Chronic graft-versus-host disease: survival impact on patients with Severe Aplastic Anemia (SAA) and Paroxysmal Nocturnal Hemoglobinuria (PNH)

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Abstract

SAA and PNH are rare and potentially fatal diseases which can be treated by allogeneic hematopoietic stem cell transplantation (HSCT). One of the most common complications after HSCT is chronic graft-versus-host disease (cGVHD). In the context of malignant diseases cGVHD can also bring the benefit of graft-versus-leukemia effect. However, in benignant diseases there is not such benefit. **OBJECTIVE:** We sought to evaluate the impact of cGVHD in survival of patients with SAA and PNH in a referral center. **DESIGN:** Four hundred and twenty one patients with SAA and PNH were identified at our database and were retrospectively analyzed from August 1983 to April 2016 at HSCT center from Federal University of Paraná (Brazil). From those, 100 patients developed cGVHD. Statistical analysis was performed using Graphpad Prism, *p* level of significance < 0,05. Kaplan-Meier method was used for survival curves. **RESULTS:** Among patients with cGVHD, 60% were male. Median age was 25 years (14-52). Eighty six percent were related transplants. Conditioning was busulfan based in 53 patients (8-12mg/kg). Only 11 patients received ATG. Immunoprophylaxis was cyclosporine and methotrexate for all cases. Mild cGVHD was present in 48% and severe cGVHD in 23% of patients. Mouth (57%), skin (55%), liver (38%), eyes (25%) and GI tract (15%) were the most frequently involved organs. Median overall survival (OS) for cGVHD patients was 70% in 13 years. Patients with moderate/severe cGVHD, had inferior survival as compared to patients with mild cGVHD (*p*=0,02). Patients who received 15 or more transfusions had significantly lower OS (*p*=0,002). No influence was seen from conditioning, year of transplant or type of donor. **CONCLUSIONS:** There was a low incidence of severe cGVHD in this cohort despite that the minority of them received ATG. Moderate and severe cGVHD and number of pre- transplant transfusions (≥15) had significant impact of OS.

Background

SAA and PNH are rare and potentially fatal diseases which can be treated by allogeneic hematopoietic stem cell transplantation (HSCT). One of the most common complications after HSCT is chronic graft-versus-host disease (cGVHD). In the context of malignant diseases cGVHD can also bring the benefit of graft-versus-leukemia effect. However, in benignant diseases there is not such benefit

Objective

We sought to evaluate the impact of cGVHD in survival of patients with SAA and PNH in a referral center.

Characteristics of Patient who developed cGVHD	
No. of patients	100
Age, median (range), years	25 (14 a 52)
Sex	
Female	60
Male	40
Disease	
SAA	90
PNH	10
Donor source	
Bone marrow	3
PBPC	97
Conditioning	
Bu-Cy (12+120)	45
Bu-Flu (8+30)	8
Cy-TBI	5
Cy (200)	38
Other	4
ATLG	11
GVHD prophylaxis	
MTX + CSA	100
Type of donor	
Related	86
Unrelated	14
Donor-recipient sex match	
Female → male	26
HLA matching	
Matched	95
Partially matched	5
Graft composition	3,68 (0,69 a 18,2)
CD34+ cellsx106/Kg, median (range)	
aGVHD	
yes	54
no	46

Materials & Methods

•421 patients with SAA and PNH were identified at our database and were retrospectively analyzed from August 1983 to April 2016 at HSCT center from Federal University of Paraná (Brazil). From those, 100 patients developed cGVHD.
•Statistical analysis was performed using Graphpad Prism, *p* level of significance < 0,05. Kaplan-Meier method was used for survival curves.

Characteristics cGVHD	
NIH Global Severity	
Mild	48
Moderate	29
Severe	23
Involved organ	
Liver	38
Gastrointestinal	15
Mouth	57
Skin	55
Eye	25
Lungs	08

Summary

Median overall survival (OS) for cGVHD patients was 70% in 13 years. Patients with moderate/severe cGVHD, had inferior survival as compared to patients with mild cGVHD (*p*=0,02). Patients who received 15 or more transfusions had significantly lower OS (*p*=0,002). No influence was seen from conditioning, year of transplant or type of donor.

Discussion

There was a low incidence of severe cGVHD in this cohort despite that the minority of them received ATG. Moderate and severe cGVHD and number of pre- transplant transfusions ≥15) had significant impact of OS.

References

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