

Isosexual peripheral precocious puberty in a girl: A rare presentation of Adrenocortical Carcinoma

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ABSTRACT

Precocity puberty was defined as the appearance of secondary sexual characteristics before the age of 8 years in girls and 9 years in boys.

precocity puberty can be due to GnRH-dependent or GnRH-independent causes. Childhood Adrenocortical Carcinoma (ACC), a rare cause of GnRH-independent precocious puberty, was hormonally active in >90% of cases. Childhood adrenal cortex cancer was aggressive childhood cancer. The tumors have a varied presentation either precocity/virilization or presentation with Cushing's syndrome or both.

Key Words: Cushing's syndrome; Adrenocortical Carcinoma; Histopathology

INTRODUCTION

Isosexual precocious puberty is a rare presentation of adrenal carcinoma in a girl. It is essential to distinguish it from an adrenal cortical adenoma by correlating it with clinical, biochemical, imaging, and histological features, as their prognosis is different.

CASE PRESENTATION

The six-year six-month-old girl presented to endocrinology OPD with a history of breast enlargement, breast pain for six months, and vaginal discharge for one month. For six months, there has been a positive history of weight gain, though the weight has not been quantified. No history of exogenous drug intake, no history of headache and vomiting, and no paroxysm (headache/sweating/palpitation). She was delivered vaginally after a full-term pregnancy; she had no surgery or medical history. On examination Tanner staging of breast and pubic hair stage III. Blood pressure is 110/80, pulse is 80/min, IAP-WHO growth chart showed height is between 3% to 10%; weight is between 25% to 50%. No features of the moon face, striae, or ecchymosis. Her bone age according to the Greulich and Pyle method is advanced (more than 2 SD).

On endocrine evaluation estrogen level was elevated (55 pg/ml), testosterone 1.58 nmol/l, serum DHEAS was more than 3 times elevated (657 ug/dl), baseline LH was 0.5, FSH<0.05, after stimulation of triptorelin 100 ug, 1 hour LH 0.14, FSH 0.50; suggested of peripheral precocious puberty. USG abdomen showed a normal ovary, and well defined hypochoic solid lesion measuring 4.8 cm × 2.25 cm was noted in the right suprarenal region which abuts hepatic parenchyma. CECT on adrenal protocol showed well-defined heterogeneously enhancing soft tissue attenuation lesion in the right adrenal measuring approx. 49 mm × 39 mm × 48 mm as shown in Figure 1, NCCCT-39 HU, arterial phase 160 HU, portovenous phase-132 HU, delayed 70 HU, absolute washout 66.67%, relative washout-46.97%, the lesion was abutting VI of the liver with the indistinct fat plane but no venous invasion, suggestive of lipid poor adrenal adenoma. 8 am cortisol was 18.2 ug/dl 11 pm cortisol 18.60 ug/dl, overnight dexamethasone suppression test was positive, low dose dexamethasone suppression test was 16.8 ug/dl (unsuppressed), morning ACTH is 9 pg/ml, plasma aldosterone was increased (498.96 pg/ml) plasma renin activity was suppressed. Urinary cortisol was elevated twice, 432 ug/24 hour, 480 ug/24 hour by ELISA. 24 hour urine metanephrine and normetanephrine were normal.

Blood pressure was controlled on amlodipine 2.5 mg twice a day. The patient underwent open laparotomy for adrenal surgery, during intraoperative tumor was a well-defined capsule separating the margin from the liver and kidney, and during intraoperative no BP fluctuation.

After surgery, on day 4 postoperative cortisol is undetectable, the patient is on a physiological dose of steroids, and blood pressure was controlled.

Histopathology was suggestive of adrenocortical carcinoma, brisk mitosis 20-25/50 high power field with capsular invasion, Ki67 index 5% to 10% as shown in Figure 2 and Figure 3. The patient underwent chemotherapy mitotane, cisplatin, etoposide, and doxorubicin. After 2 months of surgery, breast growth subsided and no new pubic hair growth occurs.

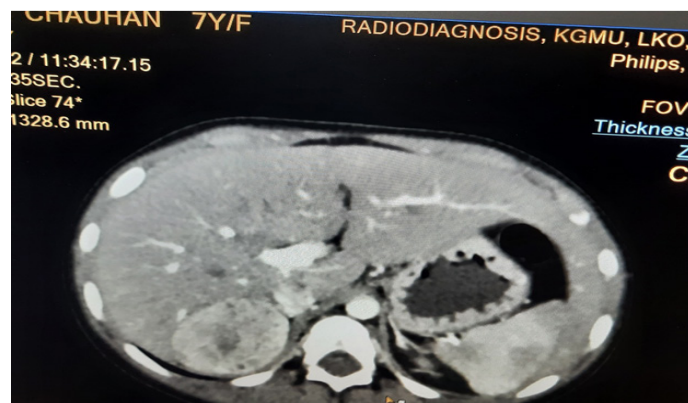


Figure 1) CECT on adrenal protocol showed well-defined heterogeneously enhancing soft tissue attenuation lesion in the right adrenal measuring approx 49mm × 39mm × 48mm

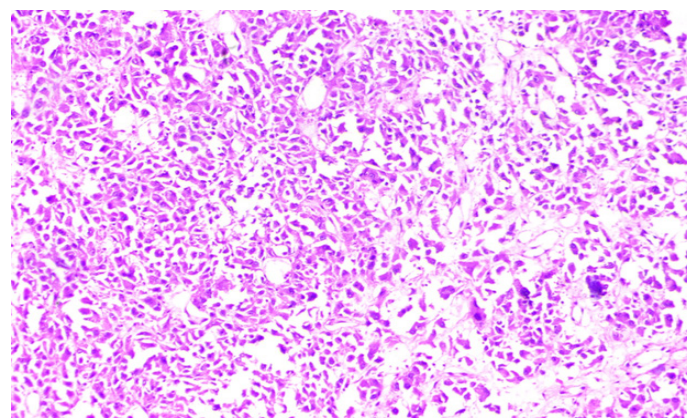


Figure 2) Showed the tumor was composed of variably size nests, trabeculae, and a sheet of tumor cells. The individual cell was large-sized chromatin and granular eosinophilic cytoplasm. Brisk mitoses were evident 20-25/50 high power field

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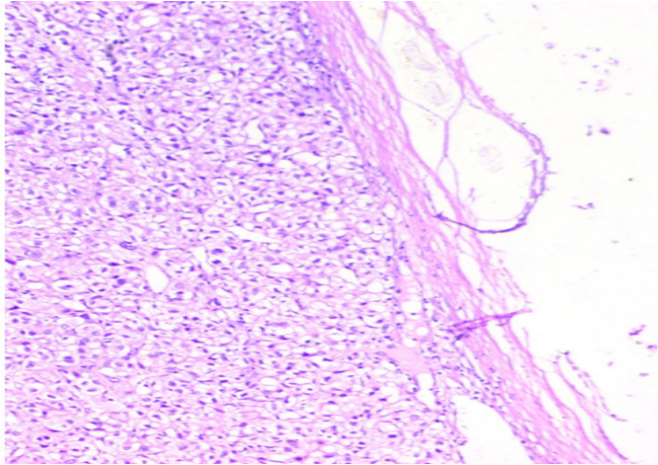


Figure 3) Tumor cell invades through the adrenal capsule.

REVIEW OF LITERATURE

Precocity puberty is defined as the appearance of secondary sexual characteristics before the age of 8 years in girls and 9 years in boys [1]. Precocity puberty can be due to GnRH-dependent or GnRH-independent causes. Childhood ACC, a rare cause of GnRH-independent precocious puberty, is hormonally active in >90% of cases.

Adrenocortical Carcinoma are very rare neoplasms of childhood (0.2% of all malignancies), with a reported incidence of only 0.2-0.3 new cases per 1 million children per year and accounting for 6% of all childhood adrenal cancers [2]. There is a slight female predilection (58.6%).

Most tumors are sporadic; however, a fraction of them may be familial. Familial ACC may be associated with Li-Fraumeni syndrome, Weidemann-Beckwith Syndrome, multiple endocrine neoplasia type 1, or Carney complex [3].

The tumors have varied presentations either precocity/ virilizing forms (pubic hair, accelerated growth, an enlarged penis, or clitoris and maturation) hirsutism and acne, or presentation with Cushing's syndrome, or both. Less often, children present with Cushing's syndrome (15%-40%), obesity, hypertension and impaired linear growth due to excessive glucocorticoids, feminization (7%) or gynecomastia due to excessive estrogens, signs of hyperaldosteronism (1%-4%) such as hypertension and hypokalemia, or a mixture of symptoms [4]. Breast enlargement is common in a boy with adrenal carcinoma but in the girl, there was no reported case in the literature. Breast enlargement with pubic hair growth (Isosexual precocious puberty) is a rare presentation of adrenal carcinoma in a girl.

The main differential diagnoses are adrenocortical adenoma. Modified

Weiss criteria were used to differentiate adenoma and Adrenocortical carcinoma. In our case is modified Weiss score was 4 and capsular invasion was present.

Surgery is the standard of care and allows the normalization of growth and the disappearance of virilization [5]. Adjuvant mitotane treatment in patients after radical surgery that has a perceived high risk of recurrence (if a tumor is more than 5 cm or lymph node metastasis, or R₁ resection and Ki67 >10%. Even after complete resection, a high risk of recurrence of ACC remains. Despite multimodal approaches including mitotane, chemotherapy with Cisplatin, Etoposide, and Doxorubicin (CED) and radiotherapy, the prognosis of ACC in children remains poor with an estimated 5 year survival rate ranging from 30% to 90% depending on the presentation of the disease [6,7].

DISCUSSION AND CONCLUSION

CECT adrenal tumor appears to be an atypical adenoma, with regular margins, no necrosis, and no invasion, but histopathology reveals Adrenocortical Carcinoma. Breast enlargement is common in a boy with adrenal carcinoma but in the girl, there was no reported case in the literature. Breast enlargement with pubic hair growth (Isosexual precocious puberty) is a rare presentation of adrenal carcinoma in a girl.

REFERENCES

1. Carel JC, Léger J. Precocious Puberty. *N Engl J Med Overseas Ed.* 2008;358:2366-77.
2. Gupta N, Rivera M, Novotny P, et al. Adrenocortical carcinoma in children: a clinicopathological analysis of 41 patients at the Mayo Clinic from 1950 to 2017. *Horm Res Paediatr.* 2018; 90:8-18.
3. Sutter JA, Grimberg A. Adrenocortical tumors and hyperplasias in childhood-Etiology, genetics, clinical presentation, and therapy. *Pediatr Endocrinol Rev.* 2006;4:32-9.
4. Ribeiro RC, Figueiredo B. Childhood adrenocortical tumours. *Eur J Canc.* 2004;40(8):1117-26.
5. Lee PD, Winter RJ, Green OC. Virilizing adrenocortical tumors in childhood: Eight cases and a review of the literature. *Pediatrics* 1985; 76: 437-44.
6. Redlich A, Boxberger N, Strugala D, et al. Systemic treatment of adrenocortical carcinoma in children: data from the German GPOH-MET 97 trial. *Klinische Pediatric.* 2012; 224:366-71
7. Wieneke JA, Thompson LD, Heffess CS. Adrenal cortical neoplasms in the pediatric population: a clinicopathologic and immunophenotypic analysis of 83 patients. *Am J Surg Pathol.* 2003;27(7):867-81