

Fatal Sepsis Due to *Stenotrophomonas Maltophilia* in Stem Cell Recipient – Case Report

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Abstract

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Background: Infections are frequent cause of further morbidity and mortality in stem cells recipients. Infection-related mortality is mainly due to severe bacterial sepsis, pneumonia and fungal infections.

Case Report: We report a 60 years old patient with AML. In the complete remission he is received high-dose chemotherapy followed by autologous peripheral blood stem cell transplantation. The patient was treated in sterile room, conditioned with HEPA filters. Antibiotic prophylaxis regimen consisted Ciprofloxacin 1.0 gr/day, Itraconazol 400 mg/day, Acyclovir 1500 mg/day, and Immunoglobulins IV 0.1 mg/kg once per week. From day +5 patient became febrile ($Ne < 0.5 \times 10^3/mL$). First line antibiotic regimen consisted third-generation anti-pseudomonal cephalosporine and aminoglycoside during a 72 h, but with no response. As a second line antibiotic therapy was introduced Vancomycin 2.0 gr/day. On day +10 from blood culture and urine culture was isolated *Stenotrophomonas maltophilia* with in vitro susceptibilities only to Ciprofloxacin (+3). Co-trimoxazole and again Ciprofloxacin in maximal doses was administered, but patient deteriorate, and in sepsis with signes of endotoxic shock he die on day +15.

Conclusion: Despite use of broad-spectrum antibiotics as prophylaxis, Gram-negative bacteria are still potentially fatal for immunocompromised patients. Microbiological monitoring on local microflora is mandatory for all transplant centers and intensive care units.

Introduction

Infection is the result of a shift in the equilibrium between host defenses and microorganism pathogenicity. Patients undergoing stem cells transplantation are at risk of neutropenia, impairment of barrier defenses, and impairment of cell-mediated and humoral immunity. This impairment leads to an immunocompromised state, allowing microorganisms to cause infection more easily, even those with limited pathogenicity. Patients undergoing stem cells transplantation experience a sequential suppression of

host defenses, allowing for various infectious processes at different phases of the transplantation process.

During an aplastic post-transplant phase bacteria and fungi are major causes of infective complications. During this phase the effect of conditioning regimen and central venous catheter are two most important factors for infections. Deep neutropenia is associated with increased risk of infection. Infection-related mortality is mainly due to severe bacterial sepsis, pneumonia and fungal infections. *Stenotrophomonas maltophilia* is an aerobic gram-negative bacillus of low virulence and is a

frequent colonizer of fluids used in the hospital setting, ie, irrigation solutions and intravenous fluids, and of patient secretions, ie, respiratory secretions, urine, or wound exudates. *S. maltophilia* usually is not capable of causing disease in healthy hosts without the assistance of invasive medical devices that bypass normal host defenses. If an intravenous infusion contains large numbers of *S. maltophilia*, then direct injection into the bloodstream may result in the signs and symptoms associated with gram-negative bacteremia. Similarly, in the urinary tract, if urological irrigation fluids that contain large numbers of *S. maltophilia* are used during an invasive urological procedure, eg, cystoscopy, then gram-negative bacteremia may occur with its attendant mortality and morbidity, which are dependent on host factors.

Case Report

We report a 60 years old patient with acute myeloblastic leukemia (FAB M2). After induction (DA therapy) and high-dose ARA-C consolidation therapy he is achieved complete remission. There was no HLA-identical sibling for related allogeneic stem cells transplantation. We perform priming with VP-16 and G-CSF for stem cells mobilization and harvest. During a two apheresis procedures total of 2.8×10^8 /kg b.w. CD34+cells were collected. In the complete remission he is received high-dose chemotherapy followed by autologous peripheral stem cell transplantation. The patient was treated in sterile room, conditioned with HEPA filters. As conditioning regimen was used Busulphan/ Cyclophosphamide regimen. As a hemorrhagic cystitis prophylaxis he is received Uromitexan and bladder irrigation through urinary catheter with saline solution Ispirof, during a days of Cyclophosphamide administration. Antibiotic prophylaxis regimen consisted Ciprofloxacin 1.0 gr/day divided in two doses, Itraconazol 400 mg/day, Acyclovir 1500 mg/day, and intravenous Immunoglobulins 0.1mg/kg once per week. From day +5 patient became febrile ($Ne < 0.5 \times 10^3$ /mL). First line antibiotic regimen consisted third-generation cephalosporine (Ceftazidime (Fortum) 3gr/day) and aminoglycoside (Amikacyn 1.5 gr/day) was administered during a 72 h, but with no response.

Chest radiography and CT scan were normal, without pulmonary infiltrates. Galactomannan test negative. As a second line antibiotic therapy we introduce Vancomycin 2.0 gr/day divided in two doses. On day +10 from blood culture and urine culture was isolated multidrug resistant *Stenotrophomonas maltophilia* with in vitro

susceptibilities only to Ciprofloxacin (+3). We introduce Co-trimoxazole and again Ciprofloxacin in maximal doses, but patient deteriorate, and in sepsis with signs of endotoxic shock he die on day +15.

Discussion

Stenotrophomonas maltophilia is an opportunistic, nosocomial pathogen that primarily affects immunocompromised patients [1, 2]. Although this organism has been considered to have limited pathogenicity, reports indicate that infection with *S. maltophilia* can cause bacteremia and other serious infections, particularly in severely immunocompromised patients [3, 4]. Treatment of infection with this organism is also complicated by the fact that isolates are frequently resistant to many of the currently available broad-spectrum antibiotics [5, 6]. Risk factors for *S. maltophilia* bacteremia include neutropenia, the presence of a central venous catheter (CVC), prolonged hospitalization, and previous therapy with broad-spectrum antibiotics [7, 8]. In uncontrolled clinical trials, crude mortality rates reported to be associated with *S. maltophilia* bacteremia have had a range of 21%–69% [9, 10]. However, many patients with *S. maltophilia* bacteremia have significant underlying illnesses. In addition, the organism is often recovered from mixed cultures. Therefore, the proportion of deaths directly attributable to *S. maltophilia* bacteremia remains unclear. *S. maltophilia* commonly colonizes the urine and potentially is pathogenic only in those with impaired host defenses, ie, patients with diabetes, systemic lupus erythematosus (SLE), cirrhosis, multiple myeloma, leukaemia and those on steroids. *S. maltophilia*, usually is resistant to third-generation cephalosporins, aminoglycosides, and antipseudomonal penicillins. *S. maltophilia* recovered from blood cultures may have come from contaminated IV fluids or from a distant infected source, eg, secondary bacteremia from the urinary tract in a patient who recently underwent instrumentation during a genitourinary (GU) procedures. Sources of *S. maltophilia* colonization include the following: IV lines and/or fluids, IV solutions, central venous catheters, personnel hands, antiseptic soaps, respiratory equipment or fluids, nebulizers, inhalation medications, Foley catheters, irrigation solutions. Medical personnel, nursing personnel, housekeeping staff, attending physicians, are potential carriers of the organism from patient to patient. Clinicians often make the mistake of treating *S. maltophilia* colonization with antibiotics, except when the pathogenic role of *S. maltophilia* is clear (ie, IV line sepsis secondary to

contaminating infusions, colonization related to IV monitoring devices, urological instrumentation resulting in colonization).

Quinolones have been shown, in comparative trials to decrease the risk for Gram-negative bacteraemia and the number of days of fever in patients with prolonged neutropenia. They are widely used for allogeneic transplantation, especially ciprofloxacin. In pharmacoeconomics studies ciprofloxacin have been shown cost-benefit effect. Antibiotic prophylaxis against *Gram-negative bacteria* predominantly increase the frequency of infection due to *Gram-positive cocci*. *Gram positive cocci* are now the most frequent bacteria isolated from all sites, especially central venous catheter. Multiresistant strains of *Gram-positive bacteria* are problem in some transplant centers. Especially *Vancomycin Resistant Enterococcus*, *Methicillin Resistant Staphylococcus Aureus*, *Penicillin resistant Streptococcus Pneumoniae* etc.

Despite use of broad-spectrum antibiotics as prophylaxis, Gram-negative bacteria are still potentially fatal for immunocompromised patients. Microbiological monitoring on local microflora is mandatory for all transplant centers and intensive care units. Effective infection control measures can minimize or limit the spread of this and other organisms in the ICU. Appropriate isolation procedures, rather than antimicrobial therapy, should be used to control the spread of *S. maltophilia*.

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