Oral clinical manifestations of graft-versus-host disease in patients submitted to allogeneic hematopoietic stem cell transplantation: an experience of a Brazilian Cancer Center

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INTRODUCTION

The graft-versus-host disease (GVHD) is an important complication of the allogeneic hematopoietic stem cell transplantation (AHCT), that affects several organs, including the mouth.

OBJECTIVE

The aim was to evaluate the incidence and clinical manifestations of oral GVHD in patients undergoing AHCT, as well as to determine predictive factors for its occurrence.

MATERIAL AND METHODS

Medical records of 147 patients who were submitted to AHCT between January 2010 to January 2015 were reviewed for clinical features and establishment of risk factors to development of oral GVHD. To evaluate the oral manifestations of GHVD were considered the following clinical features: lichenoid patterns, erythema and ulcer. Also was considered the following symptoms: xerostomia and pain.

RESULTS

Table 1:Demographic and histopathological subtypes distribution of patients.

		N	%
Gender	Male	77	52,4
	Female	70	47,6
Age	Mean ± SD	44,9 ±14,76	
	Range	14-70	
	Median	47	
Neoplasias	Acute myeloid leukemia	53	36,1
	Acute lymphoid leukemia	29	19,7
	Myelodysplastic syndrome	15	10,2
	Non-Hodgkin lymphoma	14	9,5
	Hodgkin lymphoma	11	7,5
	Chronic myeloid leukemia	8	5,4
	Aplastic anemia	5	3,4
	Chronic lymphoid leukemia	5	3,4
	Primary myelofibrosis	2	1,4
	Mixed-phenotypic leukemia	1	0,7
	Multiple myeloma	1	0,7
	Acute undifferentiated leukemia	1	0,7
	Gray-zone lymphoma	1	0,7
	B-cell lymphoma	1	0,7

Table 2: Donor features, conditioning regimen, chemotherapy and grafting information.

		N	%
Donor	Related	110	74,8
	Non-related	35	23,8
Conditioning Regimen	Reduced Intensity Conditioning	77	52,4
	Myeloablative Regimen	3	42,9
Conditioning	MTX + Cyclosporine	78	53,1
	cyclophosphamide+ MPM + Tacrolimus	27	18,4
	MTX + Tacrolimus	8	5,4
	MPM + Tacrolimus	7	4,8
	cyclosporine + MPM	5	3,4
Chemotherapy	cyclophosphamide+ MPM + Tacrolimus	5	3,4
	MTX + MPM	4	3,4
	Cyclosporine	3	2
	MTX	1	0,7
Grafting	Yes	129	87,8
	No	12	8,2

MTX: methotrexate; MPM: mycophenolate mofetil

Table 3: Incidence and topographic distribution of systemic GVHD.

		N	%
Systemic GVHD	Yes	99	67,6
	No	45	30,6
Systemic GVHD site	Skin	67	46,2
	GIT	41	28,3
	Liver	14	9,5
	Lung	10	6,9
	Eyes	6	4,1
	Vagina	2	1,4

GIT: gastrointestinal tract

Table 4: Time until oral GVHD development, clinical features and symptoms.

Time	Mean ± SD maximum Minimum	N	%
		229,37±135,05 630 45	
Oral GVHD	Yes	26	18,1
	No	121	81,9
Pain	Yes	25	96,15
	No	1	3,85
Xerostomia	Yes	17	65,38
	No	9	34,62
Oral lesions features	Ulcers	5	19,23
	Estriae	5	19,23
	Ulcers and Estriae	14	53,84
	White Plaque	2	7,69
Oral GVHD sites	Buccal Mucosa	24	92,3
	Lips	8	30,76
	Lateral border of tongue	15	57,69
	Dorsum of tongue	5	19,23
	Ventral Surface of the Tongue	3	11,5
	Floor of the Mouth	2	7,69
	Retromolar Region	1	3,8
	Palate	10	38,46
	Gingiva	2	7,69
	Buccal Vestibule	1	3,8

Table 5: Variables that influence the risk of developing oral GVHD

	RR	CI	p
Systemic GVHD	5,702	1,346 – 24,158	0,018
Age	1,013	0,985 – 1,042	0,367
Gender	0,747	0,339 – 1,648	0,471
Donor	0,737	0,268 – 2,026	0,054
Conditioning	0,79	0,327 – 1,909	0,6

RR – risk ratio; CI= Confidence interval; p – significance level

Table 6: Variables of systemic GVHD that influence the risk of developing oral GVHD

	RR	CI	p
Skin	3,485	1,345 – 9,029	0,01
Lung	3,134	1,184 – 8,298	0,021
Eyes	1,675	0,424 – 6,620	0,462

RR – risk ratio; CI= Confidence interval; p – significance level

Figure 1: Kaplan-Meier estimates of overall survival after AHCT (A), in function of oral GVHD manifestation (B) and in function of conditioning regimen type (C).

Conclusion

The mouth was the third most common GVHD affected topography. Pain, xerostomia, ulcers associated or not with white striae were the main clinical manifestations. Skin and lung GVHD were considered risk factors for the occurrence of oral GVHD.