ADRENAL REST TUMORS IN PATIENTS WITH PRIMARY ADRENAL INSUFFICIENCY

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Background

Adrenal rest tissues located in gonads may enlarge in response to chronic overstimulation by adrenocorticotropic hormone (ACTH) in diseases with ACTH hypersecretion such as poorly controlled congenital adrenal hyperplasia (CAH), Addison's disease and Nelson's syndrome. Testicular adrenal rest tumors (TART) may develop in children with CAH patients and frequency in adults may increase up to 50-95%. Adrenal rest tumors (ART) are less frequently detected in females. Moreover, ART is less frequently associated in patients with adrenal disorders other than CAH.

Aim

To investigate the presence of adrenal rest tumors in patients with primary adrenal insufficiency (PAI) excluding CAH.

Patients and Method

Twenty-four (9F, 15M) patients with PAI aged 0.5-18.3 years (mean±SD; 8.6±4.5, median 7.5 years) were included. At the time of diagnosis patients had elevated plasma ACTH, low/undetectable serum cortisol levels, hypoglycemia and in some patients hyponatremia and hyperkalemia accompanying adrenal insufficiency signs and symptoms. Detailed patient and family history was recorded. Very long chain fatty acids, 21-hydroxylase autoantibodies, adrenal steroid precursors, adrenal imaging have been performed as needed for differential diagnosis. Two of patients had findings of Allgrove syndrome and one had autoimmune Addison disease. Rest of the cohort has diagnosed as non-CAH PAI.

Frequency of consanguinity was 75%. Mean duration of follow-up was 5.7±4.1 years (median: 4.9 years, ranges: 0.17-18.3). Boys were screened by scrotal ultrasonography (US) and girls by suprapubic pelvic US.

Results

- No ovarian ART was detected in girls.
- One boy had bilateral TART (6.7%).
- The boy with bilateral TART, was diagnosed as PAI at the age of 2 years, and was receiving hydrocortisone replacement therapy. He was 6.5 years old with ACTH level >1250 pg/ml when US was performed.
- Totally 4 adrenal rest tissues were detected in that patient, one in right testis (3.5x3.5 mm), three in the left (largest one 9.5x7 mm). Additionally testicular microlithiasis was detected in 4 patients (three of them were siblings) (n=4, 26.7%).

Clinical features of patients are summarized in the Table.

Table. Clinical features of the patients with PAI

Family no		Gender	At diagnosis			At present	
			Age (y)	Cortisol (µg/dl)	ACTH (pg/ml)	Age (y)	US findings
1		F	0.21	1.0	62	5.1	Normal
2		F	0.12	0.0	>1250	5.0	Normal
3#		M	4.25	0.1	>1250	12.4	Normal
4		M	2.00	0.0	>1250	6.5	TART
5		M	0.00	0.2	>1250	0.5	Microlithiasis
6		M	4.50	0.4	>2000	5.7	Normal
7		F	0.25	0.6	680	9.8	Normal
8		M	4.00	1.7	>1250	4.2	Normal
9		F	0.25	0.0	>1250	7.5	Normal
10	a	M	5.00	8.6	>1250	7.6	Microlithiasis
	b	M	4.60	1.3	>1250	8.7	Microlithiasis
	c	M	5.70	0.1	953	14.3	Microlithiasis
11		M	0.04	0.1	958	18.3	Normal
12		F	1.00	0.7	358	7.4	Normal
13		F	2.90	<0.1	>1250	4.2	Normal
14		F	0.16	<1.0	>1250	6.1	Normal
15		F	5.00	1.7	>1250	13.7	Normal
16		M	14.8	5.0	>550	16.4	Normal
17		M	0.02	0.1	>1250	3.5	Normal
18*		M	14.0	2.7	>1250	15.2	Normal
19	a	M	0.02	1.2	>1250	4.7	Normal
	b	M	1.00	0.0	>1250	9.2	Normal
20#		F	0.60	0.1	>1250	5.7	Normal
21		F	0.50	<0.1	1250	11.0	Normal

#Patients with Allgrove (Triple A) syndrome
*Patient with autoimmune Addison disease
Patiens using mineralocorticoid replacement besides glucocorticoids are highlighted in green.

Conclusion

- ACTH overstimulation or some other yet undefined factors may predispose to TART in patients with PAI. However frequency of ART is less than seen in CAH.
- Additionally testicular microlithiasis has been found at high frequency similar to CAH patients[1]. We recommend surveillance for ART by periodic US evaluation especially in male patients with PAI.

Reference

1. Poyrazoglu S, Saka N, Agayev A, Yekeler E. Prevalence of testicular microlithiasis in males with congenital adrenal hyperplasia and its association with testicular adrenal rest tumors. Horm Res Paediatr 2010;73:443-8.