Virilising Adrenal Adenoma in Children

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Abstract

Tumours of the adrenal cortex are most commonly seen in adults but rare in children. The clinical manifestations depend on the age and sex of patients; about two-thirds of the cases virilisation is the predominant presentation, whereas many presents with both virilisation and cushingoid features. Diagnosis is confirmed by hormonal evaluation and radiological investigations. Surgical removal is the mainstay of treatment. Usually, there is a good prognosis in paediatric patients, whereas the high mortality rate reported in older literature may have been due to big tumour size, post-operative complications and inadequate steroid replacement. Here, we are presenting a series of three cases during childhood with virilising features due to adrenocortical tumours. All of them presented predominantly with features suggestive of virilisation. All patients underwent surgery and had a good outcome despite big tumour size in one of the patients. Histology revealed a benign lesion in the form of adrenal adenoma. Most virilisation and cushingoid features disappeared in the follow-up (median – 1 year). Although these tumours are rare, a high index of suspicion should be kept in children with cushingoid features, virilisation or a combination of both of them. Even if the tumour size is big, adequate steroid replacement and supportive management postoperatively have led to good prognosis in our patients.

Keywords: Adrenal adenoma, Cushing Syndrome, virilising

Introduction

Adrenocortical tumours (ACTs) are uncommon in paediatric patients and constitute 1.3% of all carcinomas in the paediatric age group. According to Surveillance, Epidemiology and End Results data of the United States, approximately 14 new patients per year are diagnosed with ACT in patients younger than 20 years of age.[1]

A number of earlier reported case series describe only a few patients of this entity over several years.[2] Most of the ACTs are sporadic; however, a few of them might be familial. There is a strong association of paediatric ACTsu with several genetic syndromes such as Carney complex, Wiedemann–Beckwith syndrome, congenital adrenal hyperplasia, Li–Fraumeni syndrome, McCune–Albright syndrome and multiple endocrine neoplasia type 1.[3]

A registry data from Brazil have shown that paediatric ACTs are more common in girls and are almost always associated with increased production of adrenal androgens. It has also shown that ACTs in the paediatric population are heterogenous and they comprise at least two subtypes with different pathogenetic mechanisms. According to them, complete resection is the definitive regardless of the type. Due to the rarity of this condition in paediatric age group, there is a requirement for a database for obtaining meaningful clinical and outcome information about such rare paediatric malignancies.[4] As these cases have been rarely reported in the Indian Medical literature; hence, we are hereby presenting three children with cushingoid and virilising features due to ACTs.

Case Reports

Case 1

A 3-year-old girl child presented to the paediatric outdoor patient department with complaints of increasing hair growth in the axilla and pubic area for the past 6 months. On examination, the child was having cushingoid facies, Stage 3 of pubic and axillary hair development with clitoromegaly, no breast enlargement, and her height was between 1st and 3rd centiles and weight was between 25th and 50th centiles. She was found

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to have hypertension (blood pressure BP = 126/88 mmHg) and there was no history of vaginal bleeding. No mass was palpable on abdominal examination. Investigations revealed increased serum cortisol after overnight dexamethasone suppression test - 18.81 µg/dL, increased serum testosterone - 79.48 ng/dL, dehydroepiandrosterone (DHEAS) - 199.9 µg/dL) with reduced adrenocorticotropic hormone (ACTH) levels - <5 pg/mL. 17-hydroxyprogesterone(17-OHP)-1.45µg/L,thyroid-stimulating hormone - 1.31 mIU/mL as well as serum electrolyte levels were normal. Complete haemogram, liver and renal function tests were in the normal range. Magnetic resonance imaging of the abdomen showed a left suprarenal lesion measuring 3.5 cm × 3 cm × 3.5 cm displacing the left kidney (adrenal adenoma). Contrast-enhanced computed tomography (CECT) of the chest was done to rule out metastasis and that too was normal. The patient had a left adrenalectomy through a left subcostal incision. The pedicle was clamped and the tumour was resected. The specimen was sent for histopathological examination, which showed abundant clear cells with finely vacuolated cytoplasm and having well-defined cell borders. There was no vascular or capsular invasion by tumour cells. The findings were suggestive of adrenal adenoma. The patient was discharged in stable condition after surgery, kept on follow-up for 1 year and 3 months and became totally asymptomatic.

Case 2

A 5-year-old girl presented with a history of excessive hair growth all over the body and acne over her face, which are gradually increasing over 2 years. On examination, thick and dark coarse hairs were present all over the body, including the face of the child. [Figure 1] Parents complain that the child is very shy and does not socialise. On general physical examination, there was buffalo hump, clitoromegaly, pubic hair and hypertension in the child, but there was no breast development. On abdominal examination, there was abdominal distention with purple striae and a mass was palpable in the right lumbar extending up to the umbilicus. It was firm, too hard in consistency and was immobile. Investigations revealed increased morning 8 am serum cortisol (>1700 mmol/L), testosterone (>75 mmol/L), DHEAS (>1500 µg/dL) and 17-OHP (12.8 ng/mL), and ACTH was very low (<5 pg/mL). Routine biochemical investigations were within normal limits.

CECT of the abdomen showed well-defined smooth marginated solid soft-tissue density mass lesion measuring 12.6 cm × 9.4 cm × 9.5 cm noted involving the right supra renal gland. There is no evidence of calcification/necrosis or haemorrhage and no significant compression of the inferior vena cava (IVC) was noticed. The patient was started on hydrocortisone before the surgery and surgery was planned. Intraoperatively, tumour measuring about 14 cm × 10 cm × 9 cm was present in the right lumbar and right hypochondrium going up to the diaphragm and pushing liver anteroinferiorly also pushing IVC but not infiltrating it [Figure 2]. Para-aortic, peripancreatic and periportal lymph nodes were not enlarged. On the cut section, the tumour has having soft gelatinous consistency. Histopathology of the specimen showed that the specimen is of adrenocortical adenoma. The patient was discharged in stable condition and on follow-up, her virilisation, as well as cushingoid features, disappeared over 7 months after surgery [Figure 3].

Case 3

A 7-year-old female child presented with excessive weight gain for around 4 months. On examination, cushingoid features in the form of abdominal striae, buffalo hump and acanthosis nigricans were present, the patient had hypertension (BP – 142/98 mmHg) and mild hair growth on the face and pubic region, which was not noticed by parents. However, there was no mass palpable on abdominal examination and there was no clitoromegaly. Blood investigations showed raised serum cortisol levels after the dexamethasone suppression test, raised testosterone levels, normal 17-OHP and very low ACTH levels. CECT abdomen showed well-defined round soft-tissue lesion measuring 31 mm × 31 mm seen in the left suprarenal gland [Figure 4]. Surgery was carried out through the left subcostal incision and the left adrenal was removed. The patient was discharged in



Figure 1: Female child having virilising features



Figure 2: Big adrenocortical tumour measuring 14 cm × 10 cm × 9 cm



Figure 3: Same female child after 8 months of surgery

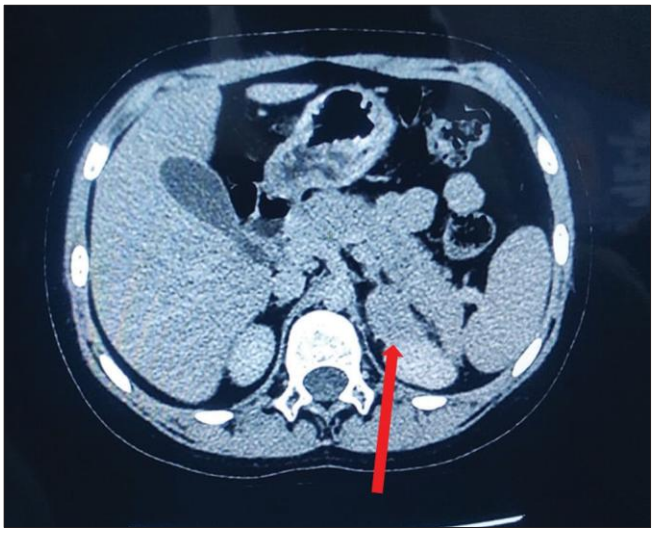


Figure 4: Contrast - enhanced computed tomography of the abdomen showing left adrenal mass (red arrow)

stable condition after a few days. Histopathology showed that the left adrenal mass measured 4 cm × 3 cm × 1.5 cm. The cut surface shows homogeneous grey-white areas, histology was suggestive of adrenal adenoma and on immunohistochemistry, cells are positive for synaptophysin, inhibin, melan A and calretinin.

Discussion

ACTs are extremely rare tumours in childhood that may be functional or non-functional. Most are benign; however, even benign can have varied presentation – either virilising forms or presentation with Cushing's syndrome, or both. It occurs more frequently in girls, predominantly unilateral, on the left side, with a peak incidence in the first decade of life.[4,5] Similarly, in our series, all of them were females, all were in first decade of life and the tumour was on the left side in two of them. Previous literature has shown that lesser number (About 50%) of adult patients and more (90%) of paediatric patients with ACTs show hormonal dysfunction.[4] Both benign and malignant ACTs can be hormonally active.[5,6] However, adrenocortical carcinomas are rarely seen than adenomas and their 5-year survival rate is 49%–55%.[4,7] Hormonal dysfunction was present in all of our patients and presented in the form of both virilising and cushingoid features.

According to the Brazil registry, the median interval between the first presenting feature of ACTs and the diagnosis was 5 months (range, a few days to 8 years).[4] However in our case series, interval between first appearance of symptoms and diagnosis was 6 months in two patients and in one patient it was 2 years. The diagnosis of ACTs is usually delayed.[8] Because of small tumours and an extensive endocrine, workup may be required before the tumour is diagnosed. Second, these children were well except for their endocrine manifestations, and in fact, many experiences accelerated growth and development. The delay in diagnosis in our cases was probably because the children were not complaining about anything and hair growth was taken as physiological/hereditary in earlier days of illness. In addition, it can be argued that retrospective parental assessment is sometimes not reliable, but in some cases, features were confirmed by photographs of the patients showing signs of overproduction of adrenal cortical hormones several years before diagnosis.

Hypertension was observed in a number of patients in earlier studies which is due to excessive production of either glucocorticoids and/or mineralocorticoids.[4,5] It has been seen in previous studies that 27% of patients with virilising or non-functional tumours also had hypertension. Tumour compression of the renal artery or increased production of aldosterone may have contributed to hypertension in these patients. Whatever the mechanism, it was seen that hypertension resolved after full tumour resection.[4] In concordance with the previously reported observations,[4,5] all three of our patients had hypertension despite having predominantly virilising features.

The prognosis of ACT was directly associated with tumour size as there is a high risk of relapse even after complete tumour resection if tumour size is big.[4,9] It seems that there is an initial phase of slow tumour progression characterised mainly by endocrine manifestations in the absence of a palpable mass, and subsequent faster tumour progression. The types of acquired genetic abnormalities which are likely to determine the tumour's proliferative potential are still unknown. Similarly, in our two patients clinical manifestations were present despite no mass was palpable on per abdomen examination.

Although virilisation by ACTs is a common phenomenon in children but lesser than in adults. In children, it has a less aggressive clinical course and responds better to surgery and other therapeutic modalities as compared to adults.[10-12] Similarly, there are chances of a good prognosis if virilisation is the sole clinical manifestation. Patients with Cushing's syndrome as either the sole clinical manifestation or combined

with other endocrine clinical syndromes (mixed), as well as those with non-functional tumours, had worse prognosis.[4] All three of our patients have both virilising as well as cushingoid features and they had a good prognosis in the form of complete disappearance of all these symptoms in an average follow-up period of 1 year after surgery. It is seen in previous literature that a small tumour carries a good prognosis if it is completely resected, whereas patients with residual disease, whether microscopic or gross, carries a poor prognosis. However, in our study, even a big-sized tumour had a good outcome till now, probably due to its complete resection. Pre-operative optimisation with hydrocortisone, prolonged surgery time to ensure complete resection and intensive post-operative care were the challenges faced during the management of these patients.

Conclusion

We have presented three cases of ACTs causing both virilising and cushingoid features in paediatric patients. Complete resection of these tumours leads to a better prognosis in these patients. A careful clinical and radiological examination, along with extensive pathological workup, is essential in making an accurate diagnosis. Early diagnosis can help in planning appropriate treatment in the form of surgery, leading to a favourable outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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