recommended, but the procedure was delayed until anticoagulation from the patient’s long-term coumadin therapy could be reversed. On hospital day 9, the patient became febrile for the first time after admission, although the most recent set of cultures from the line obtained from hospital days 3-8 had been negative. A transthoracic echocardiogram showed no evidence of valvular vegetations. A chest CT scan performed without contrast revealed a small left pleural effusion, scattered areas of atelectasis, and enlargement of pulmonary arteries compatible with the patient’s pulmonary hypertension.

Modified acid-fast stains performed on the isolate from the first positive blood culture were negative, and the isolate was referred to the Bureau of Laboratories, at the Michigan Department of Community Health (Lansing, Michigan) for further identification. By hospital day 10, the reference laboratory had determined that the organism was not a mycobacterium species. At that point, amikacin, clarithromycin, and linezolid were discontinued and vancomycin was started. The central venous catheter was removed on hospital day number 11. A culture of the catheter tip remained negative, but a peripheral blood culture obtained after removal of the catheter again grew a gram-positive rod. The patient remained febrile following removal of the catheter. No venous thrombus was identified by Doppler ultrasound evaluation of the site of his previous catheter.

Using high-performance liquid chromatography (HPLC) and other conventional biochemical tests, the isolate was identified as a Tsukamurella species. Based on this information, levofloxacin was added to the vancomycin therapy on hospital day 13. The patient’s fever subsided quickly after this change. Multiple blood cultures (eight in total) obtained over the next 10 days remained negative. Vancomycin was discontinued on hospital day 18. A new indwelling central venous catheter was inserted on hospital day 25. The patient remained afebrile and was discharged from the hospital shortly thereafter. Although there had been no overt evidence of endocarditis by echocardiogram or thrombus by Doppler ultrasound, the decision was made to treat the patient with an extended course of antibiotics owing to the prolonged bacteremia and the patient’s underlying disease. He finished a six-week course of oral levofloxacin with no further complications related to this infection.

The Tsukamurella isolate was sent to a second reference laboratory at National Jewish Health (Denver, Colorado) for susceptibility testing. The results (Table 1) demonstrate low minimum inhibitory concentration (MIC) values (<1 μg/mL) for minocycline, ciprofloxacin, and trimethoprim/sulfamethoxazole. In addition, MIC values were low (<8 μg/mL) for amikacin, kanamycin, ceftriaxone, cefepime, imipenem, clarithromycin, and linezolid. MIC values were

Key words: Tsukamurella, central venous catheter, pulmonary hypertension.

Contributions: KW, CE, WLeB, JW contributed to the conception of this project and acquisition of information regarding the case. KW drafted the original manuscript; KW, CE, WLeB, JW assisted in the revision of the manuscript, and approved the final version to be published.

Conflict of interest: the authors report no conflicts of interest.

Received for publication: 26 January 2010. Revision received: 10 March 2010. Accepted for publication: 11 March 2010.

This work is licensed under a Creative Commons Attribution 3.0 License (by-nc 3.0).

©Copyright K. Wendorf et al., 2010
License PAGEPress, Italy
Infectious Disease Reports 2010; 2:e5
doi:10.4081/1dr.2010.e5

Correspondence: Jason B. Weinberg, 7510A MSRB I, 1150 West Medical Center Drive, Ann Arbor, Michigan 48109-5684, USA.
E-mail: jbwein@umich.edu
higher for tobramycin and genta-micin (>4 μg/mL), azithromycin (>32/16 μg/mL), and amoxicillin/clavulanate (128 μg/mL).

**Table 1. Susceptibility testing of Tsukamurella sp. isolate.**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Minimum inhibitory concentration (μg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anikacin</td>
<td>&lt;8.0</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>&lt;8.0</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>4.0</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>8.0</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>&lt;8.0</td>
</tr>
<tr>
<td>Ceftipime</td>
<td>8.0</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>16.0</td>
</tr>
<tr>
<td>Imipenem</td>
<td>4.0</td>
</tr>
<tr>
<td>Minocycline</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>2.0</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>128.0</td>
</tr>
<tr>
<td>Trimethoprim/Sulfamethoxazole</td>
<td>&lt;0.5/9.5</td>
</tr>
<tr>
<td>Amoxicillin/Clavulanate</td>
<td>&gt;32/16</td>
</tr>
<tr>
<td>Linezolid</td>
<td>4.0</td>
</tr>
</tbody>
</table>

**Discussion**

CR-BSI remains a medically important problem in patients who require long-term intravenous access. The reported incidence of CR-BSI in patients with long-term indwelling central venous catheters varies from 0.3 to 9.1 infections per 1000 patient days, although higher rates have been documented in intensive care unit settings (7.7 per 1000 patient days) compared to outpatient settings (0.45 per 1000 patient days). The risk of infection also appears to increase over time, with more infections occurring after at least 30 days of catheter use.

Patients receiving continuous prostanooid infusions to treat pulmonary hypertension are at risk for CR-BSI. The rate of CR-BSI in patients with pulmonary hypertension and an indwelling central venous catheter has ranged from 0.1 per 1000 patient days to 0.89 per 1000 patient days/catheter days. These rates are comparable to rates seen in other patient populations in outpatient settings. The majority of reported cases in patients with pulmonary hypertension have been caused by gram-positive organisms, especially Staphylococcus species. Interestingly, both an overall increased incidence of CR-BSI and an increased proportion of CR-BSI caused by gram-negative pathogens have been reported in patients receiving treprostinil compared to patients receiving epoprostenol. While the presence of an indwelling central venous catheter is likely the biggest risk factor for CR-BSI in this patient population, there has been some speculation that potential immunomodulatory activities of the prostanooids may increase the risk of infection. For instance, synthetic prostacyclin analogs have been shown to inhibit bacterial phagocytosis and killing by macrophages in vitro.

In this report, we describe a case of CR-BSI caused by a Tsukamurella species. Tsukamurella species are aerobic gram-positive organisms from the order Actinomycetales. Other genera of this order, including Nocardia, Gordonia, Streptomyces, Rhodococcus, Mycobacterium, and Corynebacterium, are closely related to Tsukamurella species; this may explain the easy misidentification of Tsukamurella in the literature. Tsukamurella species typically are found primarily in soil and sludge. Tsukamurella was first isolated in humans from the sputum of patients with chronic lung disease in 1971 by Tsukamura and Mizuno. The organism was known as Gordona aurantia until 1988, when it was first proposed as a genus based on gene sequence analysis. Seven Tsukamurella species have been identified, but only five have been reported to cause infections in humans, including T. inchonensis, T. paurometabola, T. pulmonis, T. stranjardiae, and T. tyrosinosolvens. The first case of bacteremia caused by T. pulmonis was reported in 1998 in an immunosuppressed patient. Tsukamurella species may be misidentified as atypical Mycobacterium species when conventional mycobacterial testing is used initially in the identification of a gram-positive bacillus. Given the difficulty of identifying Tsukamurella isolates using routine laboratory techniques, it is likely that some cases of Tsukamurella CR-BSI have been incorrectly attributed to other pathogens. Of the Tsukamurella species associated with CR-BSI reviewed here, five were first identified as Corynebacterium, one as Nocardia, four as Rhodococcus, two as Bacillus, and one as a nontuberculous mycobacterium. Final identification as Tsukamurella species often depended on the use of techniques that are not readily available in most clinical microbiology laboratories, such as HPLC or 16S rRNA sequencing.

In vitro testing suggests that Tsukamurella isolates may be susceptible to quinolones, macrolids, carbapenems, trimethoprim/sulfamethoxazole, and aminoglycosides. Low MIC values for ciprofloxacin, imipenem, and trimethoprim/sulfamethoxazole (Table 1) suggest that this was true for the isolate that we describe in this report. The activity of other classes of antibiotics varies in other reports. Susceptibilities may vary even within a class of antibiotics, as with the aminoglycosides for the isolate described here (Table 1). Importantly, antibiotics that are common empiric choices when a gram-positive rod is isolated may not have sufficient activity against Tsukamurella species. For instance, although MIC values for vancomycin were not
available for the isolate obtained from our patient, other reports have documented MIC values for vancomycin between 2 and 8 μg/mL. Many antibiotics have been used to treat Tsukamurella CR-BSI, particularly trimethoprim/sulfamethoxazole and quinolones by themselves or in combination with other antibiotics. Because of the varying susceptibilities of Tsukamurella species and the relative lack of clinical experience with Tsukamurella CR-BSI, appropriate identification of a Tsukamurella species and subsequent susceptibility testing are therefore essential to facilitate appropriate antimicrobial therapy. In the setting of CR-BSI caused by a Tsukamurella species, treatment in our patient and in all other previously reported cases,[16,20,23,27,28] ultimately required the removal of the infected catheter in addition to antimicrobial therapy.

In summary, it is important to consider Tsukamurella species in cases of CR-BSI, particularly when specific identification of a gram-positive bacillus is difficult or delayed or when a patient fails to respond promptly to empiric antibiotic therapy. Our report highlights the potential for Tsukamurella species, while most often associated with CR-BSI in immunocompromised patients, to cause disease in other patient populations including otherwise immunocompetent patients treated with intravenous prostanoids for pulmonary hypertension.

References


