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Short Communication

A Survey of Bacterial Infections in Bone Marrow Transplant Recipients

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Abstract

Background: Bone marrow transplant (BMT) recipients are prone to bacterial, viral and fungal infections. Bacterial infection is considered as one of the common and serious complications in bone marrow transplant recipients. The aim of this study was to determine the rate of bacterial infections in bone marrow transplant recipients.

Methods: Fifty-two blood and 25 catheter samples were obtained from 23 patients who were hospitalized in bone marrow transplantation unit in Shariati Hospital in Tehran. Bacterial strains were isolated and identified by the standard conventional bacteriological methods. Antimicrobial susceptibility was performed according to the guidelines from NCCLS using 18 different antibiotics.

Results: The strains of *Staphylococci*, *Streptococcus viridans*, *Pseudomonas aeruginosa* and *Escherichia coli* were isolated from 8(66.7%), 1(8.3%), 2 (16.7%) and the 1(8.3%) cases, respectively.

Conclusion: Current study indicated that the bacterial infections particularly those caused by the Gram-positive cocci were still as important problem in bone marrow transplant.

Keywords: *Bacterial infections, Bone marrow transplantation, Drug resistance, Iran*

Introduction

Microbial infections are one of the major problems against successful organ transplantation and can cause high morbidity and mortality among transplant recipients (1).

Bone marrow transplant (BMT) recipients are prone to bacterial, viral and fungal infections. Because of the severe immune suppression associated with BMT, microbial infection is considered as a common and serious complication in these patients. Opportunistic infections are major causes of morbidity and mortality following bone marrow transplantation (2- 4).

Several factors that have caused tremendous changes in transplant practices include technological advances in stem cell procurement, introduction of hematologic growth factors to speed engraftment, development of new immunosuppressive regimens to control graft-versus-host disease (GVHD), development of technology to perform graft engineering with removal of T lymphocytes in toto or subpopulations of T lymphocytes, use of molecular techniques to optimize donor and recipient matching, advances in blood banking, and development of international donor registries (5-10). Because of such changes in transplant practices, along with the advent of new antimicrobial agents, and development of infection control measures affecting pathogen exposure, alterations in the interplay between host and potential pathogens have occurred. Shifts in the incidence and types of opportunistic pathogens are taking place (9, 10).

Several historically important infectious syndromes are today well controlled; others have diminished in importance early after transplant but are more problematic later. New emerging pathogens are being recognized due to selection

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pressures from antimicrobial usage and new hosts, such as recipients of alternate donor allogeneic transplant procedures, with even more profound and prolonged immune suppression. Such shifts and new syndromes pose continuing new challenges to the transplant clinician. Bone marrow transplants are traditionally divided into 3 types: autologous, syngeneic, or allogeneic. Autologous transplants use a patient's own stem cells to replace those damaged by high-dose cytotoxic drug therapy. Syngeneic transplants are grafts from a patient's identical twin donor. Autologous and syngeneic transplants involve the fewest complications because of the identical human leukocyte antigen (HLA) matching of graft and host. HLAs are encoded on the major histocompatibility complex (MHC) and are the major determinant of graft-host compatibility, as opposed to the ABO compatibility sought in most solid organ transplants (9- 14).

Allogeneic transplants are the use of a graft from another person, and are associated with complications from graft rejection, graft versus-host disease (GVHD), and infection from continued immunosuppression (14).

The purpose of current study was to determine the rate of bacterial infections in bone marrow transplant recipients who were hospitalized in bone marrow transplantation unit in Shariati hospital in Tehran, capital of Iran.

Materials and Methods

Fifty-two blood and 25 catheter samples were obtained from 23 patients hospitalized in bone marrow transplantation unit in Shariati Hospital in Tehran. The clinical specimens were inoculated to Brain Heart Infusion (BHI) broth and were incubated at 37 ºC overnight. Then, during the one month of period, subculturing was carried out daily on blood agar at 37 ºC overnight. Positive cultures were more studied to determine the type of isolated strains by standard conventional bacteriological methods. Antimicrobial susceptibility test was performed according to the standard CLSI guideline (15), using Sensi-disks (Becton-Dickinson) of trimethoprin-sulfamethoxazol, ampicillin, carbenicillin, nalidixicacid, cloxacillin, gentamycin, tetracyclin, amoxicilline, erythromycin, cephalothin, nitrofurantoin, doxcycline, chloramphenicol, kanamycin, tobramycin, penicillin G, polymixine B, bacitracin on Mueller-Hinton agar (Oxoid) plates.

Results

Twenty-three recipients of bone marrow transplantation (14 males and 9 females; mean age 28 yr ranged from 4 to 37 yr) were subjected. Underlying disease in the patients included major thalassemia (13 cases, 56.5%), myelofibrosis (1 case, 4.3%), aplastic anemia (3 cases, 13.0%), acute lymphoblastic leukemia (1 cases, 4.3%), chronic myelogenous leukemia (2 cases, 8.7%) and acute myelogenous leukemia (3 cases, 13.0%).

From the 23 cases studied, 21 (91.3%) and 2 cases (8.7%) had been received allogeneic and autologous transplants, respectively. Twelve blood specimens obtained from recipients of bone marrow transplantation showed bacteremia.

As shown in Table 1 the strains of *Staphylococci*, *Streptococcus viridans, Pseudomonas aeruginosa* and *Escherichia coli* were isolated from 8(66.7%), 1(8/3%), 2(16/7%) and 1(8/3%) bacterimic samples, respectively.

The strain of *Streptococcus viridans* was resistant to all of the antibiotics tested. More than 50% of *Staphylococci* strains were resistant to trimethoprin-sulfamethoxazol, ampicillin, carbenicillin, nalidixicacid, cloxacillin, gentamycin, tetracyclin, nitrofurantoin, doxcycline. *E. coli* showed resistance to ampicillin, carbenicillin, trimethoprin-sulfamethoxazol, and tetracycline. *Pseudomonas aeruginosa* strainss were susceptible only to cloxacillin, kanamycin, and bacitracin, however one isolate was also susceptible to polymixine B.

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Table 1: Age and bacterial agent distribution of bone marrow transplant recipients

Age-groups (Yr)	Bacterial agents				Total
	Staphylococci	*S. viridans*	*P. aeruginosa*	*E. coli*	
0-15	4	1	1	-	6
≥16	4	-	1	1	6
Total	8	1	2	1	12

Discussion

Cytotoxic conditioning regimens used in the pre-transplant stage have a profound effect on the host's immune system during the preengraftment period. Severe neutropenia becomes ordinary at this stage. The risk of infection grows, with patients whose neutrophil counts dropping below 100/mm^3 being at increased risk over patients whose counts are between 100/mm^3 and 500/mm^3. The patient's barrier defenses are often compromised because of indwelling IV catheters and regimen-related toxicity of the mucous membranes of the oropharynx (mucositis), respiratory tract, and gastrointestinal tract, which provide a route of systemic entry for organisms that typically colonize these areas. Changes in oral mucosa appear by day 10, usually begin to resolve by day 20, and occur in up to 70% of patients receiving allogeneic transplants and in a smaller but substantial number of patients undergoing autologous or gynogenic transplants (11, 12). This mucositis has been identified as a significant risk factor for developing bacteremia with alpha-hemolytic *Streptococci* (viridans group *Streptococci*), which normally colonize the oropharynx. Bacteremia with these organisms has been associated with poor outcomes, a significantly prolonged length of stay, and increased cost of therapy (13, 14).

In this study, we found one case of viridans *Streptococci* which showed resistance to almost all tested antibiotics. This finding is similar to results reported by Mossad et al. (9). In recent years, causative bacterial pathogens of bacteremia in patients with neutropenia have shifted from gram-negative to gram-positive organisms (12). We found similar results in which the gram-positive bacteria were the most prevalent cause of bacteremia. Similar finding was reported by Tomas et al. (10). They reported that virtually all patients had at least one febrile episode. Gram-positive germs were most commonly present, 85% of the isolates, and coagulase-negative *Staphylococci*, especially *S. epidermidis*, was reported as the most prevalent strain (60%).

Indwelling IV catheters often give rise to bacteremia with organisms that normally colonize the skin, such as coagulase-negative *Staphylococci*. It is often difficult to determine the clinical significance of a blood culture positive for coagulase-negative *Staphylococci* in the nonneutropenic patient population; many clinicians have traditionally regarded growth in one blood culture bottle only as a contaminant, and have been content to withhold empiric therapy in the absence of other signs of infection. Efforts have been made to correlate this theory with the emergence of clinical symptoms, but have had little success (13).

The positive predictive value of all coagulase-negative staphylococcal blood cultures (including those with growth in only one bottle) was reported as 26% in a previous study (16, 17). Coagulase-negative *Staphylococci* have become the most common organisms isolated from blood cultures in many institutions, followed by viridans *Streptococci*, *Streptococcus pneumoniae*, and *Enterococcus* species (5).

Our results showed coagulase-negative *Staphylococci* as the most common organisms isolated from blood. The other isolated organisms were gram- negative bacteria as the same as the other

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studies (12). Sparrelid et al. (18), showed 164 patients (33%) had at least one positive blood culture. Gram-positive cocci (alpha-*Streptococci* and coagulase-negative *Staphylococci*) were found in 146 of 164 cases (89%). Gram-negative bacteria were present in only seven cases.

In conclusion, the results obtained from the current study indicated that the bacterial infections particularly those caused by the gram-positive cocci are still as important problem in bone marrow transplant.

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