case report

Heterosexual precocity: rare manifestation of virilizing adrenocortical oncocytoma

Sridhar Subbiah,[a] Uma Nahar,[b] Ram Samujh,[c] Anil Bhansali[a]

From the [a]Department of Endocrinology, [b]Department of Pathology and [c]Department of Pediatric Surgery, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

Correspondence: Anil Bhansali · Department of Endocrinology, PGIMER, Chandigarh,India · drsridharjipmer@gmail.com

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Adrenocortical oncocytomas are extremely rare, and most of the tumors are benign and nonfunctioning. To our knowledge, only 30 cases have been reported in English published studies, and most patients are 40 to 60 years of age. So far, in the pediatric age group, only three cases of functioning adrenocortical oncocytoma have been reported. We report a case of functioning adrenocortical oncocytoma in a 3 1/2-year-old female child who presented with premature pubarche, clitoromegaly, and increased serum dehydroepiandrosterone sulfate and testosterone. She was managed successfully with right adrenalectomy, and the tumor histology was consistent with adrenal oncocytoma.

Adrenocortical neoplasm is the most common cause of heterosexual precocity in a girl child. Among the adrenal masses, functioning adrenocortical oncocytoma is a rare cause of heterosexual precocity. Oncocytoma is defined as a neoplasm composed of oncocytes, which are large cells with an abundant eosinophilic and granular cytoplasm.[1] The term "oncocyte" was first used by Hamperl[2] in 1950, while describing the histological features of Hurthle cell thyroid neoplasm. Oncocytomas have been reported in a variety of anatomic sites, most frequently in the thyroid, kidney, salivary gland, and pituitary.[1] An oncocytoma arising from the adrenal gland is an extremely rare finding, with only 30 cases reported in English published studies. They are usually benign and nonfunctioning, with most reported patients being 40 to 60 years of age.[3] To our knowledge, among the reported nine functioning adrenocortical oncocytoma, only three were presented in the pediatric age group, and the youngest age reported was 6 years.[4]

Because of unusual occurrence of functioning adrenocortical oncocytoma in childhood, we report a case of adrenocortical oncocytoma in a 3½-year-old female child presenting with heterosexual precocity.

CASE

A 3 1/2-year-old female child was brought by her parents with complaints of premature development of pubic hair growth, noted since 1 year prior to admission. She had no history of facial or axillary hair growth, menstrual spotting. She was born at full-term by normal vaginal delivery without any perinatal problems and had no history of hospitalization previously. Her mother gave no history of androgen drug exposure during the pregnancy.

On examination, her body weight was 13 kg (10th percentile), height was 93 cm (10th percentile), target height 157 cm (<3rd percentile), and body mass index was 15.03 kg/m^2. Her blood pressure was 100/80 mm Hg. The physical examination revealed hair growth on the pubic area (**Figure 1a**) and clitoromegaly (**Figure 1b**). Her Tanner stage was A1P3B1. No signs of Cushing syndrome were noted. Abdominal examination found no mass palpable in the adrenal and hypochondrial regions. Laboratory values are shown in **Table 1**. Complete blood count, liver, and renal function tests were normal while the hormonal profile showed increases in some values (**Table 2**). Her bone age was less than 4 years.

The abdominal CT scan showed a well-defined hypodense lesion measuring 38×36 mm, seen in the right adrenal region without any calcification or necrosis (**Figure 2**). Based on the above clinical, biochemical, and radiological investigations, the patient was diagnosed with a right adrenal mass presenting as heterosex-

Figure 1A. Hair growth over the pubic area.

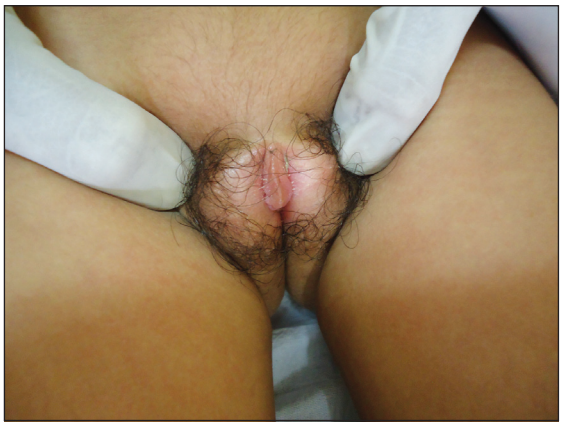

Figure 1B. Clitoromegaly.

Table 1. Laboratory test results.

Laboratory test	Value	Normal range
Hemoglobin (g/dL)	11.2	
Serum sodium (mml/L)	142	135-145
Serum potassium (mmol/L)	4.1	3.5-5.0

Table 2. Hormonal profile.

Laboratory test	Value	Normal range
Serum dehydroepiandrosterone sulfate (µg/dL)	1000	35-430
Testosterone (nmol/L)	5.37	0.2–2.0
Luteinizing hormone mIU/mL	0.01	2.4–12.6
Follicle-stimulating hormone (mIU/mL)	0.493	3.5-12.5
Estradiol (pg/mL)	20.86	12.5-166
17-hydroxy progesterone (ng/mL)	6.22	0.7–5.0
0800 hr cortisol (nmol/L)	563.2	150-550
Adrenocorticotropic hormone (pg/mL)	9.0	10-20
0800 hrs serum cortisol was non suppressible after overnight (ONDST) (nmol/L)	431.9	<50 nmol/L
Low dose dexamethasone suppression test (nmol/L)	367.5	<50 nmol/L

ual precocity. She underwent a right open adrenalectomy and her postoperative course was uneventful. The resected tumor was well encapsulated measuring 2.5×2.0 cm in diameter and 20 g in weight. The histopathological examination of the tumor revealed diffuse sheets of tumor cells with a large, round, abundant eosinophilic granular cytoplasm (**Figures 3A, 3B**). No capsular or vascular invasion was noted. Immunohistochemistry of the tumor cells was negative for chromogranin A stain (**Figure 4**). Overall features were consistent with benign adrenocortical oncocytoma.

After the removal of the adrenal lesion, the patient was re-evaluated after 1 month. Her serum total testosterone (5.37 vs <0.087 nmol/L) and serum dehydroepiandrosterone sulfate (>1000 vs 130 µg/dL) levels decreased dramatically to a normal range. The patient was advised to follow up at 6-month intervals.

DISCUSSION

The differential diagnosis of contrasexual precocity in a female child includes late onset congenital adrenal hyperplasia (21-hydroxylase and 11 beta-hydroxylase deficiency), androgen-secreting adrenal mass including adrenal carcinoma, virilizing ovarian tumor (arrhenoblastoma), polycystic ovary syndrome, and rarely a syndrome of glucocorticoid resistance.[5] The clinical manifestations of virilization in children include accelerated growth and skeletal maturation, clitomegaly, hirsutism, acne, and premature pubarche.

Oncocytic tumors have been described mostly in the kidney, thyroid, and salivary glands.[1] Adrenal oncocytomas are very rare. The mean age of the patients were 43.5 years (range, 6-72 years), with a female predominance of 2:1. These tumors are more common on the left side (1:2). Most of the tumors are benign and nonfunctional, and hence incidentally detected.[3]

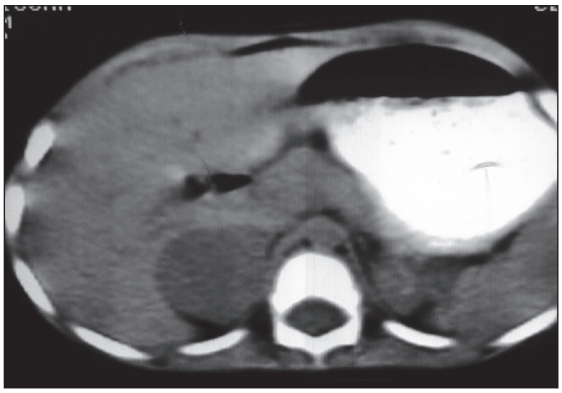

Figure 2. Abdominal CT scan showing a well defined hypodense lesion measuring 38×36 mm, seen in the right adrenal region without any calcification or necrosis.

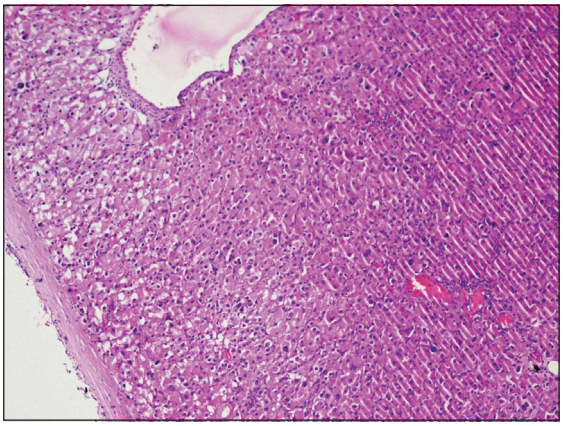

Figure 3A. Microphotograph showing a thin capsular tumor with diffuse sheets of large cells (HE ×140).

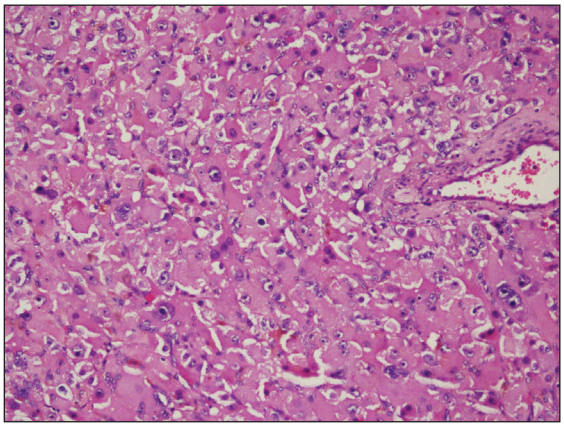

Figure 3B. Microphotograph showing the higher magnification of the tumor cells which are large, round, having abundant eosinophilic cytoplasm (HE ×540).

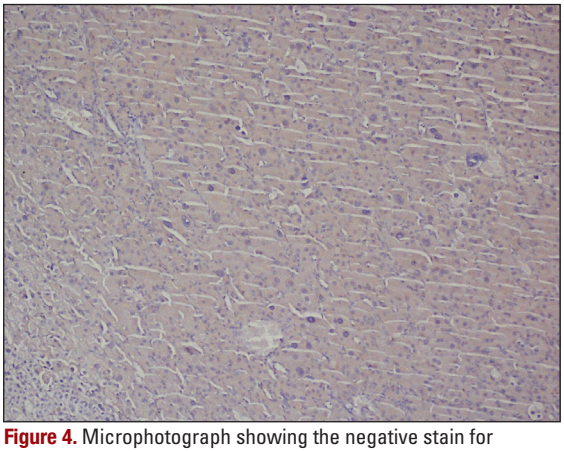

Figure 4. Microphotograph showing the negative stain for chromogranin A (IHC ×280).

Functioning adrenocortical oncocytomas are very rare; so far only 9 cases have been reported studies published in English.[4,6,7] Among the reported 9 functioning oncocytomas, 6 were in the age group of 40 to 60 years, with female predominance (M:F, 4:5). All females presented with features of virilization, whereas gynecomastia and Cushing syndrome (2 in each) were the presenting features in males. So far, only three functioning adrenal oncocytomas have been reported in the pediatric age group (6, 12, and 14 years).[4,6] All reported children presented with virilization and heterosexual precocity, similar to our case. The underlying mechanisms of the hyperfunction in oncocytomas are yet unexplained.

It is often difficult to differentiate benign from malignant adrenocortical oncocytoma. Most studies demonstrated that a combination of clinical, biochemical, and, in particular, histological features (Weiss score)[8] can distinguish adenoma from carcinoma. The presence of fibrous encapsulation in contrast imaging is suggestive of oncocytoma. However, our patient did not have this finding. Rarely, pheochromocytoma can have cells with an eosinophillic cytoplasm resembling oncocytes. Apart from clinical and biochemical features, immunohistochemical studies, like chromogranin A, are helpful to differentiate pheochromocytoma from oncocytoma. In our case, immunohistochemistry for chromogranin A was negative (**Figure 4**). The treatment of functioning tumor is surgical excision irrespective of size, whereas the nonfuctioning oncocytomas require removal only if the size is more than 6 cm. In conclusion, adrenal oncocytomas, although rare, should be considered in the differential diagnosis of virilizing adrenal tumor.

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