

8-year-old male with
premature adrenarche

Endorama

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[CC]

- CC: Transfer of endocrinology care for premature adrenarche and bone age advancement at 8 yr old
- Initial presentation to outside Endocrinology at 4-9/12 years

[HPI]

- H/o Opsoclonus-myoclonus syndrome
 - Tx'd w/ ACTH therapy
- Px at 4-9/12 years old with BO and pubic hair, intensified mood swings x3mo
- Acne- attributed to ACTH tx
- Height at the 90th percentile
 - W/o accelerated growth

[PMH]

- Term BW-8 lb, 5 oz; BL-22 in
- Opsoclonus-myoclonus syndrome dx at 20 months
 - Lost motor and speech milestones, seizures
 - Negative eval for neuroblastoma
 - Tx'd w/ ACTH intermittently since 21 months
 - IVIG monthly

Family History

- Mom:
 - Menarche- 16 years
- Dad:
 - Growth spurt at 14 yrs
 - Goiter s/p lobe removed
- Healthy older sister, younger brother
- No hx of sexual precocity, autoimm dz, adrenal dz, sudden deaths,

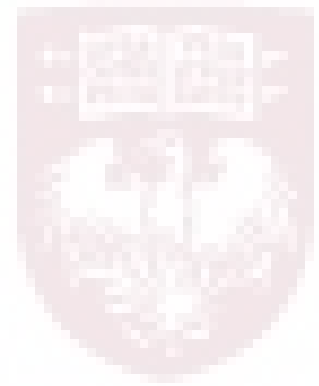
[ROS]

- Fatigue
- + Acne; No skin color changes, no salt cravings
- No PU/nocturia, No PD
- Headaches exacerbated by IVIG
- Speech delay
- Gait abnormality

[Physical examination]

- HR: NL, BP:121/76
- Cushingoid
- Skin: Two small (2.5 x 1.5 cm) hypopigmented areas on each side of his abdomen
- T2 PH; L testis 1.5 ml, R testis not palpated

[Assessment? Investigation?]



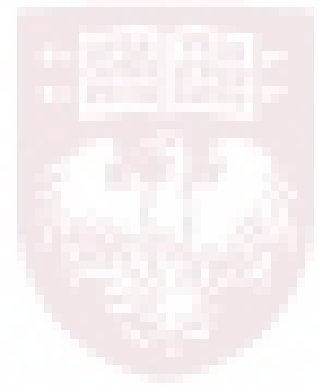
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Results

- LH: 0.1 mIU/mL
- FSH: 0.7 mIU/mL
- Testosterone: 8.7 ng/dL
- 17-OHP: 30 ng/dL
- DHEA-S: 50 mcg/dL
- AD: 44 ng/dL
- Bone age: 6.5 years at 4-9/12 years (1 yr 9 months advanced)
- Adrenal US: negative

[Thoughts?

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[Thoughts?]

- Exaggerated premature adrenarche

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Interval history- 5-3/12 yr

- Stable physical examination
- LH: 0.1 FSH: 0.6 Test: 25.5 ng/dL
- DHEA: 55 ng/dL
- BA: 7.25 yr (2 years advanced)

Interval history

- Followed q 3-6 months
 - Stable prepubertal exam
 - Prepubertal Gn, Adrenarchal DHEA-S, Testosterone ~20-30 ng/dL

[Interval history- 7/10-12 yr]

- Testicular volume ~3ml
- T3 PH



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Interval history

- BA: 11.5 years (3 yr 8 mo advanced)
- Prepubertal LH, FSH
- Testosterone: 28.4 ng/dL (<3-10)
- DHEA-S: 70 mcg/dL

Interval history

- Lupron stim test:
 - LH: $<0.07 \rightarrow 0.98$
 - FSH: $0.6 \rightarrow 6.9$
 - Testosterone: 29.4 ng/dL
- ACTH test
 - Cortisol: $6.6 \text{ mcg/dL} \rightarrow 28.5$
 - Testosterone: $16.2 \text{ ng/dL} \rightarrow 27.1$

Interval history

	Pre	Post
17-OHP	25	271
17-OH Preg	--	851
DOC	7	63
Deoxycortisol	12	55
DHEA	304	529
AD	59	117
Testosterone	20	33
Cortisol	6.6	28.5

Transfer of care- HPI, PMH

- Hx of OMS, s/p ACTH tx
- Premature adrenarche + BA advancement
- Euthyroid autoimmune thyroid dz
- Pulse decadron, q.mo IVIG
- Synthroid

Physical examination

- P-83 BP- 105/58
- 136.8 cm (>90th%) HA: 9-8/12
- 34.9 kg (90-95th%; 75th% for height)
- WD, WN; NAD
- NL thyroid exam
- NL CV, Resp, Abd
- GU: T3 PH, T1 AH, R testis-1.5, L-1.7

[Transfer of care]

- BA: 11.75 yr at 8-2/12 years
 - PH: 67.3 inches
 - MPH: 72 inches



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Interval history-

- Stable prepubertal physical exam
- Prepubertal gonadotropins, testosterone
- Advancing bone age
 - 9 yr → 12.8 yr PH:65.8
 - 10-2/12yr → 13.7 yr PH:64.3

[Interval history-

- Stable prepubertal physical exam
- Prepubertal gonadotropins, testosterone
- Advancing bone age

UC →

- 9 yr → 12.8 yr PH:65.8
- 10-2/12yr → 13.7 yr PH:64.3

[Last visit- 10-7/12 yr]

- Ht: 75-90th%
- Poor wt gain
- AGV: 4.33 cm/year

- Prepubertal

Questions

- What is the relationship between ACTH therapy and premature adrenarche?
- What is the connection between all of his diagnoses?

[OMS]

- Dancing eyes, myoclonus, ataxia
- Personality changes
- Developmental regression
- Most frequently paraneoplastic (NB)
- ? Autoimmune
- Tx: ACTH, steroids, IVIG, cyclophosphamide, rituximab

ACTH and premature adrenarche

Table 1. Steroid levels (means \pm SE) before and after acute and chronic ACTH

	Controls		PA patients							
	Basal values	Basal values	P	Acute ACTH		P*	Chronic ACTH		P*	P†
				A.V.	I.		A.V.	I.		
17-OHP ng/dl \pm SE	48.6 11.9	69.3 11.3	0.05	155.7 8.5	86.4 19.3	0.001	276.6 11.6	207.3 25	0.001	0.05
A ng/dl \pm SE	35.1 13.5	45.4 7.7	0.05	65.2 12	19.8 4.1	n.s.	189 7.5	143.6 14	0.001	0.01
S ng/dl \pm SE	52 3.6	46 7.7	n.s.	85.5 2.9	39.5 3.2	0.05	533.5 19.3	487.5 18.2	0.001	0.001
F μ g/dl \pm SE	13 1.8	14 1.7	n.s.	24.6 1.5	10.6 1.4	0.05	44.6 3.2	20.6 1.3	0.001	0.001
5P ng/dl \pm SE	50 7	74.4 7.1	0.05	141.7 5.6	67.3 17.7	0.01	214.1 7	139.7 10.4	0.01	0.01
DHA ng/dl \pm SE	77 6.3	329.2 41.7	0.001	452.7 38	123.5 46.8	n.s.	1140 50	810.8 48	0.01	0.01
DHA-S μ g/dl \pm SE	30 16	169 54	0.001	189.1 41	20.1 5	n.s.	470 37.6	301 47	0.01	0.01

17-hydroxyprogesterone (17-OHP), Androstenedione (A), 11-deoxycortisol (S), Cortisol (F), 5-Pregnenolone (5P), Dehydroepiandrosterone (DHA), Dehydroepiandrosterone sulphate (DHA-S).

A.V.: Absolute value; I.: increments.

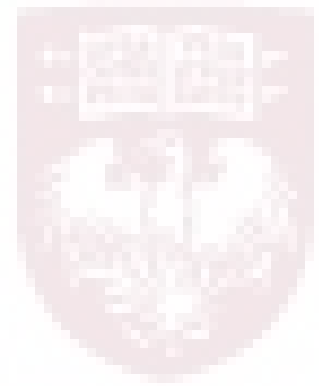
P: Statistical significance vs controls.

*P: Statistical significance vs basal values.

†P: Statistical significance vs acute ACTH test.

n.s.: not significant. SE: Standard Error; dl: 100 ml.

[OMS + PA + UC]



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[Patient]

- Monitoring puberty and growth
- Plan to assess HPG axis in 6-12 months
- Considering growth augmentation
 - OMS
 - UC

References

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