

The late effects after the hematopoietic stem cells transplantation (HSCT) for patients with non-neoplastic disease



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Background

- As a curative therapy, HSCT has been used for patients with non-neoplastic diseases such as aplastic anemia, primary immunodeficiency, and some congenital metabolic diseases. (1)
- Regarding late adverse effects of HSCT for non neoplastic disease, few studies have been reported
- Therefore, clinical details are not elucidated yet.

Aim of our study

- Clarify the details of late effects of HSCT for non-neoplastic patients

Objective and Method

- Since 1983 to 2013, 73 of non-neoplastic disease patients of our institute were received HSCT, and 19 patients were followed up to date
- We retrospectively analyzed the late effects of post-HSCT patients with non-neoplastic diseases

Case List: Growth retardation*1 and gonadal failure*2 were observed in three patients each

No	Disease	Conditioning	Sex	Age	Age at HSCT	after HSCT	Height (SDs)	T (ng/ml) or E2(pg/ml)	LH(mIU/ml)	FSH(mIU/ml)
1		FLU+BU	M	2yo	3m	2yrs	-0.66	<0.04	0.4	2
2	SCID	FLU+BU	M	3yo	7m	3yrs	-2.23	<0.04	<0.2	<1.0
3		FLU+L-PAM	M	6yo	1y1m	5yrs	+0.25	<0.04	<0.2	1.5
4	Severe Congenital	FLU+BU+ATG FLU+CY	M	3yo	2yo	1yr	-4.89	<0.04	<0.2	2
5	Neutropenia	TBI+FLU+CY+LPAM+ATG	M	5yo	2yo	3yrs	+1.06	<0.04	<0.2	1.6
6		Unknown	M	33yo	19yo	14yrs	-2.38	9.59	2	3.1
7	WAS	BU+CY+ATG	M	3yo	1yo1m	2yrs	-4.77	<0.04	<0.2	2.1
8	(wiskott-aldrich syndrome)	BU+CY+ATG	M	10yo	1yo5m	9yrs	-3.01	<0.04	0.2	2.8
9		BU+CY+ATG	M	30yo	21yo	9yrs	-0.45	6.51	2.3	18.9
10		BU+CY	M	7yo	5yo	2yrs	-1.19	<0.04	<0.2	<1.0
11	XHIM	BU+CY	M	18yo	3yo	15yrs	-0.22	6.38	5.5	20.2
12	(CD40L deficiency)	Unknown	M	17yo	3yo	14yrs	-0.93	4.15	8.1	14.1
13		BU+CY	M	15yo	3yo	12yrs	-0.29	5.52	2.4	8.1
14		TBI+FLU+CY+ATG	M	13yo	12yo	1yr	-1.92	7.25	2	1.7
15	Aplastic Anemia	FLU+LPAM+ATG	M	13yo	9yo	4yrs	-0.38	5.57	3.62	40.9
16		CY+LTI	F	41yo	14yo	26yrs	+0.70	<5	<0.2	1.4
17	Chronic Mucocutaneous Candidiasis	FLU+BU+ATG	F	14yo	12yo	2yrs	-2.78	<5	17.5	69
18	Ectodermal dysplasia with immunodeficiency	FLU+L-PAM+ATG	M	4yo	1yo3m	3yrs	+0.57	<0.04	<0.2	1.5
19	Hemophagocytic syndrome	BU+CY	F	11yo	1yo	11yrs	-0.44	<5	34.4	148

FLU: Fludarabine, BU: Busulfan, L-PAM: melphalan, CY: cyclophosphamide, ATG: Anti-Thymocyte Globulin

*1: Less than -3.0SD With Decreased Growth rate

*2: Hypogonadotropic hypogonadism or receiving HRT

Due to X linked diseases, 16 of 19 patients were male.

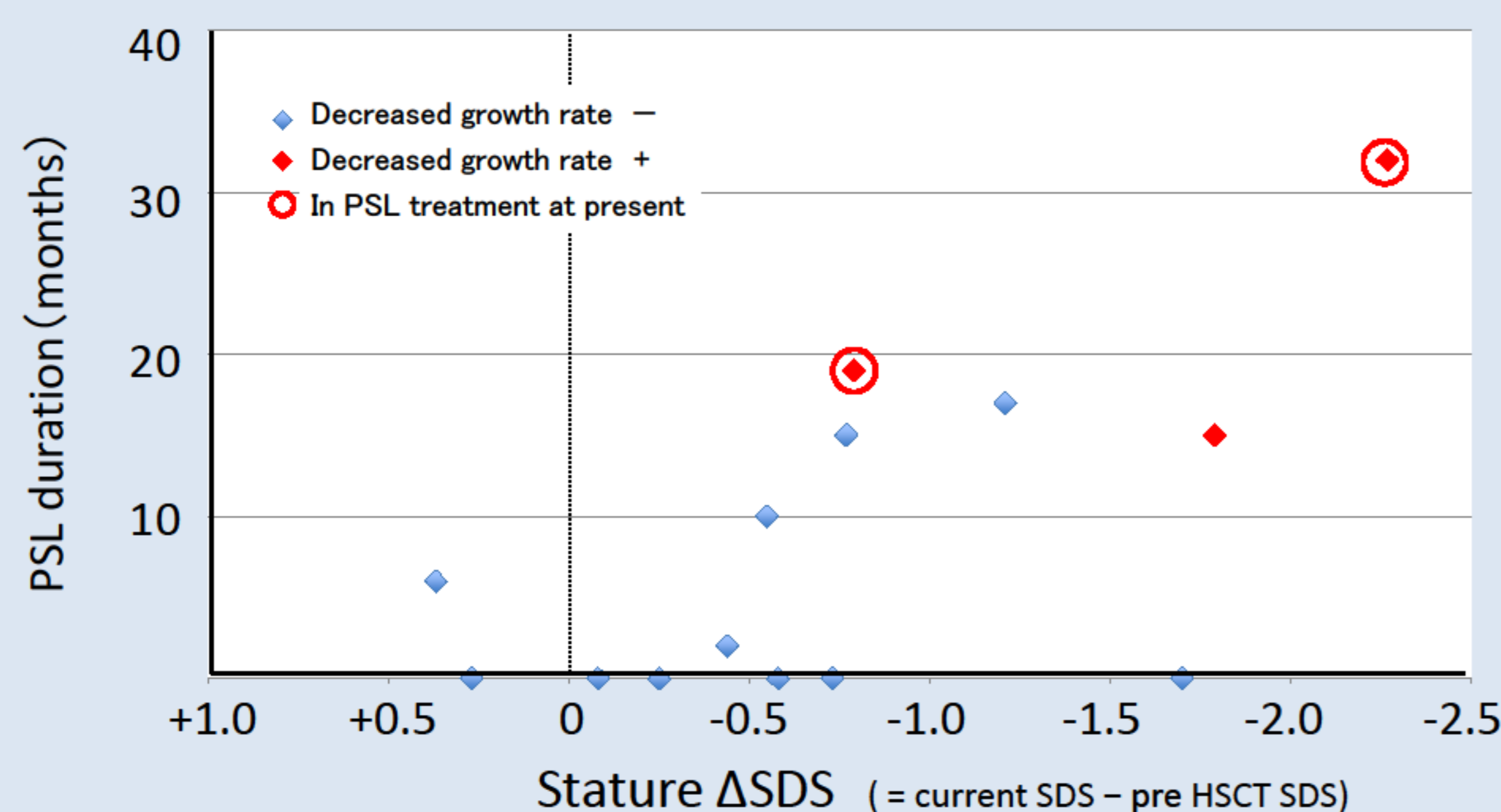
Result 1 :Growth retardation due to PSL for cGVHD

1) cGVHD was a significant risk for growth retardation

Growth Retardation	+	-	Fisher exact test, p=0.036
cGVHD+	3cases	4cases	
cGVHD-	0case	12cases	

- Growth retardation was observed in 3 cases (#4,7,8)
- Neither cases received radiation therapy
- Thyroid function and IGF-1 were normal in all cases

2) Longer PSL treatment would impair growth



Conclusion

- Careful observation is necessary for non-neoplastic patient after HSCT.

Result 2 : All three female patients showed gonadal failure

Case No.	#16	#17	#19
Conditioning	CY	Flu+BU+ATG	BU+CY
Radiation	-	-	-
Age	41yo	14yo	11yo
Sex	F	F	F
Tanner Stage	No data	No data	B1
LH (mIU/ml)	<0.2*	17.5	34.4
FSH (mIU/ml)	1.4*	69.0	148.0
E2 (pg/ml)	<5*	<5	<5
AMH (ng/ml)	<0.16		<0.16
Notes	Since 20yo, HRT (+)		

- All three patients were treated with alkylating antineoplastic agents
- Male patients did not show obvious gonadal failure, suggesting ovaries were more susceptible for alkylating antineoplastic agent⁽²⁾

Summary

- Even for non-neoplastic disease, HSCT had late adverse effects in growth and gonadal function.
- The prevalence of gonadal failure would be higher in female patients.

References

- Horowitz MM et al, Thomas' Hematopoietic Cell Transplantation. Blackwell Publishing Ltd.: Malden, 2004, pp 9-15.
- Gerard Socie et al, May 1, 2003; Blood: 101 (9).

