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Does microbial contamination influence the success of the hematopoietic cell transplantation outcomes?

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ABSTRACT

Introduction: Microbial contamination can be a marker for faulty process and is assumed to play an important role in the collection of hematopoietic progenitor cell (HPC) and infusion procedure. We aimed to determine the microbial contamination rates and evaluate the success of hematopoietic cell transplantation (HCT) in patients who received contaminated products.

Patients-methods: We analyzed microbial contamination records of HPC grafts between 2012 and 2015, retrospectively. Contamination rates of autologous donors were evaluated for at three steps: at the end of mobilization, following processing with dimethyl sulfoxide, and just before stem cell infusion. Grafts of allogeneic donors were assessed only before HCT.

Result: A total of 445 mobilization procedures were carried out on 333 (167 autologous and 166 allogeneic) donors. The microbiological contamination of peripheral blood (323/333 donations) and bone marrow (10/333 donations) products were analyzed. Bacterial contamination was detected in 18 of 1552 (1.15 %) culture bottles of 333 donors. During the study period 248 patients underwent HCT and among these patients microbial contamination rate on sample basis was 1.3 % (16/1212). Microbial contamination detected in nine patients (7 autologous; 2 allogeneic). In 8 of 9 patients, a febrile neutropenic attack was observed. The median day for the neutropenic fever was 4 days (0–9). None of the patients died within the post-transplant 30 days who received contaminated products.

Conclusion: The use of contaminated products with antibiotic prophylaxis may be safe in terms of the first day of fever, duration of fever, neutrophil, platelet engraftment and duration of hospitalization.

1. Introduction

Autologous and allogeneic hematopoietic cell transplantations (HCT) are commonly used for the treatment of hematological diseases. In stem cell products, microbial contamination incidence was 0.2–26.3% [1–14]. It can be caused by inadequate decontamination of skin at the needle puncture site, indwelling catheter site during the harvesting, ex vivo processing, cryopreservation, and the pre-infusion thawing process and contamination by laboratory staff or equipment [1–10]. Microbial contamination can be a marker for faulty process and is assumed to play an important role in the collection of hematopoietic progenitor cell (HPC) and infusion procedure. On the other hand, its requirement is

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unclear for the success of HCT and infusion procedure. In a variety of studies, it was reported that microbial contamination of stem cells did not cause any adverse events in patients who received contaminated HPC products [1–8]. Therefore, in this study, we aimed to determine our microbial contamination rates during collection, processing and infusion steps of HPC products and then evaluate the success of HCT in patients who received contaminated HPC products.

2. Material and method

2.1. Patients

Microbial cultures of 445 HPCs of 333 donors (167 autologous and 166 allogeneic) with various hematologic disorders between February 2012 and January 2015 were retrospectively analyzed. The age of the patients ranged between 16 and 72 years. The demographic characteristics of the patients were presented in Table 1. Clinical outcomes of the patients who received contaminated products were recorded and analyzed.

2.2. Stem cell collection

Stem cells were collected by bone marrow (BM) harvesting and peripheral blood progenitor cell (PBPC) apheresis. PBPCs were mobilized with 10 μg/kg daily doses of recombinant human granulocyte colony stimulating factor (GCSF; filgrastim or lenograstim). The insertion of a central venous catheter under sterile conditions was succeeded by the collection of cells. In collecting the HPCs, a continuous-flow blood cell separator spectra optia apheresis system (TerumoBCT, USA), was used. The cell separator was included in processing three total blood volumes at each of the collections, which was made in order to collect at least 3×10^6/kg and 5×10^6/kg CD34 + cells for multiple myelomas and other indications, respectively. Collections were continued until the above threshold dose of PBPCs was obtained unless any donor complication related to mobilization was observed necessitating termination of the apheresis procedure. When mobilization with G-CSF failed, further mobilization with G-CSF plus chemotherapy, G-CSF and plerixafor or BM harvesting was performed in autologous donors. Also, HPC collections were performed via BM harvesting under general anesthesia for the donors of patients diagnosed with aplastic anemia or donors refusing PBPC mobilization.

2.3. Microbial sampling

Microbial cultures of HPCs for autologous HCT candidates were performed in three phases: (1) subsequent to the marrow harvesting or PBPC apheresis, (2) following the process with cryoprotective agent DMSO (Dimethyl sulfoxide), and (3) just before the infusion of thawed HPCs. On the other hand, HPCs of allogeneic donors were analyzed only following marrow harvesting or PBPC apheresis. Two culture bottles each consisting 1 ml of HPC product were evaluated at all phases. For each patient who could receive autologous or allogeneic HCT, a total of 6 or 2 culture bottles (samples) were analyzed for microbial contamination. HPC products were inoculated into BacT/ALERT 3D automated system blood culture bottles. These bottles were incubated in the same automated system for at least seven days. The bottles with positive signals were subcultured in 5% sheep blood agar, chocolate agar, eosin methylene blue agar and Sabouraud dextrose agar. An automated identification system (VITEK 2 Compact, bioMerieux, Marcy-10 Etoile, France) was used to identify the microorganisms. Antimicrobial susceptibility testing was performed in accordance with the Clinical and Laboratory Standards Institute (CLSI) guideline. Patients routinely received systemic antibiotic prophylaxis, generally including a fluoroquinolone, trimethoprim- sulfamethoxazole (TMP-SMX) and acyclovir, fluconazole. For patients who received products with documented microbial contamination, appropriate antibiotics such as vancomycin were started as soon as an occurrence of febrile neutropenia or any sign of blood stream infection. Otherwise, no preemptive therapy was commenced following HCT with contaminated HPC product.

2.4. Statistical analysis

Descriptive statistics were presented as median and range. Mann–Whitney U test was used for the comparisons of the first day of fever, duration of fever, engraftment days and duration of hospitalization between groups. $P < 0.05$ was considered to be of statistical significance.

3. Results

Between February 2012 and January 2015, a total of 333 donors (167 autologous and 166 allogeneic) were mobilized and 445 HPC products were obtained. We analyzed 1552 culture bottles and bacterial contamination was

Table 1
Characteristics of patients.

Gender		Age	Diagnosis				Donor type		HPC* source	
Male	Female		Leukemia	Lymphoma	Multiple myeloma	Others†	Allogeneic	Autolog	Bone marrow	PBPC**
132	116	32	135	49	47	17	166	82	10	238
53%	47%	(16–72)	(54%)	(20%)	(19%)	(7%)	(67%)	(33%)	(4%)	(96%)

* HPC: Hematopoietic progenitor cell.
** PBPC: Peripheral blood progenitor cell.
† Others: Paroxysmal nocturnal hemoglobinuria, myelodysplastic syndromes, aplastic anemia, testicular tumor.