Abstract: PB3129

Title: DOWN SYNDROME AND HEMATOPOIETIC STEM CELL TRANSPLANTATION: RISKS AND CHALLENGES

Abstract Type: Publication Only

Topic: Stem cell transplantation - Clinical

Background:

Besides solid neoplasms, Down Syndrome (DS) confers a risk of 10 to 20 X of developing acute leukemia (AL). Hematopoietic Stem Cell Transplantation (HSCT) is an effective therapy in DS patients (pts) with high-risk malignant diseases and often is the only potentially curative option; however, the number of pts receiving HSCT is significantly low, making data on the outcomes of allogeneic and autologous transplant scarce, due to considered suboptimal candidates for associated pathologies, increased chemotherapy toxicity, and concerns about conditioning intolerance, although recent reports suggest that disease relapse is the main barrier to successful transplantation in DS pts, rather than HSCT related mortality.

Aims:

To describe characteristics of DS pts with oncohematological diseases who underwent HSCT; and analyze their outcomes (morbidity, mortality, and transplant-related toxicities).

Methods:

Cases report of 4 DS pts receiving autologous or allogeneic HSCT at Hospital Privado Universitario de Córdoba, Argentina, from January 2020 to July 2023; data was obtained by electronic medical records reviewing (clinical and epidemiological characteristics, HSCT setting and outcomes).

Results:

In a median follow up (f.u) of 17 months, four pts were included (Table 1), median age 5 years old; no sex predominance. Heart defects were the most frequent congenital abnormality; one pt had transient abnormal myelopoiesis at birth developing later myeloid AL, and one has congenital hypothyroidism. Median time from diagnosis to transplant was 8.4 m; three pts received allogeneic HSCT for AL and one autologous HSCT for neuroblastoma, all received the stem cell graft in first complete remission (1CR); 50% received BM and 50% PB as cell source. All pts received myeloablative conditioning, with Busulfan full dose; 75% experienced grade ≥II mucositis and febrile neutropenia. The average time to neutrophils and platelets engraftment was 14 and 20 days (11 to 22; 13 to 37); none had graft failure. All developed grade I skin graft-versus-host disease (GVHD) and received topical treatment, one pt developed moderate chronic pulmonary GVHD, receiving systemic and inhaled steroids. We observed one cytomegalovirus reactivation. Until the end of f.u none relapsed or died.

Summary/Conclusion:

In our pts HSCT was effective and well tolerated; since complications post transplant were transient and responsive to support treatment, and no transplant-related mortality was observed. Those findings support our opinion that DS pts should promptly undergo HSCT as a curative treatment if it is indicated, to reduce the probability of later relapse of their primary disease.

TABLE N°1: Characteristics of Reported Cases

Characteristics	Case 1	Case 2	Case 3	Case 4
Sex	Male	Female	Male	Female
Age at transplant (years)	1.6	2.6	20.3	7.7
Diagnostic	VHR[1] AML[2] (7 monosomy)	HR[3] Neuroblastoma N-Myc +	HR ALL-B[4]	HR ALL-B
Associated Congenital Malformation	AVSD[5]	ASD[6]	-	Congenital hypothyroidism
TAM[7]	Yes	No	No	No
Pre- transplant status	1st CR[8]	1st CR	1st CR	1st CR
Transplant	Allogenic	Autologous	Allogenic	Allogenic
Donor type	HLA 11/12 unrelated donor	-	HLA-matched sibling donor	HLA-matched sibling donor
Cell Source	PB[9]	BM[10]	PB	BM
Patient/donor CMV[11]	+/+	-	+/+	+/+
Conditioning regimen/ intensity	Busulfan Fludarabine	Busulfan Melfalan	TBI[12] Fludarabine	TBI Fludarabine
GVHD[13] prophylaxis	ATG[14] CSA[15]-Mtx[16]	-	Tacrolimus Mtx	CSA
Time to Engraftment (days) Neutrophile Platelets	 13 13	 22 37	 13 15	 11 15
Acute GVHD (organ/grade)	Skin Grade I	-	Skin Grade I	Skin Grade I
Chronic GVHD (organ/grade)	N/A[17]	-	Lungs Moderate	N/A
Transplant-Related Toxicity	GIII Mucositis Febrile neutropenia	GII Mucositis Febrile neutropenia	GIII Mucositis IAC[18] Febrile neutropenia	GI Mucositis
CMV reactivation	No	N/A	Yes	No

1- VHR: Very High Risk / 2- AML: Acute Myeloid Leukemia / 3- HR: High Risk / 4- ALL: Acute Lymphoblastic Leukemia 5- AVSD: Atrioventricular Canal Defect / 6- ASD: Atrial Septal Defect / 7- TAM: Transient Abnormal Myelopoiesis / 8- 1st CR: First Complete Remission / 9- PB: Peripheral Blood / 10- BM: Bone Marrow / 11- CMV: Cytomegalovirus / 12- TBI: Total Body Irradiation / 13- GVHD: Graft-Versus-Host Disease / 14- ATG: thymoglobulin / 15- CSA: Cyclosporine / 16- MTX: Methotrexate / 17- N/A: Not Applicable / 18- IAC: Catheter-Associated Infection

Keywords: Allogeneic bone marrow transplant, Down Syndrome, Autologous bone marrow transplant