case report

Successful treatment of multiresistant *Achromobacter xylosoxidans* bacteremia in a child with acute myeloid leukemia

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Achromobacter xylosoxidans is an aerobic gram-negative bacillus and important cause of bacteremia in immunocompromised patients. We describe a leukemia pediatric patient with severe neutropenia who developed bacteremia with *A xylosoxidans* resistant to multiple antibiotics, and treated the patient with tigecycline and piperacillin-tazobactam in addition to supportive medications.

Achromobacter xylosoxidans is a nonfermenting, aerobic, motile, gram-negative bacillus. It was first described by Yabuuchi and Ohyama in 1971 from purulent ear drainage of patients with chronic otitis media.[1] Affected individuals are usually immunocompromised, but nosocomial outbreaks have also been defined.[2] The treatment of infections caused by this organism is difficult due to the lack of a standard therapy and resistance to several antibiotics.

CASE

A 13-year-old male patient was diagnosed as acute myeloid leukemia (M0). Two febrile neutropenia attacks were detected until the fourth course of chemotherapy. Perianal hyperemia and induration were detected as a focus of infections. We did not identify any bacteria from the abscess drain and multiple blood cultures that were taken during the period of fever. Fever, cough, and pain in the perianal region reappeared at the eighth day of the initiation of new chemotherapy with CLASP (ARA-C, L asparaginase). Meropenem and amikacin were initiated. Laboratory findings revealed absolute neutrophil count 400/mm^3 and C-reactive protein 74 mg/dL. Fever regressed after 72 hours of antibiotherapy but reappeared on the 10th day of antibiotherapy with the progression of anal lesion and deterioration of his general condition. Chest X-ray, echocardiography (for ruling out endocarditis), and abdomen ultrasonography did not reveal any pathologic lesion, and galactomannan was negative. The computerized tomography of thorax showed left lung upper lobe pneumonic infiltration. Blood culture was repeated, and antibiotics were switched to piperacillin-tazobactam. On the 20th day of the CLASP therapy, *A xylosoxidans* growth was detected in the blood culture. Repeated 4 blood cultures yielded the same microorganism. Repeated cultures were also taken from perianal abscess to confirm that it is the source. But we did not isolate any microorganism from anal cultures. The susceptibility of the organism to antimicrobial agents by a disk diffusion method (Kirby-Bauer method) on Mueller-Hinton agar showed the strain was resistant to imipenem, meropenem, ciprofloxacin, amikacin, cefepime, ceftazidime, colistin, and TMP-SMZ and intermediately susceptible to piperacillin-tazobactam. Tigecycline was added to the piperacillin-tazobactam therapy, and granulocyte transfusions were applied for 3 consecutive days for supportive therapy. The susceptibility test was repeated using E-test (Oxoid), and minimal inhibitory concentrations (MICs) of meropenem and tigecycline were found to be >32 μg/dL and 3 μg/dL, respectively. Fever was controlled after 5 days, and no further growth of *A xylosoxidans* was detected after the sixth day of antibiotherapy. Antibiotics were discontinued after 21

days. As there was still the loss of epithelial tissue in the perianal region, colostomy was performed. At the 36th days of the CLASP therapy, he recovered fully including the perianal region. Colostomy was closed 2 months later, and bone marrow aspiration revealed remission. Bone marrow transplantation could not be performed because of the absence of a matched donor. He is still in remission within 2-year follow-up.

DISCUSSION

Though accepted as an opportunistic microorganism with low pathogenicity, *A xylosoxidans* can lead to serious infections in immunocompromised individuals.[3,4] Bacteremia is a significant infection and may be catheter related or associated with a gastrointestinal pathologic lesion. In a 10-year analysis of 54 cases with *A xylosoxidans* bacteremia, 96% of cases were nosocomial and 42 (77%) patients had an underlying illness.[5] Nosocomial infections are usually waterborne (disinfectant solutions, intravenous fluids, dialysis solutions), but even normal stool colonized by *A xylosoxidans* can be a source. Our patient did not have a central venous catheter, but severe neutropenia and a large perianal abscess could have been the leading factors for the development of infection.

A xylosoxidans is uncommonly isolated from a clinical material. It is susceptible to anti-pseudomonal penicillin, TMP-SMZ, and carbapenems and resistant to second- and third-generation cephalosporins and gentamycin. The hyperproduction of β-lactamases has been implicated in resistance.[6] Antimicrobial combinations such as piperacillin plus gentamycin, azitromycin plus doxycycline, and azitromycin plus TMP-SMZ have been tested with favorable results. Susceptibility to the fluoroquinolones is variable. High concentrations of colistin inhibit most strains.[7] Recently Teng et al described successful use of colistin in complicated peritonitis due to multidrug-resistant *A xylosoxidans*.[8]

Our patient's strain was resistant to multiple antibiotics including meropenem and TMP-SMZ. Tigecycline was reported to have a great potential in managing several emerging pathogens in cystic fibrosis including *A xylosoxidans*.[9] Since *A xylosoxidans* growth was detected while the patient was on piperacillin-tazobactam, we added tigecycline to the treatment regimen. Tigecycline is chemically a minocycline derivative active against many gram-positive and gram-negative organisms, including methicillin-resistant Staphylococcus aureus, vancomycin-resistant enterococci, and extended spectrum β-lactamase–producing *Escherichia coli* and *Klebsiella pneumoniae*. Jacquier et al determined the in vitro susceptibility of doripenem, meropenem, imipenem, tigecycline, and colistin against 166 unusual nonfermenting gram-negative bacilli recovered from clinical samples.[10] Tigecycline showed a moderate activity against *A xylosoxidans* (MIC50=4 mg/L; 44% susceptible), while 76% of isolates were susceptible to meropenem. The susceptibility of A. xylosoxidans isolates to colistin was 28% (MIC50=4 mg/L, MIC range=0.5 to ≥32).

The emergence of systemic infections caused by multidrug-resistant bacteria is a serious concern for high-risk individuals. Tigecycline has a bacteriostatic effect for many microorganisms, so monotherapy for bacteremia might have resulted in treatment failure. Though it cannot be advised as a first-line therapeutic agent in Achromobacter infections, it can be considered in multidrug-resistant isolates given that the isolate is sensitive in susceptibility studies.

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