

# An extremely rare cause of Cushing Syndrome in Childhood



Dr Amith Ramcharan<sup>1,2</sup> FCP (Paeds) Cert Paed Endo; Dr Yasmeen Ganie<sup>3</sup> FCP (Paeds) Cert Paed Endo

1. The Paediatric and Adolescent Diabetic and Endocrine Unit, Red Cross War Memorial Children's Hospital and Groote Schuur Hospital, Cape Town, South Africa
2. Department of Paediatrics and Child Health, Faculty of Health Sciences, University of Cape Town, South Africa
3. Division of Paediatric Endocrinology, Inkosi Albert Luthuli Central Hospital, Durban, South Africa

## Case Vignette

- 3 year 4 month old female patient A.T.M
- Referred from Stanger Regional Hospital
- Initially presented to base hospital with history of:
  - Body swelling for 1 month
  - Diarrhoea for 1 week
- Clinical examination at referral hospital revealed the following:
  - A body mass index that classified as overweight
  - Hirsutism
  - Hypertension
  - Phenotypic features suggestive of Cushing Syndrome

Investigations at Stanger Regional Hospital		
Investigation	Result	Reference Range
Midnight Cortisol (nmol/L)	671	28-662
Midnight Cortisol-Sedated (nmol/L)	645	28-662
24hr urine cortisol (nmol/L)	6280	85-807
Abdominal Ultrasound	Normal kidneys and adrenals. No masses identified.	

## Clinical Examination

### Anthropometry:

- Weight: 16.7 kg (between 0 and -2SD)
- Height: 94 cm (between 0 and -2SD)
- BMI: 19.0 (between 2 and 3) = Overweight

### Vitals:

- BP 159/118mmHg
- Pulse 139 bpm

## General Examination

- No dysmorphic features
- Oedema - knees
- Cushingoid facies, facial plethora, facial hirsutism
- Acanthosis nigricans nape of neck
- Dorsal cervical fat pad present
- Pseudo-gynaecomastia
- Central adiposity
- No striae or bruising or acne
- Tanner: P1 A1 B1
- No thyroid masses palpable
- No evidence of latent hypocalcaemia

## Systemic Examination

### Abdomen

- Abdominal distension with no visible veins.
- Hepatomegaly of 2cm below the costal margin.
- No renal or other abdominal masses palpable.

## Assessment

- Phenotypic Cushing Syndrome
- Hypertension
- Hirsutism

### Diff Diagnosis:

- Adrenal carcinoma
- Cushing Disease
- Ectopic Cushing:
  - Adrenal Carcinoma
  - Cushing Disease
  - Ectopic Cushing

## Laboratory

Investigation	IALCH	Normal Range
FSH (IU/L)	1,2	
LH (IU/L)	<0,1	
Testosterone (nmol/L)	1,6	0.1-0.3
17OHP (nmol/L)	5,1	0,5-3,1
DHEAS (umol/L)	3,5	0,1-0,6
Androstenedione (nmol/L)	12,2	0,2-1,4
Aldosterone (pmol/l)	29,3	33-943
Renin (mIU/l)	23,4	
Urine Catecholamines	Negative	
Thyroid Function Tests	Normal	
<b>Tumour Markers:</b>		
Alpha Feta Protein (ug/L)	745	0,6-11,1
Beta HCG(IU/L)	<2	0-9
CEA(ug/L)	<0,5	0,0-5,0
CA 125(kU/L)	223	0-35
CA 19-9(kU/L)	71	0-31

## Screening Tests for Cushing Syndrome

Investigation	IALCH	Normal Range
Midnight Cortisol (nmol/L)	1329	28-662
Midnight ACTH (pmol/L)	"51.7"	1.1-10.2
Morning cortisol (nmol/L)	1133	28-911
Morning ACTH (pmol/L)	"45.1"	1.1-10.2
24hr UFC (nmol/L)	Specimen 1: 1344 Specimen 2: 1929	28-807

Overnight Dexamethasone Suppression Test 9am Cortisol = 907 nmol/L FAILED SUPPRESSION

## Imaging

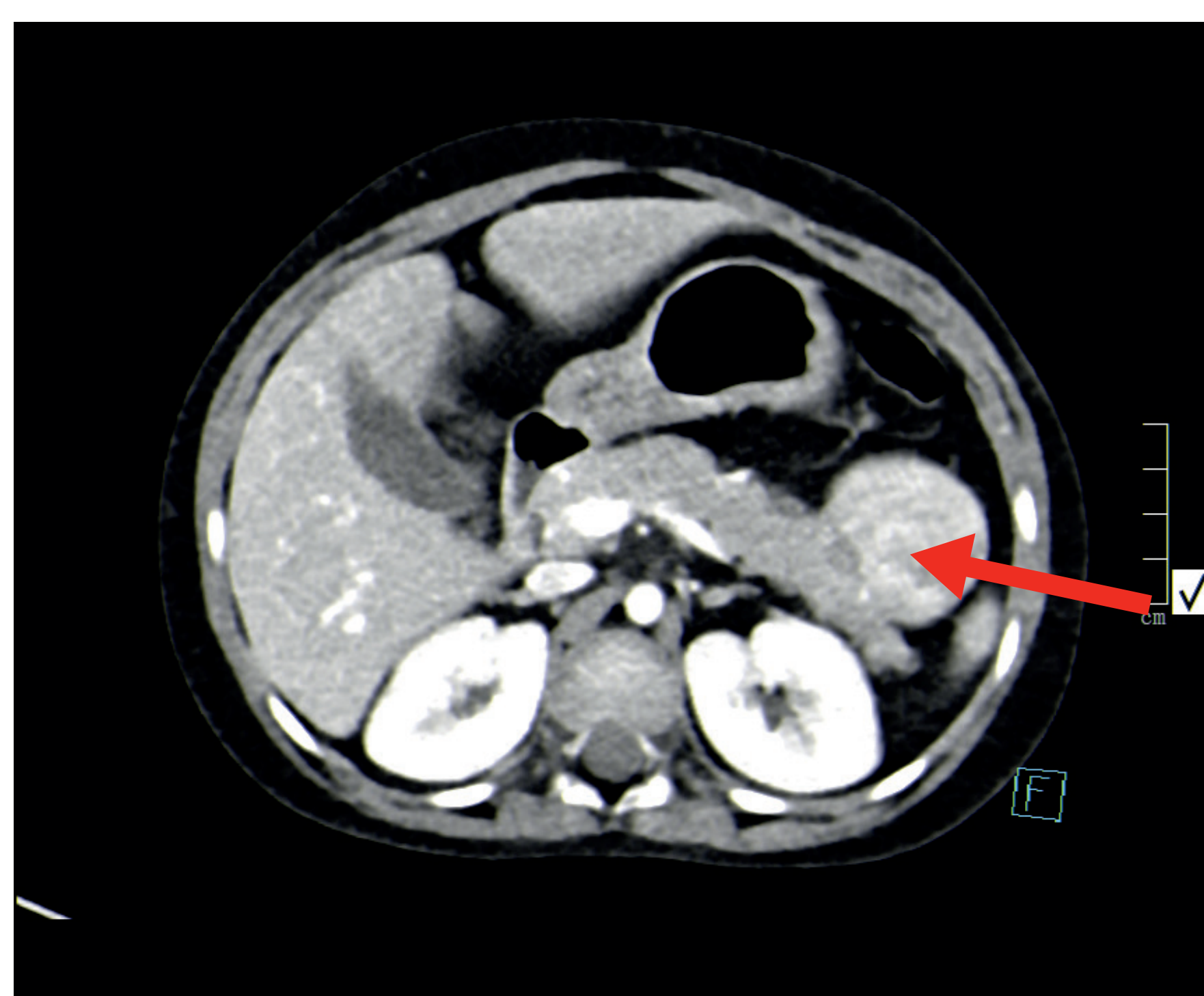
### Abdominal Ultrasound

Solid, heterogeneous, well defined, 3.3 x 3.7cm mass noted in the Left peri-renal space at the level of the mid pole of the left kidney.

### Conclusion:

Left peri-renal solid highly vascular mass noted. Highly suggestive of an adrenal mass however position and morphology is not typical of adrenal mass.

## CT Abdomen Chest



There is heterogeneously enhancing well circumscribed exophytic mass lesion with foci of intra-lesional necrosis noted in relation to the tail of the pancreas. The mass measures 4.6 x 3.9 x 4.5 cm.

### Excision Biopsy

#### Distal Pancreas:

Features are those of a solid pancreatic tumour with diffuse epithelial marker immunopositivity, patchy neuroendocrine immunopositivity, diffuse ACTH immunopositivity and focal Alpha-Fetoprotein immunopositivity.

The histomorphological features and patchy neuroendocrine immunopositivity favour a pancreatoblastoma.

Lymphovascular invasion is not identified.

## Final Assessment

Ectopic ACTH Dependent Cushing Syndrome secondary to AFP producing Pancreatoblastoma

## Management and Progress

- Prior to surgery blood pressures were stabilized
- There was complete laparoscopic removal of the tumour (50g) (45 x 15 x 40mm)
- Hydrocortisone was commenced immediately post surgery
- Chemotherapy deferred:
  1. Low trend AFP and low mitotic count on histology
  2. Complete excision of tumour
- Discharged home on oral hydrocortisone

## Post-Operative Investigations

Investigation	IALCH	Normal Range
Morning cortisol(nmol/L)	58	28-911
Alpha Feto Protein(ug/L)	6.0	0.6-11.1
DHEAS (umol/L)	<0.4	0.1-0.6
Testosterone (nmol/L)	0.5	0.1-0.3
Androstenedione (nmol/L)	<1.1	0.2-1.4

## Cushing Syndrome in Children

- Rare in childhood
- Female predominance
- Classical clinical features include:
  - Weight gain
  - Growth failure
  - Hypertension
  - Compulsive overachieving behavior
- Causes include:
  - Exogenous administration of glucocorticoids and ACTH
  - Pituitary adenomas
  - Adrenal Tumours
  - Ectopic ACTH production

## Ectopic ACTH producing Tumours

- Rare in children
- Accounts for less than 1% of Cushing Syndrome in adolescents
- Tumours that secrete ACTH include small cell carcinoma of the lung, carcinoid tumours of the bronchus, thymus and pancreas, pheochromocytomas and neuroendocrine tumours particularly that of the gut and pancreas.

## Pancreatoblastoma

- Pancreatic neuroendocrine tumour known to produce ACTH
- Very rare malignant, slow growing tumour
- One third present with metastases at presentation
- An incidental abdominal mass is the most common form of presentation
- The head and tail of the pancreas is the most common site while the liver is the most frequent site of metastatic disease
- Complete surgical resection of the tumour is the treatment of choice
- Chemotherapy maybe beneficial prior to surgery to reduce tumour size
- Even though these tumours are curable, long-term surveillance for recurrence is mandatory

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