Adrenocortical Tumours in Children – A Case Series

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Introduction

Paediatric adrenocortical tumours are rare and typically presents with virilising symptoms and signs. Clinical presentation can be similar to other virilising conditions such as congenital adrenal hyperplasia.

Methods

We described three retrospective cases of adrenocortical tumours diagnosed and managed at our institution over the past 10 years (2008-2017).

Results

All three girls presented with signs and symptoms of virilisation. Diagnosis of adrenocortical tumour was confirmed by laboratory findings, diagnostic imaging and histopathology. Of which, one patient was misdiagnosed and treated for congenital adrenal hyperplasia for 7 months. All three patients underwent complete resection of tumour and the affected adrenal gland. Hormone levels returned to normal after surgical resection. Two patients had subsequent recurrence – one had right lung metastasis while the other had local tumour recurrence. Treatment included surgical resection of tumours and systemic chemotherapy (mitotane, doxorubicin, cisplatin and etoposide). Both patients achieved complete remission since completion of chemotherapy.

Table 1: Clinical Data of Three Patients With Adrenocortical Tumours

Patient	Gender	Age at first signs	Age at first consult (years)	Age at diagnosis (years)	Clinical presentation
1	F	7.7	8.7	8.7	Pubic hair (P3), acne, skin pigmentation, deep voice, clitoromegaly
2	F	12	14.6	14.6	Primary amenorrhoea, hirsutism, deep voice
3	F	0	0.3	1.3	Clitoromegaly, hirsutism, deep voice

Table 2: Laboratory findings at diagnosis (*ND*: Not done)

	Patient 1	Patient 2	Patient 3	Normal values
Electrolytes				
Sodium (mmol/L)	140	141	137	*138-145*
Potassium (mmol/L)	3.5	4.1	4.8	*3.4-4.7*
Adrenocortical hormones				
Progesterone (nmol/L)	1.96	9.54	*ND*	*<0.32-52.28*
17alpha-OH progesterone (nmol/L)	>36.6	34.2	4.45	*0.6-5.5 <3.3 (<1 year old)*
Aldosterone (pmol/L)	284.8	120.8	*ND*	*97.3-834.0*
8am Cortisol (nmol/L)	228	207	*ND*	*101-536*
DHEA-S (micromol/L)	40.4	71.6	2.9	*1.1-11.8*
Androstenedione (nmol/L)	60.7	67.6	*ND*	*0.1-2.8*
Total Testosterone (nmol/L)	9.9	33.2	22.5	*0.4-2.0*
Estradiol (pmol/L)	79	96	83	*77-2382*
Hypothalamic-pituitary-adrenal axis				
Plasma renin (mcg/L/hr)	*ND*	1.09	18.36	*0.66-3.08*
Adrenocorticotropic hormone (ng/L)	5.5	*ND*	4.9	*Oct-60*
Short synacthen test	Failed	Passed	*ND*	-
Germ cell tumour markers				
Alpha-fetoprotein (ug/L)	<2	*ND*	5	-
Beta-human chorionic gonadotropin (IU/L)	<1.2	*ND*	<1.2	*<5*
Hormonal profile				
Follicle stimulating hormone (IU/L)	<0.1	3.2	0.2	*1.35-17.06*
Luteinizing hormone (IU/L)	<0.09	1.44	<0.09	*0.38-60.33*
Prolactin (ug/L)	17.9	17.7	14.5	-
Free thyroxine (pmol/L)	12.6	13.2	14.9	*10.3-25.7*
Thyroid stimulating hormone (mIU/L)	0.84	2.81	1.68	*0.50-4.50*

Table 3: Diagnostic imaging results at initial diagnosis

Patient	Ultrasound of abdomen and pelvis	MRI Abdomen (transverse x anteroposterior x craniocaudal)	Metastatic screen
1	Right suprarenal mass Normal ovaries and uterus	Right suprarenal mass that is heterogeneous and mildly enhancing and measures 5.5cm by 4.7cm by 4.1cm	CT Thorax showed no pulmonary metastasis Post-operative PET/CT scan showed no FDG-avid metastasis
2	Right suprarenal mass Probable right ovarian dermoid Normal left ovary and uterus	Right suprarenal mass that is fairly well-circumscribed and measures 10.9cm by 11.1cm by 11.5cm	CT Thorax showed no pulmonary metastasis Bone scan showed no scintigraphic evidence of osseous metastasis
3	Mass anteromedial to the upper pole of the right kidney	Right adrenal mass that is well-defined and enhancing and measures 3.2cm by 3.0cm by 3.2cm	CT Thorax showed no pulmonary metastasis

Table 4: Surgical and histopathological findings with reference to propose Criteria by Wieneke at al[8]

		Patient 1	Patient 2	Patient 3
Tumour weight (g)		67	371	Well below 500
Tumour size (cm)		7.5 x 4.5 x 3.5	10.5 x 9.5 x 6.5	3.0 x 2.5 x 2.3
Periadrenal extension		No	Yes	No
Invasion into vena cava		No	No	No
Venous invasion		No	No	No
Capsular invasion		Focal invasion seen	No	No
Lymph node biopsy		Negative for malignancy	Not done	Not done
Presence of tumour necrosis		Yes	Yes	No
Mitoses		Up to 23 per 50 HPF*, atypical mitoses seen	Up to 8 per 50 HPF, atypical mitoses seen	6 per 50 HPF
Immunohisto-chemistry	**p53 positive cells (%)**	100	Rare cells, <10	100
	Ki67 index (%)	Up to 50	10	Oct-20
Tumour staging[4]		II	II	I

*HPF: High power fields

Table 5: Post-operative outcomes

	Patient 1	Patient 2	Patient 3
Hormone levels			
DHEA-S micromol/L)	0.4	3.3	4.4
Total Testosterone (nmol/L)	<0.4	0.6	<0.4
17-OHP (nmol/L)	1.3	1.5	0.2
Androstenedione (nmol/L)	6.9	*ND*	*ND*
Recurrence	12 months post operation	12 months post operation	No
	Metastatic adrenocortical carcinoma in right lung	Local recurrence (4.6cm by 4.2cm by 5.2cm) in retroperitoneum on the right side posterolateral to the right kidney	
Tumour markers used	DHEA-S, total testosterone, 17-OHP, androstenedione	DHEA-S, total testosterone, 17-OHP	DHEA-S, total testosterone, 17-OHP
Surveillance scans	PET/CT scan, MRI abdomen and CT Thorax	US abdomen	US abdomen
Endocrine complications	**Mitotane-induced adrenal insufficiency** – on hydrocortisone (since December 2013) and fludrocortisone (since February 2015) **Mitotane-induced hypothyroidism** – on levothyroxine since April 2015	**Mitotane-induced adrenal insufficiency** – on hydrocortisone (since June 2016)	**Adrenal suppression** from prolonged high dose steroid use (since October 2016)

Conclusion

In summary, this descriptive analysis of our case series over past 10 years concurs with many findings in the literature. Based on our experience, we feel that it may be prudent to perform ultrasound abdomen (with emphasis on the adrenal glands) for all girls who present with virilising features.