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Agrobacterium radiobacter bacteremia in oncologic and geriatric patients: presentation of two cases and review of the literature

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Summary
Introduction: We report here two cases of *Agrobacterium radiobacter* bacteremia. These cases were observed at the same institution over a short time period (3 months).
Case reports: The first patient was a female cancer patient receiving third-line chemotherapy for ovarian carcinoma. When she developed bacteremia, she was neutropenic and had an indwelling catheter that was removed as part of the treatment. The second case was a geriatric patient admitted from home with bacteremia, clinical signs of septic shock, and concomitant acute cholecystitis.
Outcome: Both patients responded promptly and completely to antibiotherapy. No recurrence was observed.

Introduction

Agrobacterium radiobacter is an agricultural soil bacterium that survives in the ground as a saprophytic organism. It is a Gram-negative aerobic bacillus that can be an opportunistic pathogen, often associated with indwelling catheter infection.[1,2] Predisposing factors are leukopenia, neutropenia, low CD4+ lymphocyte count, hospitalization, concurrent AIDS-related infectious complications, indwelling catheter, and instrumentation.[3]

A. radiobacter bacteremia has most frequently been reported in the HIV-infected population, but recently cases in other compromised patients have been published. Oncologic and geriatric patients belong to this last category. In this population, bacteremia is also frequently due to an indwelling catheter infection. We report here a single institution's experience of two cases of *A. radiobacter* bacteremia. These two cases were observed over a short time period (3 months) on two different hospital wards. In one patient, the catheter was believed to be the cause of infection, while for the second, the origin remained obscure. We discuss here the epidemiology and characteristics of *A. radiobacter* infections in the light of our two cases.

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Case 1

In December 2001, a 42-year-old woman was diagnosed with FIGO (Fédération Internationale de Gynécologie et d'Obstétrique) stage IV ovarian carcinoma. She underwent debulking surgery followed by multiple lines of chemotherapy treatment. The first line consisted of six courses of carboplatin (area under the curve (AUC) 6) and taxol 175 mg/m^2 administered every 3 weeks. For this treatment, a Bard Port® indwelling catheter was placed. In December 2002, CA-125 started to rise and peritoneal carcinomatosis was diagnosed. A second treatment with topotecan (1.25 mg/m^2 for 5 days every 3 weeks) was started. In October 2003, a new chemotherapy was started with carboplatin (AUC 6) and Caelyx® (30 mg/m^2 every 4 weeks) due to a third increase of CA-125 with peritoneal relapse. In November 2003 while perfusing the port for a routine post-chemotherapy blood control, she presented malaise, fever, and shivers. Physical examination was normal with the exception of a high body temperature (39 °C). There was no sign of septic shock and these symptoms lasted 48 hours. Her white blood cell count on admission was 1.96×10^9/l, with 51.5% neutrophils (1×10^9/l), 38.8% lymphocytes (0.8×10^9/l), and 9.7% monocytes (0.2×10^9/l). C-reactive protein (CRP) was 1.9 mg/dl (normal <1 mg/dl). She was treated empirically with intravenous (IV) ceftazidime (2 g/8 h) and rapidly became afebrile. The antimicrobial susceptibility to antibiotics was determined before definitive identification of the pathogen. It showed sensitivity to third-generation cephalosporins, beta-lactams, carbapenems, amikacin, ciprofloxacin, meropenem, and co-trimoxazole. The identification of the pathogen came later: three blood samples obtained one through the port and two through peripheral veins were positive for *A. radiobacter*. The identification of *A. radiobacter* was confirmed in a bacteriology reference laboratory. The port was suspected to be the origin of the infection and was then removed after 7 days of IV antibiotic treatment (ceftazidime 2 g/8 h). A culture of the removed port remained sterile. A total of 10 days of IV ceftazidime was administered, then the patient was discharged with oral ciprofloxacin. Three weeks after oral antibiotherapy, a new port was implanted and chemotherapy was continued. To-date no further infection has been observed in this patient.

Case 2

An 80-year-old man was hospitalized for fainting, high fever, septic shock, and acute renal failure. He was living at home and had a history of epilepsy, stroke, gastric hemorrhage, chronic renal failure, and bladder catheter for prostate hypertrophy. Physical examination revealed signs of septic shock with a blood pressure of 100/70 mmHg, tachycardia 108 beats per minute, and peripheral cyanosis. His body temperature was 38.8 °C. There was tenderness with a rebound in the right upper quadrant. Laboratory tests showed: 11.2×10^9/l leukocytes with 81% neutrophils, CRP 10 mg/dl, and moderately increased liver enzymes. Computed tomography of the abdomen showed an acute cholecystitis without signs of biliary tract enlargement. Urine culture obtained through the bladder catheter remained sterile, while three blood cultures showed the presence of *A. radiobacter*. IV ciprofloxacin (800 mg per day), metronidazole (1500 mg per day), and amikacin (1 g on day 1 followed by 500 mg once daily) were empirically started. Antibiotherapy was not modified, except that metronidazole was stopped when the pathogen was identified since this was sensitive to most usual antibiotics except aztreonam. In addition, the medical evolution was favorable: amikacin was stopped after 5 days and ciprofloxacin IV after 10 days. At day 11 the patient was discharged with oral ciprofloxacin (1 g daily) for an additional 3 weeks. He then underwent an elective laparoscopic cholecystectomy. At microscopic evaluation there were signs of residual acute cholecystitis. Gall culture remained sterile. The bladder catheter was not changed and there was no recurrence of *A. radiobacter* bacteremia.

Discussion

A. radiobacter is an environmental bacterium present in rhizospheres. It is a motile, glucose non-fermenting, Gram-negative bacillus, oxidase positive, strongly urease positive, and able to hydrolyze esculin.[4] It is an active carbohydrate oxidizer. This bacterium is mostly encountered in soils and plants.[5] Isolation in clinical specimens is very rare. *A. radiobacter* can be distinguished from other species – *Agrobacterium rhizogenes*, *Agrobacterium rubi*, and *Agrobacterium tumefaciens* – as the only one that has been described not only as a plant pathogen but also as a human pathogen, although of low virulence. However, a case of *A. tumefaciens* bacteremia has recently been reported.[6] In the literature, about 40 cases of infection with *A. radiobacter* have been recorded. More than half of the patients presented with bacteremia, peritonitis, urinary tract infection, endocarditis, or cellulitis.[7,8] Immunosuppression, the presence of central venous catheters, nephrostomy tubes, intraperitoneal catheters, and prosthetic valves were predisposing factors. The first-line antibiotic therapy for *A. radiobacter* disease has not been definitively determined. The vast majority of reported patients responded to different antimicrobial therapies, and this strategy was often combined with removal of suspected catheters.[9]

The antimicrobial susceptibility patterns of these organisms appear to be quite variable.[8] In different reports, cure was obtained with a wide range of different antimicrobial agents including: association of beta-lactams plus aminoglycosides, co-trimoxazole and imipenem, ampicillin or beta-lactams associated with beta-lactamase inhibitors, third generation cephalosporins, imipenem, co-trimoxazole, and fluoroquinoles alone. Alnor et al. suggested that ciprofloxacin be the first choice.[4] These reports came mostly from observations in HIV-infected patients. The outcome of infection was favorable in all cases described, and no direct mortality was observed.

If most observations were reported in HIV-infected patients, the isolation of *A. radiobacter* in oncologic patients is, however, uncommon. In the literature, Paphitou and Rolston recently reported a case of catheter-related bacteremia due to *A. radiobacter* in a neutropenic patient.[10] Castagnola et al. reported other cases in a population of children with Broviac® catheters for cancer treatment.[11] Children were receiving antineoplastic chemotherapy or bone marrow transplantation, and all episodes were diagnosed in the absence of granulocytopenia. In addition, Amaya and Edwards reported *A. radiobacter* bacteremia in five pediatric patients. All cases were related to catheter infection.[12] Hammerberg et al. described the isolation of *A. radiobacter* from a central venous catheter in a patient undergoing chemotherapy who had been neutropenic.[1] Dunne et al. reported infection with *A. radiobacter* that was isolated in blood cultures from an immunocompromised child cancer patient who had a transcutaneous catheter.[13]

Gram-positive bacteria are most frequently responsible for indwelling catheter infections, however other pathogens can be found, particularly in neutropenic patients, for instance: yeasts, fungi, Gram-negative bacilli, and corynebacteria. In oncologic patients some criteria are important to judge the severity of infections: the location of infection, the catheter device (central venous catheter or port), and the gravity of symptoms (septic shock or not). The eradication of the infection from the chamber of the indwelling catheter is more difficult and the principle of treatment in this kind of infection is antibiotherapy and removal of the catheter.[9]

In the second case, we observed *A. radiobacter* bacteremia in a man who was not being treated for cancer. However he could be considered an immunocompromised patient since he was old and suffered from chronic renal failure. In addition, he had a permanent bladder catheter. We discovered concomitantly to the bacteremia an acute cholecystitis, probably secondary to the systemic infection. The cholecystitis was later histologically confirmed when the gallbladder was removed by elective surgery. The origin of the bacteremia was not found, but it is of note that the urine remained sterile and that the infection never recurred despite the fact that we did not change the bladder catheter. An interesting point is the fact that the patient was admitted from home when the bacteremia was diagnosed. Unfortunately the personal habits of this patient were not recorded in order to determine a possible risk behavior.

A. radiobacter bacteremia has rarely been described in the geriatric population. Our second case suggests that despite not being severely immunosuppressed by HIV infection or cancer treatments, the geriatric population, frequently suffering from multiple organ dysfunction, can be prone to develop infections due to this pathogen. In 1985 Freney et al. presented the case of an elderly patient receiving artificial ventilation who developed *A. radiobacter* bacteremia.[14] This patient was the second case of *A. radiobacter* human infection ever reported, and unfortunately the source of infection was not found. More recently Yu et al. described a 78-year-old patient with chronic obstructive pulmonary disease treated with corticosteroids who developed *A. radiobacter* bacteremia in the intensive care unit.[15] Finally, a patient with corticosteroid use and diabetes mellitus who developed *A. radiobacter* bacteremia has recently been published.[16]

In a larger published series of 13 patients with *A. radiobacter* bacteremia, Lai et al. reported that 76% of patients (10 patients) had underlying hematological malignancy or solid-organ cancer. Six patients (46%) had febrile neutropenia and most of the infections were catheter-related (54%). Finally 92% of infections were hospital-acquired, although not due to nosocomial spread, and all patients survived.[17]

On at least one occasion pseudobacteremia with *A. radiobacter* has been reported. These false-positive blood cultures collected in newborns were due to an environmental source and faulty blood inoculation techniques.[18]

In conclusion, *A. radiobacter* may play a pathogenic role in oncologic patients, especially if indwelling devices are present. In addition the geriatric population with its possible multi-organ dysfunction can be vulnerable to this pathogen. Complete cure can be achieved with appropriate antibiotics and removal of the infected catheter.[9] The prognosis of the infection is usually good.[17]

Conflict of interest: No conflict of interest to declare.

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