Clinical characters of adrenocortical tumors in Chinese childhood

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Abstract: Kidney cancer includes both cancer of the renal parenchyma and cancer of the pelvis (ie transitional cell cancer). In adults, 85%-90% of kidney cancer cases are renal cell cancer. Renal cell cancer accounts for 2% - 3% of all malignancies in western countries and 1% -2% in Japan. The incidence of renal cell cancer is high in Western, and Northern Europe and North America while it is low in Asia. Children with adrenal tumors adrenal tumor is most common, children with precocious puberty may consider this disease, its clinical manifestations was different from adults, should be combined with clinical, laboratory and imaging features comprehensive diagnosis. The incidence of renal cell cancer has been increasing worldwide. Although the incidence of renal cell cancer in Japan is lower than the rates in the other industrialized countries, there is no doubt that it is increasing.
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Key words: tumor; adrenal tumor; adrenal cortex; Cushing's syndrome

1. Introduction

Great strides have been made in the understanding of molecular mechanisms of adrenocortical tumor. This has led this field to the enviable position of having a range of molecularly targeted therapies. Large sequencing efforts are now revealing more and more risk factors responsible for tumour development and progression, offering new targets for therapy. adrenocortical tumor is a rare disease, the world's children under the age of 15, the incidence is only 0.3/million-0.38 / million [1]. Adrenocortical tumors accounted for 0.2% of all childhood tumors, the peak age of onset is less than 5 years of age [2]. As the source of the heterogeneity of adrenal tissue and the children may have a tumor of embryonic tissue sources, various types of adrenal tumors of children, due to the clinical manifestations,are different. clinical manifestations of adrenal tumors and adrenal abnormalities were high cortisol symptoms,alone or mixed performance, high aldosterone hyperlipidemia is rare. Different from adult,children with adrenocortical tumors or abnormal adrenal androgen increased more common. In this paper, we would like to introduce the result of our studies, which evaluate the risk factors of renal cell cancer in a Chinese population. This study retrospectively analyzed the symptoms, laboratory tests and imaging inspection, compared the the clinical features between adrenal adenoma and adenocarcinoma, to improve the cognitive ability of clinical manifestations and diagnosis.

2. Methods and Materials

84 cases were reviewed for the pathologic diagnosis of adrenocortical tumor between 2000 and 2010. They were diagnosed as adrenal tumors (adenomas 43 cases, adenocarcinoma 41 cases, Table 1), containing 36 males and 48 females, male:female is 3:4. Mean diagnosis age at (5.63 ± 2.84) years. 57 cases (67.9%) are less than 5 years; 27 cases (32.1%) are more than 5 years. 13 cases adrenal tumors, 4 cases was found by prenatal B super, the other 9 cases was born for the clitoris hypertrophy, represented a penis enlargement and appeared acne after born 1 week, 7 cases is adenoma, 6 patients were adenocarcinomas, There was no evident difference in gender, onset doctor age, no tumor family history. the clinical characteristics, endocrine change, imaging findings，pathological diagnosis and the relationships were statistically analyzed by this research.

3. Statistical analysis

All the data were presented as mean±standard deviation or as percentage. Chi-squared test were used to analysis the difference of genotypic and allelic frequencies between patients and controls by SPSS 11.0 software. A P-value of less than 0.05 was viewed as statistically significant.

4. Results

43 cases (51.2%) performed precocious puberty, 31 cases (36.9%) precocious puberty were girls, and 12 cases were boys (14.3%). There is statistically significant difference between men and women (P <0.05).9 patients had hypertension,5 cases even caused paralysis led clinic. 9 cases had no abnormal symptoms, discoveryed due to abdominal pain, bloating, and (or) treatment abdominal mass, or accidental (Table 1).

Table 1. Main patient characteristics and outcomes

Clinical manifestations	cases	（%）
Precocious puberty	43	51.2
Earlier pubic hair	30	35.7
Penis enlargement	23	27.4
clitoris hypertrophy	11	13.1
Breast development	14	16.7
Growth acceleration	8	9.5
voice low	2	2.4
Other	9	10.7
Abdominal mass	7	8.3
Abdominal pain/abdominal distention	7	8.3
Fever, emaciated, tired	5	5.6
Physical examination/examination revealed	2	2.4
Cushing's syndrome	32	38.1
Central obesity	27	32.1
Hairy	20	23.8
Acne	14	16.7
High blood pressure	10	10.7
Hyperthyroidism appetite	7	8.3
Much blood quality	1	1.2

79 cases detected the blood levels of sex hormones, 75 cases (94.9%) testosterone increased, The value is higher than the corresponding age and 1.93 ~ 201.4 times of the upper limit.23 cases (27.7%) examined DHEA sulfate (DHEAS), 18 patients (21.4%) increased, adenoma and adenocarcinoma DHEAS level have no difference. 51 (60.7%) were detected estradiol (both have higher testosterone at the same time), 34 patients (40.5%) value increased,which is higher than the corresponding age and developmental level of 1.24 to 18.78 times. 21 cases with estradiol elevated DHEAS. 18 patients carryed dexamethasone suppression test, 3 cases of testosterone can be suppressed (Table 2).

Table 2 sex hormone levels in children with adrenocortical tumors

Sex hormones	N	negative	positive	positie（%）
testosterone	75	4	75	94.9
DHEAS	23	5	18	78.3
estradiol	51	17	34	66.7

76 cases (90.5%) blood lactate dehydrogenase (LDH) were more than the normal range (114 ~ 240 U / L), 29 adenomas (34.5%) increased,41 (48.8%) adenocarcinoma increased, both the positive rate is differences (P <0.05). Adenocarcinoma blood LDH average (724.1 ± 415.3) U / L, LDH adenoma average (412.7 ± 115.2) U / L, both were significantly different (P <O. 01).serum LDH of Adenoma and adenocarcinoma is the biochemical and endocrine markers,they were the only statistically significant difference. Table 3.

Table 3 adrenal cortical tumors in children with serum LDH enzyme

serum LDH	N	negative	positive	positie（%）
adenoma	43	14	29	67.4
adenocarcinoma	41	0	41	100

In this study,adenocarcinoma and adenoma underwent B-ultrasound and CT.Only 17.6% B ultrasonic diagnosis were consistent with pathology, so the B- ultrasound as a means of detection of cancer screening. 2 cases were misdiagnosed as adrenal neuroblastoma,the final pathological diagnosis was adrenal cortical carcinoma. CT diagnosis was only 31.7% in line with the pathology, including 3 cases adenoma,because the tumor has a large central necrosis,which was diagnosed by adenocarcinoma image, while the small cancer can not be qualitative.Therefore, clinicians must be combined with comprehensive clinical and laboratory tests，not to pander to the initial imaging diagnosis.

5. Discussions

Kidney cancer includes both cancer of the renal parenchyma and cancer of the pelvis (ie transitional cell cancer). In adults, 85% -90% of kidney cancer cases are renal cell cancer [3]. Renal cell cancer accounts for 2% - 3% of all malignancies in western countries [4-7] and 1% -2% in Japan[7-8].The incidence of renal cell cancer is high in Western, and Northern Europe and North America while it is low in Asia [3-5,7].children adrenal tumors can be divided into the adrenal cortex and medulla by adrenal tissue sources, and Children with adrenocortical tumors， which a simple expression of peripheral precocious puberty，was the most common, followed by both peripheral precocious puberty and Cushing syndrome,Cushing's syndrome again for the performance alone, finally, no endocrine abnormalities.Up to now,little attention has been paid to interethnic variability or individual differences, whereas，this is an important aspect in the current TKI era [9].Some studies have found that 125 children with cortical tumors purely peripheral precocious puberty accounted for 51.2%, simple Cushing's syndrome 0.8%, both 42%, non-functional 4.8% [10]. Children's non-iatrogenic Cushing's syndrome is more than 80% due to adrenal tumors, Cushing's syndrome in adults is more common. In this study, 43 precocious puberty (51.2%), 31 cases early-maturing girls (36.9%), and 12 boys (14.3%), precocious performance ratio between men and women was significant difference ($P<0.05$).Clinical manifestations of female masculinity and male peripheral precocious was puberty performance.27 Cushing's syndrome with central obesity in 32 cases, 9 patients had high blood pressure, stroke and 5 cases even caused paralysis led clinic. This is clearly different from adults with symptoms of Cushing's performance-based. So the peripheral precocious puberty in children should be on high alert.Adrenal androgen secretion is mainly DHEA, DHEAS and androstenedione [11], feminine sexuality cortical tumor cell aromatase activity was significantly higher in normal adrenal Cushing's syndrome and to the performance of cortical tumor cells. Studies confirmed the adrenal cortex tumor cells of ACTH and angiotensin lI (Ang Ⅱ) receptor expression, the expression of all kinds of P450 enzymes, exogenous ACTH can increase its activity [12], so the adrenal cortex hormones can be increased in the male various types of adrenal hormone secretion. No matter what age, gender，95%blood DHEAS are from the adrenal gland, the adrenal lesions prompted DHEAS. In this study, 79 cases examined the blood hormone levels, 75 patients (94.9%) testosterone increased， detection value is higher than the corresponding age.23 cases (27.7%) examined DHEA sulfate (DHEAS), 18 patients (21.4%) increased adenoma and adenocarcinoma.DHEAS level was no difference. 51 (60.7%) were detected estradiol (both have higher testosterone at the same time), the detection value increased in 34 patients (40.5%),Which is higher than the corresponding age.23 cases DHEAS were elevated. The incidence of renal cell cancer has been increasing around worldwide.The rapidly increasing incidence of renal cell carcinoma may be partly explained by the rising numbers of the new imaging techniques and diagnosis[13].the diagnosis of B ultrasound and CT is a common diagnosis of adrenal tumor, CT scanning is considered as the imaging diagnosis of adrenal cortical carcinoma and the primary means. Tumors were large, uneven density, with irregular low-density area or hemorrhage, and there is a strengthen uneven calcification as the typical CT, CT found the tumor, but three cases is negative in B ultrasound[1]. If CT is still negative and cortisol decreased, we should regularly review B ultrasound or CT. For the diagnosis of CAH patients, if poorly controlled disease, adrenal gland should be regularly reviewed by B ultrasound,to see whether hyperplasia of the adrenal adenoma. This study for the occurrence of abnormal adrenal and sex characteristics (or) symptoms of Cushing's patients underwent B ultrasound and CT. Only 17.6% B ultrasonic diagnosis was consistent to pathology, so the B ultrasonic is as a means of cancer screening. 2 cases were misdiagnosed as adrenal neuroblastoma, the final pathological diagnosis was adrenal cortical carcinoma.only 31.7% CT diagnosis wasin line with the pathology, including 3 cases adenoma,because the tumor has a large central necrosis,which was diagnosed with adenocarcinoma, while the small cancer can not be qualitative.Therefore, clinicians must be combined with comprehensive clinical and laboratory tests,not pander to the initial imaging diagnosis. In summary, the adrenal cortex tumor showed the signs of clinical abnormalities and (or) Cushing's syndrome, or no endocrine abnormalities.laboratory tests and common hormone increased the cortisol circadian rhythm disappeared and the clinical features of cancer,Unlike adults, children with adrenogenital disorders increased performance of the more common androgen. A few may be due to adrenal cortical tumors,early B ultrasonic exceptions have been misdiagnosed as CAH. In short,the distribution of children's tumor type and clinical manifestations are different from adults, we should summarize the clinical characteristics according to the early identification of adrenal tumors, clinical presentation, laboratory examination, imaging studies， We can make the final diagnosis timely，accurate treatment decisions and prognosis. Further studies may be necessary to provide a better understand of this important clinical issues,because the number of renal

cancer cases was small in our studies.

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Refereces

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