CORTICOTROPIN-INDEPENDENT CUSHING SYNDROME IN A 2-YEAR-OLD GIRL: DIAGNOSIS AND TREATMENT ARE NOT A STRAIGTHFORWARD ROAD

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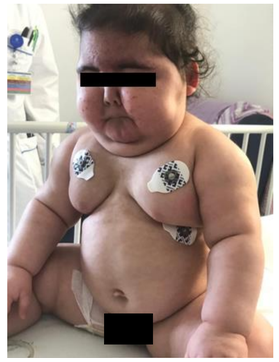
INTRODUCTION

- Endogenous Cushing Syndrome (CS) in the paediatric age group is a rare disease, and corticotropin-independent forms are even less frequent.
- In childhood, it carries a significant burden, not only because of the prolonged hypercortisolism long-term effects, but also for the treatment-associated morbidity.

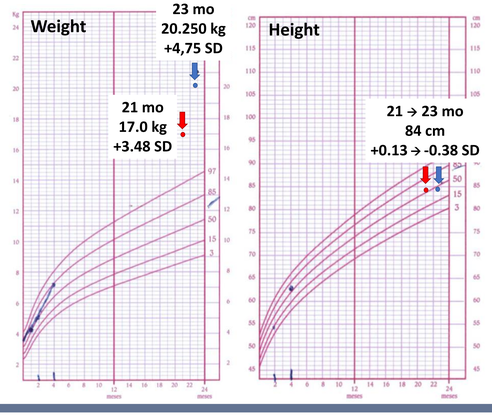
CASE REPORT

- 23 month-old girl
- Irritability, depressed mood
- Rapid weight gain + gross motor skills and language regression in the previous 4 months

- BP 164/114 mmHg (>> 99th centile)
- Morbid central obesity: BMI-SD +7.36
  Waist to height ratio: 73%
- Hypertrichosis
- "Full moon" and facial acne
- Cervical *acanthosis nigricans and b*uffalo hump



Photos were taken after parental consent.



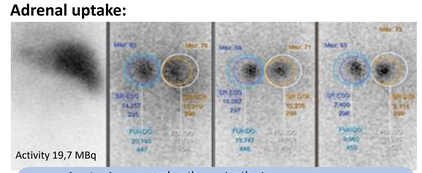
Cortisol (µg/dL)	32.5 ↑	HOMA-IR	5.7 ↑	Total cholesterol (mg/dL)	223 ↑
ACTH (pg/mL)	<5.00 ↓	Fasting glycose (mg/dL)	89	LDL cholesterol (mg/dL)	154 ↑
24h urine cortisol (NR: 28.5-213.7 µg)	462.6 ↑	HbA1c (%)	4.8	Triglycerides (mg/dL)	160 ↑
				Vitamine D25 (ng/mL)	6.9 ↓

Loss of cortisol circadian rhythm
0a.m.: 35.9 µg/dL | 5a.m.: 42 µg/dL | 8a.m.: 32.5 µg/dL
Negative dexamethasone supression test (0.3 mg/m^2): cortisol 33.1 µg/dL
Normal urinary metanephrins

Adrenal MRI: normal adrenal glands
Head CT-scan and MRI: normal hypothalamus-pituitary axis;
leukoencephalopathy and diffuse cortical-subcortical atrophy
Skeleton X-ray: generalized osteopenia

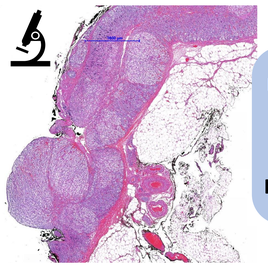
Chest-abdomen-pelvis scintigraphy
^{131}I-NP-59
(1,6-beta-iodomethyl-19-norcholesterol)

Adrenal activity supression: Metyrapone 15mg/kg, q6h, 1 wk
Thyroid uptake blockage: Lugol solution 32.5mg/day
Adrenal uptake:



Uptake index at 3rd, 5th and 7th day:
- Right adrenal gland - **0.55% » 0.71% » 0.69%**
- Left adrenal gland - **0.53% » 0.67% » 0.63%**
(NV: 0.33% of the given dose)

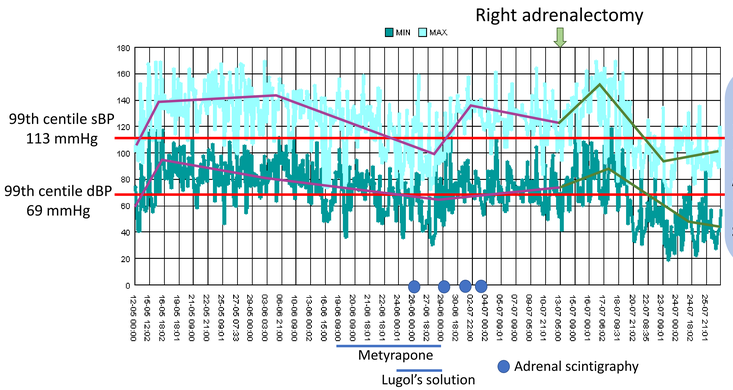
Right adrenalectomy



Homogeneous adrenal gland:
- 3.6 x 2.5 x 0.5cm (normal)
- six nodular lesions (0.5-1.2 cm)

Benign Nodular Hyperplasia

Mendeliome**: Variants of Undetermined Significance**
Waiting for parents' genetic study



Anti-hypertensive therapy
Propanolol (max 1 mg/Kg/day)
Enalapril (max 0,63 mg/Kg/day bid)
Amlodipine (max 0,2 mg/Kg/day bid)
Furosemide (max 1,5 mg/Kg/day 4 id)
Spironolactone (max 1 mg/Kg/day bid)

Follow-up	HOSPITAL		HOME		
	Admission	Discharge	2 weeks	2.5 months	7.5 months
Cortisol (µg/dL)	32.5	**7.90**	**15.60**	**16.50**	**19.40**
ACTH (pg/mL)	<5.00	**6.00**	**53.40**	**<5.00**	**<5.00**
HOMA-IR	5.7	**1.6**	0.5	1.3	2
Total cholesterol (mg/dL)	223	141	**181**	**179**	**239**
LDL cholesterol (mg/dL)	154	72	**102**	**123**	**175**
Triglycerides (mg/dL)	160	132	121	93	86
Aldosterone (ng/dL)	4.1	2.9	17.7	4.5	5.8
Active renin (µIU/mL)	8.3	-	-	97	**329.1**

CONCLUSIONS

- Some forms of adrenal cortisol hyperproduction may not be readily apparent on routinely used imaging techniques, posing additional difficulties in the diagnosis in pediatric patients.
- Scintigraphic studies are a safe and effective diagnostic option even in young children.
- Unfortunately, despite the attempt, unilateral adrenalectomy did not solve bilateral micronodular adrenal hyperplasia. The remotion of the other gland, and posterior replacing hormonal therapy will be inevitable.

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