Virilizing Adrenal Adenoma causing precocious puberty in a girl- a rare presentation

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ABSTRACT

Precocious puberty is a common complaint in paediatric medicine these days with numerous causative factors. The differential diagnosis is broad with androgen producing adrenal adenoma being one of them though very rare cause.We report a case of heterosexual precocious puberty presenting with early adrenergic features and finally diagnosed to have unilateral adrenal adenoma as the cause, a rare condition not commonly reported in the literature. The patient was transferred to our paediatric surgery department and was operated with left adrenalectomy. Histopathological examination of the excised mass revealed adrenocortical oncocytoma.

Conclusion: Precocious puberty has wide differential diagnoses and work up. Cases presenting with virilizing signs should alert clinician for probable cause of androgen producing adrenal tumour, a rare condition not commonly reported in paediatric age group in literature. Early identification and intervention may halt the accelerated maturation with maintaining subsequent physiological growth potential.

Keywords: Adrenal adenoma, androgen, Precocious puberty, Virilization

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INTRODUCTION

Adrenocortical tumors are rare in childhood, with an incidence of 0.3-0.5 cases per million child years[1]. They occur in all age groups but most commonly in children younger than 6 years and are more frequent (1.6 fold) in girls. The presentation of an adrenal adenoma can vary, with

isolated androgen production causing precocious puberty being an uncommon presentation. We report a case of heterosexual precocious puberty due to androgen producing adrenal adenoma (oncocytoma) of which only 3 cases have been reported in literature till date.

Case presentation: A 40 months old female child presented with features of precocious puberty with early adrenergic features. Patient was thoroughly evaluated with history, physical examination with special reference to genitalia, relevant investigations and diagnosed to have unilateral adrenal adenoma as a source of androgen production and was transferred for surgical treatment and histopathological evaluation. No conflict of interest

CASE REPORT:

A 40 months old female child presented with progressive enlargement of genitalia, increased body hair and sexual hair and deepening of voice for 1.5 years. She was a product of non consanguineous marriage, delivered through normal vaginal route without any h/o antenatal maternal drug intake or radiation exposure, with uncomplicated postnatal period. There was no h/o fever, radiation exposure or exposure to drugs and herbal products, vision problem, headache, head trauma, skin pigmentation, cold intolerance, abdominal pain or mass, vaginal bleeding. She had increased appetite and oily skin with acne over forehead. Bladder and bowel habit were normal.

On examination she had muscular built with stable vital parameters (temp-37^0c,HR-74/min, RR-22/min, BP-100/70 mm Hg). Anthropometry revealed accelerated growth with increased body wt (actual-19.8 kg, expected-14.6 kg, >2SD 19.2); height-101 cm (expected-97.7 cm); US: LS-1.06 (expected-1.3); arm span-101.5 cm; MAC-18 cm; HC-50 cm (expected-48.8 cm); increased BMI-19.31(expected-15.3,>2SD-18.4).

She had coarse facies with acne, male pattern (temporal recession) of hair line (Figure 1), increased body hair,facial-axillary-pubic hair, oily skin with normal eyes and 20 temporary teeth.

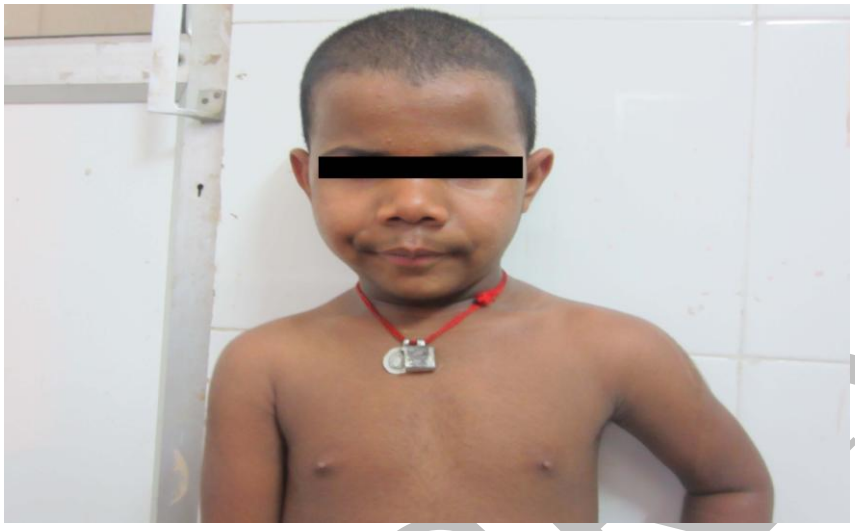

Figure 1: Clinical profile, coarse facies with temporal recession

Genitalia showed normal vaginal and urethral opening with pale vaginal mucosa, enlarged labia majora and minora, clitoromegaly (length 4 cm) and male pattern distribution of pubic hair (Figure 2). SMR staging showed pubic hair stage PH_3 and breast $B_{3.}$ Abdominal examination revealed no mass or organomegaly and CNS examination was found to be normal.

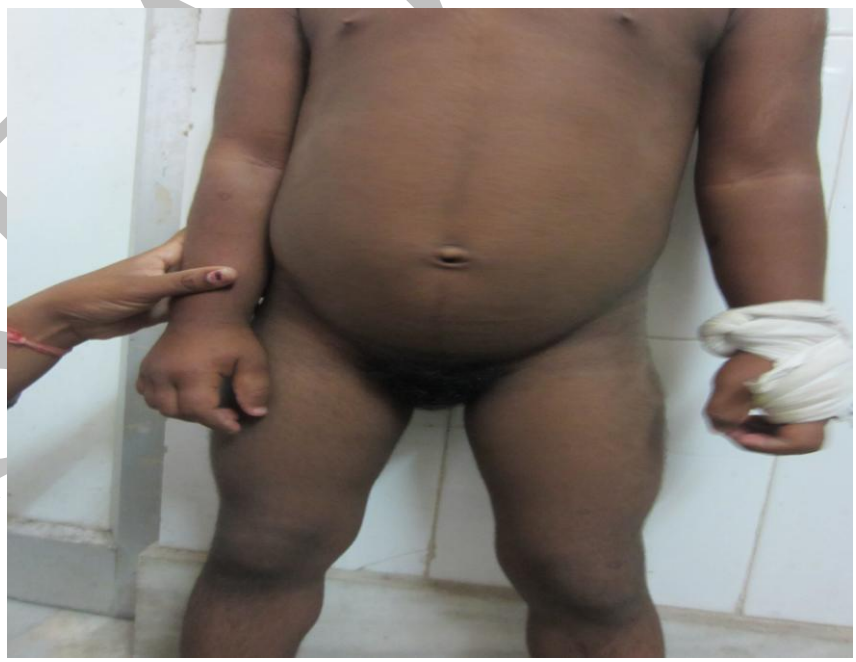

Figure 2: Genital showing PH3 pubic hair

LABORATORY INVESTIGATIONS

Initial investigations showed CBC-(Hb-11.6 gm% RBC-6.25 million/mm^3, WBC-12380 /mm^3; $N_{39}L_{51}E_{09}M_{01}B_{00}$, platelet-6.22 lakhs/$mm^3$), urine RE 1+ protein, c/s- no growth, RBS-69 mg/dl, electrolytes normal(Na^+-140 mmol/L, K^+-4.8 mmol/L, Ca^{++}-1.06 mmol/L). Blood urea, serum creatinine and lipid profile were also found to be within normal range (Ur-18 mg/dl, Cr-0.5mg/dl, cholesterol -110mg/dl, TG-85 mg/dl, HDL-30mg/dl). Hormonal assay revealed normal thyroid profile (TSH-1.2477 micro IU/ml, fT_3-3.31 pg/ml, fT_4-086ng/dl). FSH was markedly decreased(less than 0.05 mIU/ml) and LH_2 was absent (LH_2-0.00 mIU/ml). Morning cortisol-8.87micro gm/dl (normal), 17 alpha hydroxyl progesterone 2.10 ng/dl with marked elevation of testosterone (> 3000.00ng/dl) and DHEA-S(402.1 micro gm/dl).

X-ray left wrist identified 8 carpal bones suggestive of bone age at least 11 year (Figure 3).

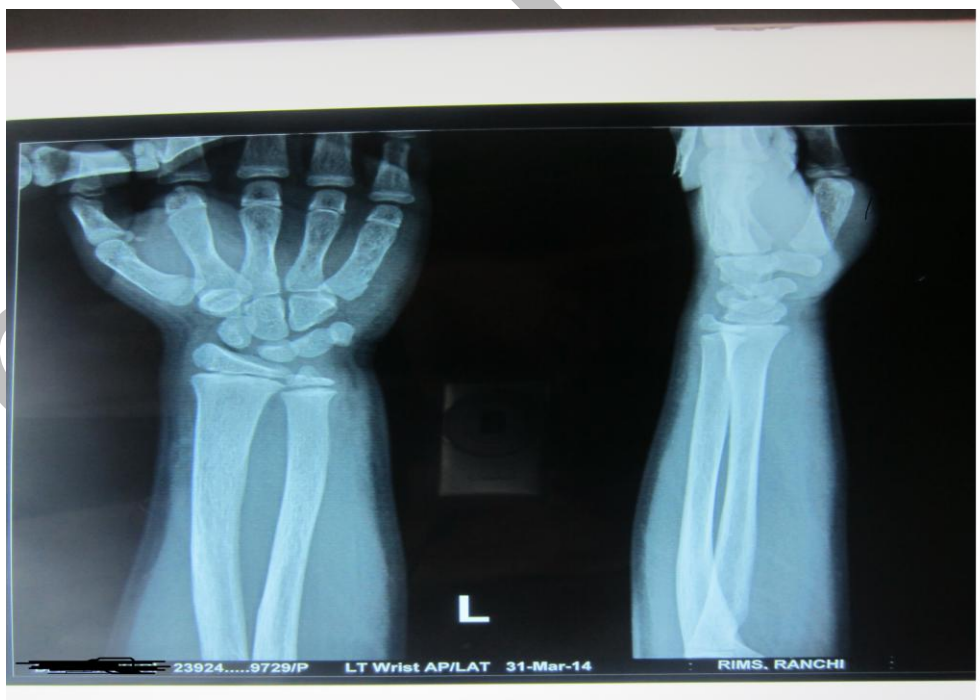

Figure 3: X-ray left wrist showing 8 carpal bones

USG abdomen and pelvis showed a localised cystic lesion with calcified foci within it of size 4.4x3.5 cm adjacent to but separate from the upper pole of left kidney with normal appearing uterus without visualisation of ovaries. MRI abdomen and pelvis identified a well defined T2 hyperintense lesion of approximately 42 x 41 x 38 mm size with regular margins arising from left adrenal gland with internal flow voids. No evidence of internal calcification or necrosis or involvement of adjacent renal parenchyma was noted. Also there was no significant paraaortic lymphadenopathy. Paediatric uterus was seen without any evidence of mass lesion.No significant follicles was seen in either ovary (Figure 4).

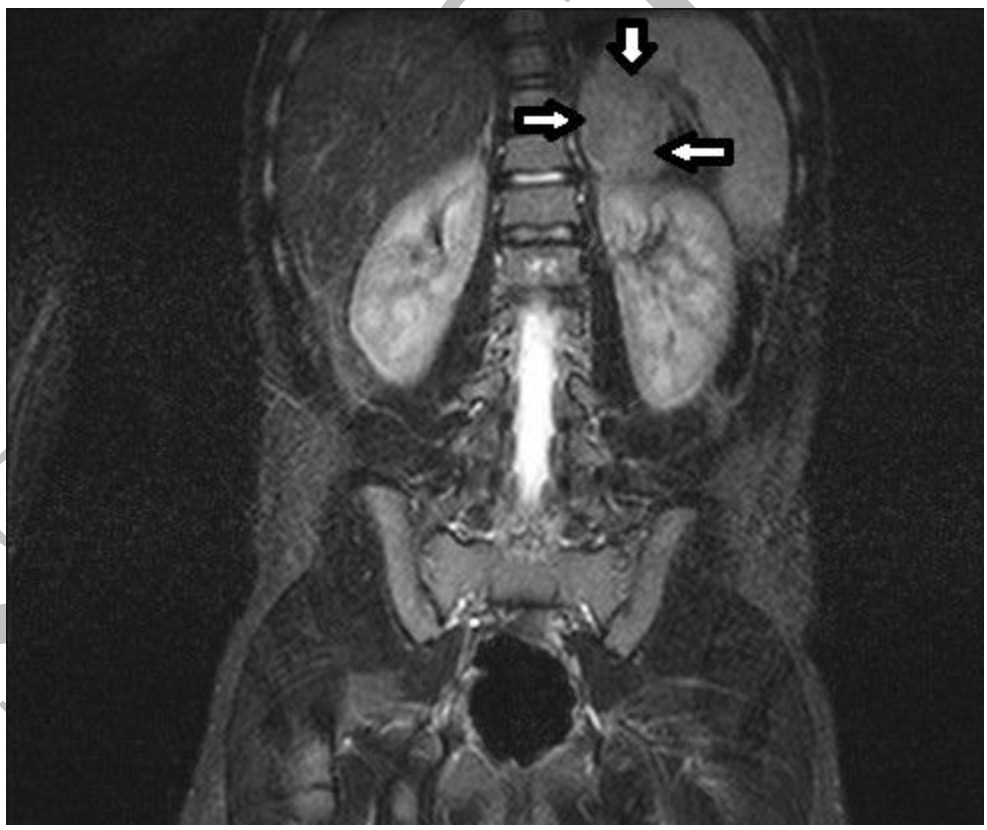

Figure 4: MRI abdomen showing left adrenal adenoma

Patient was transferred to pediatric surgery department and operated with left adrenalectomy. Histopathology showed back to back arrangement of cells in trabecular, sheets

and nests arrangement separated by fibrous septa and blood vessels. The cells were uniform granular with finely granular eosinophilic cytoplasm and hyperchromatic neuclei (Figure 5).

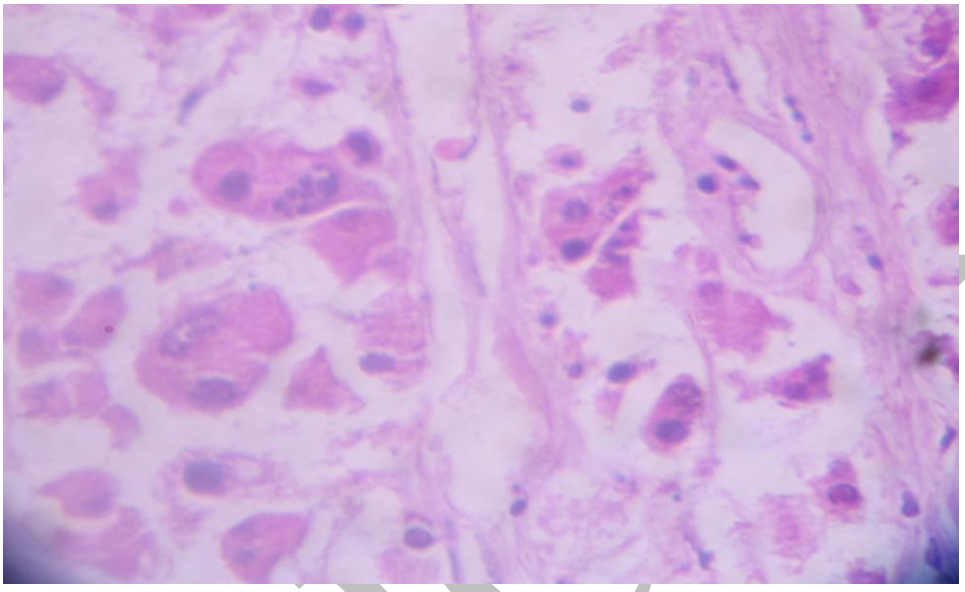

Figure 5: Histopathology of the operated mass showing polygonal cells with eosinophilic cytoplasm and hyperchromatic nuclei.

No mitotic figures or vascular invasion seen (Figure 6). All features was suggestive of Oncocytic Adrenocortical Adenoma (oncocytoma).

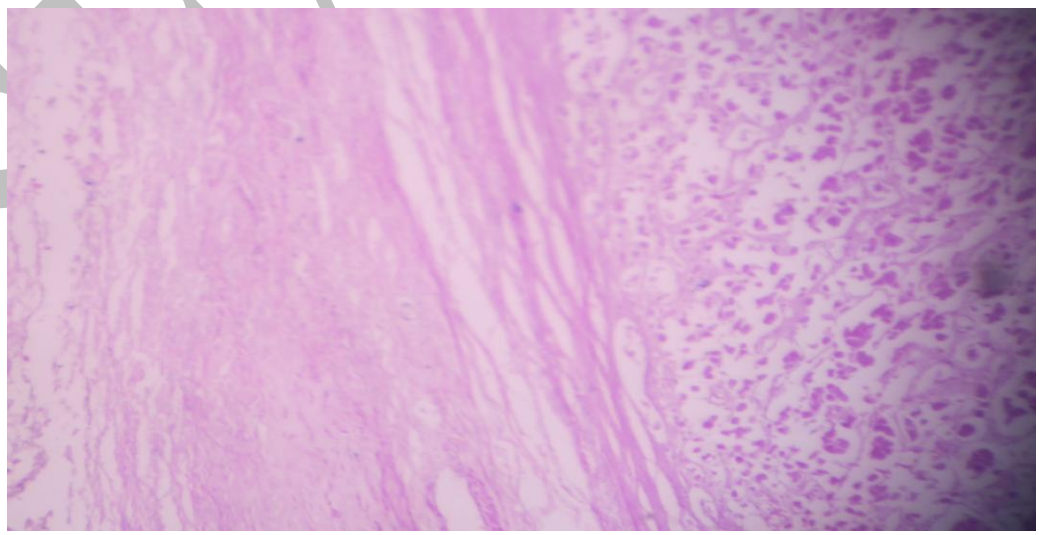

Figure 6= Histopathology showing no vascular or capsular invasion by tumor cells

DISCUSSION

In our index case masculinising features of previously normal female child with clitoral enlargement, growth acceleration, acne, deepening of voice, premature pubic and axillary hair development with advanced bone age, isolated high testosterone, DHEA-S, decreased LH, FSH, and radiological impression of adrenal adenoma(left) which was confirmed on tissue biopsy as adrenocortical oncocytoma with normal appearing uterus prove it as a case of heterosexual peripheral precocious puberty due to androgen producing adrenal tumour.

Precocious puberty has broad differential diagnosis and work up that should be completed. Clues to the paediatrician to a virilising tumour include masculinising signs of precocious puberty, abnormal hormonal levels and imaging suggestive of adrenal adenoma. Overall adrenocortical tumours are rare in childhood with an incidence of 0.3- 0.5 cases per million child years.[1,2] They occur in all age groups but most commonly in children younger than 6 years of age and are more frequent (1.6 fold) in girls. 2-10% of cases the tumours are bilateral[1].

The hormone secreting adrenal adenoma causes Cushing syndrome, primary aldosteronism, or much less commonly virilisation or estrogen secretion[3]. Functional tumour secrete steroid independently from the ACTH or rennin angiotensin system. In one study from a series of 1004 adrenal incidentaloma found that 85% were non functional, 15% were functional.

In the functional group 9.2% causes Cushing syndrome , 4.2% were pheocromocytoma and 1.6% were aldosteronoma[3]. So far in paediatric age group only 3 cases of functional adrenocortical oncocytoma causing precocious with similar presentation have been reported[3,4].

CONCLUSION:

Precocious puberty has wide differential diagnoses and work up. Cases presenting with virilising signs should alert clinician for probable cause of androgen

producing adrenal tumour, a rare condition not commonly reported in paediatric age group in literature.

List of abbreviations:

h/o- history of
temp- temperature
HR- heart rate
RR- respiratory rate
BP- blood pressure
Wt- weight
SD- standard deviation
Kg- kilogram
Cm- centimetre
US- upper segment
LS- lower segment
MAC- mid arm circumference
HC- head circumference
BMI- body mass index
SMR- sexual maturity rating
CNS- central nervous system
ICT- intra cranial tension
CBC- complete blood count
WBC- white blood corpuscle
RBC- red blood corpuscle
Hb- haemoglobin
RE- routine examination
C/S- culture sensitivity
RBS- random blood sugar
Na^+- sodium
K^+- potassium
Ca^{++}- calcium
Ur- urea
Cr- creatinine
TG- triglyceride
HDL- high density lipoprotein
TSH- thyroid stimulating hormone
fT_3- free tri-iodothyronine
fT_4- free thyroxine
pg- pictogram
ng-nanogram
ml- millilitre
dl- decilitre
FSH- follicle stimulating hormone
LH- luteinising hormone
DHEA-S- dihydrepiandrosterone sulphate
ACTH- adrenocorticotrophic hormone

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