Best Practice & Research Clinical Haematology 28 (2015) 155–161

Contents lists available at ScienceDirect

Best Practice & Research Clinical Haematology

journal homepage: www.elsevier.com/locate/beha

Role of intestinal microbiota in transplantation outcomes

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Keywords:
Allo-HSCT
Bacteremia
Diversity
Intestinal microbiota
Microbial dominance
Metronidazole
Mortality
Survival

A B S T R A C T

While allogeneic hematopoietic stem cell transplantations have a curative potential, infections and graft-versus-host disease remain significant problems. The intestinal microbiota can influence responses to cancer chemotherapy and the role of the microbiota in affecting allogeneic hematopoietic stem cell transplantation outcomes is increasingly appreciated. The following paper discusses the most recent developments in this area.

Introduction

The intestinal microbiota comprises microbial populations that colonize the human gastrointestinal tract and has been shown to play a crucial role in human health by mediating resistance to infection

Abbreviations: allo-HSCT, allogeneic HSCT; HSCT, hematopoietic stem cell transplantation; VRE, vancomycin-resistant Enterococcus.

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http://dx.doi.org/10.1016/j.beha.2015.10.013
1521-6926/

[1–3]. Studies of the microbiome of humans have revealed that healthy individuals harbor diverse microbial populations in the gut. The majority of bacterial taxa belong to the Firmicutes and Bacteroidetes phyla and bacteria belonging to the Actinobacteria, Proteobacteria, Verrucomicrobia, and Fusobacteria are also represented [1]. The composition of the intestinal microbiota differs from person to person, which can have implications in health and disease [4]. For example, the composition of the intestinal microbiota has been associated with malnutrition, obesity, and autoimmune disorders such as rheumatoid arthritis [5–7]. Recently, two studies have indicated that the intestinal microbiota can influence the immune response to systemic cancer chemotherapy and disruption of the intestinal microbiome was associated with resistance to cancer therapy [8,9]. It has become clear that the intestinal microbiota not only mediates resistance to colonization by pathogens but also modulates immune function by promoting differentiation of different T-cell phenotypes. Given that infections and graft-versus-host disease are significant problems associated with allogeneic hematopoietic stem cell transplantation (allo-HSCT), the study of intestinal microbiota may provide clues to improve outcomes among allo-HSCT patients [10]. The following discussion provides a brief summary on the impact of intestinal microbiota in allo-HSCT outcomes.

Intestinal microbiota and bacteremia in allo-HSCT

Although allo-HSCT represents a potentially curative treatment option for some patients with hematologic malignancies, systemic infection and bacteremia are frequent complications [10]. An initial study of the fecal samples from five patients undergoing allo-HSCT showed that the composition of the intestinal microbiota can change dramatically following allo-HSCT (Fig. 1) [11]. While all patients presented with a diverse intestinal microbiota before allo-HSCT, three of the patients showed dramatic fluctuations in the composition of the microbiota after allo-HSCT. In two of these patients, vancomycin-resistant *Enterococcus* (VRE) was shown to dominate the gastrointestinal tract before the onset of VRE bacteremia. However, the exact reason for this intestinal domination by VRE was not clear in this study.

To identify correlative factors that explain the loss of diversity of the intestinal microbiota and the intestinal domination by certain microorganisms following allo-HSCT, a larger longitudinal study with 94 allo-HSCT patients was performed [12]. Fecal samples were collected from these 94 patients pre-allo-HSCT and for up to 35 days post-allo-HSCT. These samples were characterized for intestinal

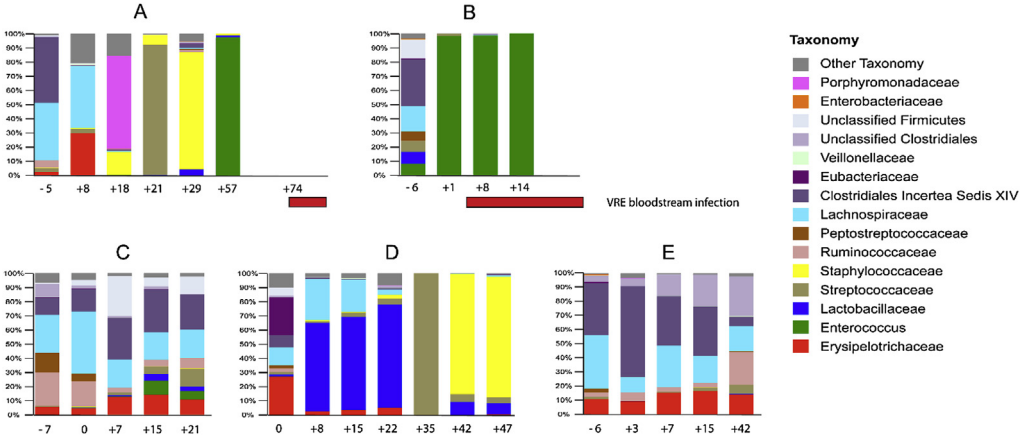

Fig. 1. VRE dominates the intestinal microbiota in humans prior to invading the bloodstream [11]. Stool samples from 5 patients (A–E) were studied prior to and during the transplant period. Each bar on the graph depicts the microbiota of 1 stool sample. Days the samples were collected relative to the day of transplant are indicated along the x-axis. The red horizontal bars indicate the timing of vancomycin-resistant *Enterococcus* bloodstream infections in patients A and B. Republished with permission of Journal of Clinical Investigation, from Vancomycin-resistant *Enterococcus* domination of intestinal microbiota is enabled by antibiotic treatment in mice and precedes bloodstream invasion in humans, Ubeda C et al., volume 120, number 12, copyright 2010; permission conveyed through Copyright Clearance Center, Inc.