

Early recognition of adrenal insufficiency after hematopoietic stem cell transplantation during childhood

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Introduction and objectives

We try to analyze the prediction capacity of variable factors to diagnose adrenal insufficiency.

Methods

We analyzed clinical and laboratory data of 22 children (Male = 13) who have been checked regular dose ACTH stimulation test for suspected symptoms after HSCT (Lymphoid leukemia=5, Myeloid leukemia=9, Non-malignant=8) at the Catholic HSCT center from Feb 2013 to Feb 2017 at Seoul St. Mary's Hospital. A normal response of ACTH stimulation test was defined as a stimulated serum cortisol >18.1 mcg/dL and an increment from base line of at least 7.2 mcg/dL was considered a partial response.

Table 1. Patient characteristic and treatment variables

No	22
Gender	
Male	13 (59 %)
Female	9 (41 %)
Age (years)	
at HSCT	7.86 ± 4.85
at ACTH stimulation	9.46 ± 5.40
Currently on steroid treatment	13 (59 %)
Disease status	
Lymphoid leukemia	5 (23 %)
Myeloid leukemia	9 (41 %)
Non-malignant	8 (36 %)
GVHD	19 (86 %)
aGVHD	13 (59 %)
cGVHD	13 (59 %)

Table 2. The proportions based on obese or central obese category in total obese adolescents

Poor feeding	8
Lethargy or sleeping tendency	7
Nausea or vomiting	6
Fever	5
Elevated ACTH or Low cortisol	2
Facial flushing	2
Hyperkalemia	1
Diaphoresis	1
Fatigue	1
Hypoglycemia	1
Edema	1
Epigastric pain	1
Dizziness	1

Table 3. Hormone levels of ACTH stimulation test (Mean ± SE)

	Adrenal insufficiency (n = 16)	Response (n = 6)	P - value
Age at ACTH test	9.10 ± 1.45	10.43 ± 4.47	0.579
Basal cortisol	2.79 ± 0.87	5.48 ± 1.62	0.181
30 minutes cortisol	4.90 ± 1.03	14.85 ± 3.47	0.034
60 minutes cortisol	3.82 ± 0.68	16.14 ± 3.00	0.008

Results - I

The suspected symptoms of AI that patients had before ACTH test were as follows: Poor feeding=8, Lethargy or sleeping tendency=7, Nausea or vomiting=6, Fever=6, Elevated ACTH or Low cortisol=2, Facial flushing=2, Hyperkalemia=1, Diaphoresis=1, Fatigue=1, Hyponatremia=1, Hypoglycemia=1, Edema=1, Epigastric pain=1, Dizziness=1. Sixteen (72.7%) out of 22 patients underwent ACTH test was diagnosed as AI, 3 patients were partial AI and 3 patients were normal.

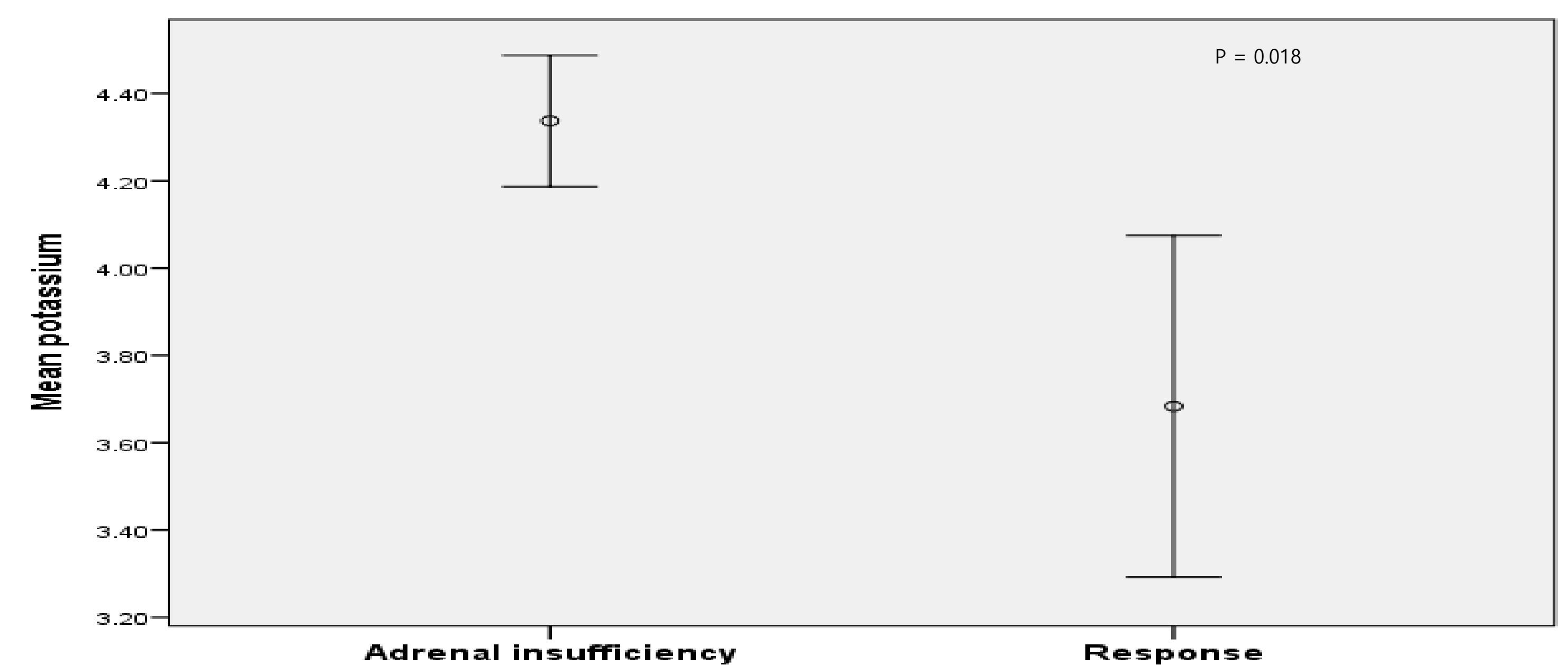
Table 4. Clinical data and hormones levels before ACTH stimulation test

	Adrenal insufficiency (n = 16)	Response (n = 6)	P - value
Gender			0.597
Male	10 (62.5 %)	3 (50 %)	
Female	6 (37.5 %)	3 (50 %)	
Age at HSCT	7.39 ± 1.28	9.12 ± 1.73	0.438
Currently on steroid treatment	12 (75 %)	1 (16.7 %)	0.013
Pre cortisol	4.79 ± 1.74	7.49 ± 6.37	0.706
Pre ACTH	38.86 ± 13.36	24.04 ± 6.81	0.339
FBS	96.68 ± 10.27	102.00 ± 10.82	0.727
Sodium	138.31 ± 0.96	140.33 ± 1.33	0.246
Potassium	4.34 ± 0.75	3.68 ± 0.20	0.018
Chloride	102.81 ± 1.04	104.50 ± 1.59	0.396
WBC	7420.0 ± 1128.8	4927 ± 460.31	0.055
BUN	10.8 ± 2.20	8.43 ± 1.98	0.437
Cr	0.47 ± 0.44	0.40 ± 0.04	0.272

Table 5. Logistic regression analysis to evaluate the factors that can predict adrenal insufficiency

	Univariate			Multivariate	
	Odds ratio	95 % CI of OR	P - value	Odds ratio	P-value
Age	0.954	0.799-1.138	0.600		
Sex	1.667	0.251-11.07	0.597		
Currently on steroid treatment	15.0	1.325-169.87	0.029	112.3	0.084
Base cortisol	0.823	0.634-1.067	0.141		
FBS	0.996	0.97-1.02	0.761		
Sodium	0.797	0.538-1.181	0.259		
Potassium	317.5	1.247-80849	0.042	40029	0.125
Chloride	0.875	0.644-1.188	0.391		

Figure 1. Serum potassium of Adrenal insufficiency and Response group



Results - II

In AI group, serum cortisol levels after 60 minutes (3.82 ± 0.68 vs. 16.14 ± 3.00 , $P < 0.008$) was lower and serum K level (4.34 ± 0.75 vs. 3.68 ± 0.20 , $P < 0.018$) before ACTH stimulation test was higher than normal or partial response group. There were no significant differences age at HSCT, Age at ACTH test, serum FBS, Na level before ACTH test between AI and normal or partial response group.

In a univariate logistic regression analysis, serum K level before ACTH test (OR=317.5; 95% CI, 1.1-191705.1, $P < 0.042$) and proportion of steroid users at ACTH stimulation (OR=15.0; 95% CI, 1.325-169.87, $P < 0.029$) were higher was associated with AI.

Conclusion

Serum potassium level and current steroid use could be potential factors for early detection of adrenal insufficiency.

These results emphasize the need to pay attention to the small signal including serum normal upper limit K level of children after HSCT for early detecting AI.