Original article

Infectious diarrhea in autologous stem cell transplantation: high prevalence of coccidia in a South American center

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ABSTRACT

Background: Diarrhea is frequently seen in autologous stem cell transplantation. Although toxicity related to conditioning is the most common cause, infectious pathogens can play a distinctive role particularly in certain regions and environments.

Methods: The role of enteropathogens was investigated in 47 patients submitted to autologous stem cell transplantation at a Brazilian center between May 2011 and May 2013. All patients who presented with diarrhea consented to stool sample analysis to identify the etiological agents including coccidia, *Strongyloides sp.*, *Clostridium difficile* and other pathogenic bacteria.

Results: Thirty-nine patients (83%) had diarrhea, among whom seven (17.5%) presented with coccidia, three (7.5%) with *Candida* sp., one (2.5%) with *C. difficile*, and one (2.5%) with *Giardia lamblia*. There was a tendency toward a higher incidence of diarrhea in older patients (p-value = 0.09) and those who received conditioning with lomustine, etoposide, cytarabine, and melphalan (p-value = 0.083). Furthermore, the number of days of neutropenia was higher in patients with diarrhea (p-value = 0.06).

Conclusions: The high frequency of diarrhea caused by coccidia shows the importance of investigating and correctly identifying etiological agents and highlights the possible varieties of intestinal infections in patients who undergo autologous stem cell transplantation.

Introduction

Diarrhea is one of the most prevalent causes of morbidity in patients who undergo autologous stem cell transplantation (ASCT), resulting in a significant impairment to the patient's quality of life.[1–3] The causes of diarrhea are mainly related to the toxicity of high-dose chemotherapy schemes, irritation of the epithelia and mucosa of the digestive tract and various infectious conditions.[1]

Clostridium difficile bacteria is a known cause of diarrhea of nosocomial origin[4] in addition to being associated with the use of broad-spectrum antimicrobials.[5] There is also a strong association between intestinal infections and opportunistic germs that are present and largely described in groups of immunocompromised patients submitted to chemotherapy as well as those with oncological diseases or acquired immunodeficiency syndrome (AIDS), such as strongyloidiasis, cryptosporidiosis, isosporiasis, and candidiasis.[6]

The empirical use of antimicrobials to treat these microorganisms is common practice in some ASCT centers.[1] However, there are few studies regarding the etiology or the infections that may be involved in diarrheal events, especially in Brazil. The objective of this study is to identify the main etiologies of diarrhea in our environment.

Methods

Once approval of the study was granted by the institutional research and ethics committee, all patients evaluated and submitted to ASCT at the bone marrow transplantation unit of the University Hospital of the Universidade Federal de Juiz de Fora (UFJF) between May 2011 and May 2013 were enrolled in this study consecutively.

All patients were evaluated by a parasitological stool examination and treated according to the pathogen found prior to ASCT since no patient presented with diarrhea at the time of the transplant procedure. Diarrhea was defined as the presence of two or more watery or loose fecal discharges within a 24-hour period. Diarrhea was classified as infectious in nature in cases in which enteric pathogens, intestinal parasites, or fungi were isolated or in the case of a positive test for A/B toxin for *C. difficile*. Afebrile patients who presented with diarrhea with no isolated infectious agents were considered as having chemotherapy-induced diarrhea and the others were defined as having diarrhea of an unspecified cause.

Parasitological stool examinations using the merthiolate-iodine-formalin and Baermann-Moraes techniques were conducted in three samples to assess the causes of infections in patients presenting with diarrhea. Fresh samples were collected for the direct assessment of fungi and coccidia as well as the assessment of the combined A and B *C. difficile* toxins using an enzyme-linked immunosorbent assay. Fresh stool cultures were performed for *Shigella* sp., *Salmonella* sp., and *Escherichia coli*. Other samples were collected from patients who stopped having diarrhea for 24 hours but suffered further episodes at any time, and a new sample for *C. difficile* was collected from patients who presented with diarrhea and a new episode of fever.

All patients received prophylactic acyclovir from the beginning of the chemotherapy conditioning up to neutrophil engraftment without prophylaxis for bacteria and fungi. Cefepime was the empirical antimicrobial used initially for all patients in the event of fever during neutropenia.

Statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS) software version 21, in which Pearson's chi-squared test or Fisher's exact test for categorical variables as well as the Mann–Whitney test for variables with non-normal distribution were used. p-values < 0.05 were considered statistically significant.

Results

This study enrolled 47 patients (Table 1). Among these patients, 39 had diarrhea, including one patient who had two distinct episodes giving a total of 40 events of diarrhea in the study period. Fourteen patients presented with diarrhea induced by chemotherapy, with no relationship between the conditioning chemotherapy protocol used and the presence of diarrhea, and 14 events were classified as having other causes. Among the 12 cases of infectious diarrhea, the most common agents were coccidia in seven cases, among which four cases were of *Cryptosporidium* sp. and in three cases it was not possible to determine the genus of the isolated coccidia. The second most frequent pathogen was *Candida* spp. in three cases, including one case where *Cryptosporidium* sp.

Table 1 – Patient, disease and transplantation characteristics.

	With diarrhea	Without diarrhea	Total	p-value
Patients – n (%)	39 (83)	8 (17)	47 (100)	
Gender – n (%)				0.60
Male	20 (43)	4 (8.5)	24 (51)	
Female	19 (40)	4 (8.5)	23 (49)	
Age (range/mean) – years	16–65	19–56	46.2	0.13
Underlying disease – n (%)				0.47
Multiple myeloma	25 (53)	4 (8.5)	29 (61.5)	
Non-Hodgkin's lymphoma	4 (8.5)		4 (8.5)	
Hodgkin's lymphoma	8 (17)	3 (7)	11 (24)	
AML	2 (4)	1 (2)	3 (6)	
Conditioning – n (%)				0.08
MEL 200	22 (47)	4 (8.5)	26 (45.5)	
CBV	3 (7)	3 (7)	6 (14)	
LEAM	9 (18.5)		9 (18.5)	
Busulfan base schemes	5 (10)	1 (2)	6 (12)	
Febrile neutropenia (range/mean) – days	1–15	1–7	4.97	0.06

AML: acute myeloid leukemia; MEL 200: melphalan 200 mg/m^2; CBV: cyclophosphamide, carmustine, and etoposide; LEAM: lomustine, etoposide, cytarabine, and melphalan.