

10 yo boy w/Chiari/pseudotumor
seen for obesity

8/22/13

Jess Hwang

HPI

- Kids at school have been teasing him about his weight and the skin darkening around his neck
- 127lb was peak weight
- Quit desserts/soda and has lost 8lb in 12 months
- Exercise: Just Dance, planks, jumping jacks

HPI cont.

- No steroid since 2010 (had been on 2 month course of decadron for headaches)
- Headaches treated with excedrin, topamax
- No peripheral vision problems
- 6/2011 negative sleep study
- Used to see a therapist for his labile mood

More History

PMH

Chiari malformation
(s/p decompression)

Pseudotumor (s/p LP
shunt)

Distal ulnar fracture
2012

SHx

Negative

Meds

Topamax 75 mg BID

FHx

MGM: CAD, DM

PGM: DM

Sister: ?autoimmune
disease

ROS

Constitutional: 8lb weight loss in 12 months
but it has been very difficult losing weight

HEENT: wears glasses

CV: no chest pain

Resp: no shortness of breath

Neuro: +chronic headaches

GI: no nausea, vomiting, diarrhea

Skin: skin darkening

Physical Exam

Vitals: 110/65, 118, 135 cm (4'5"), 54 kg (119lb), BMI 29.4

Gen: no distress

HEENT: visual fields grossly normal, wears glasses

Neck: no thyromegaly, no nodules

CV: RRR

Pulm: CTA bilaterally

GI: soft, non-tender, obese abdomen, no striae

GU: prepubertal, testes 2.1 cm B, no axillary hair

Skin: acanthosis nigricans

Neuro: A+O, normal reflexes

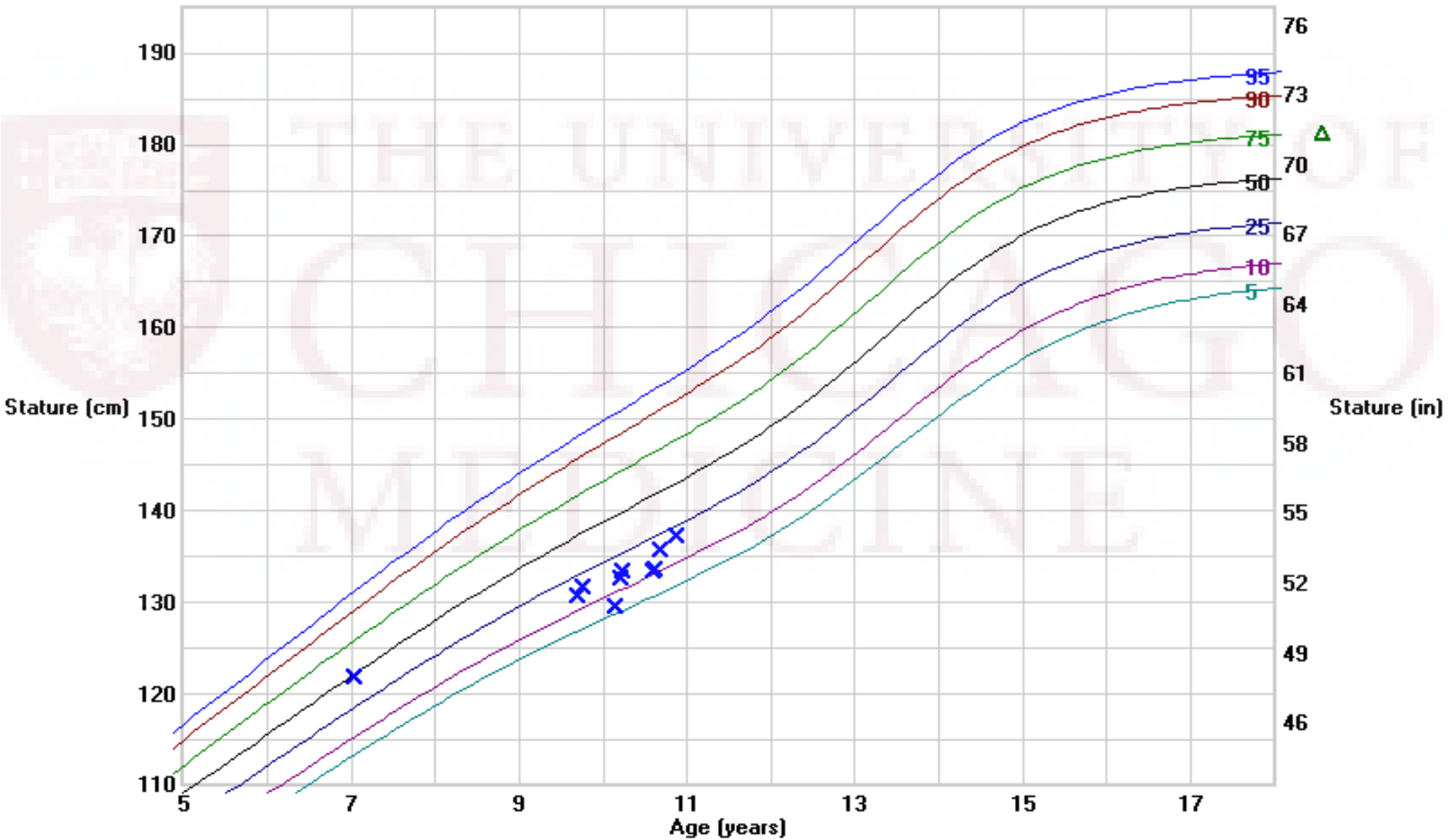
2009→2013



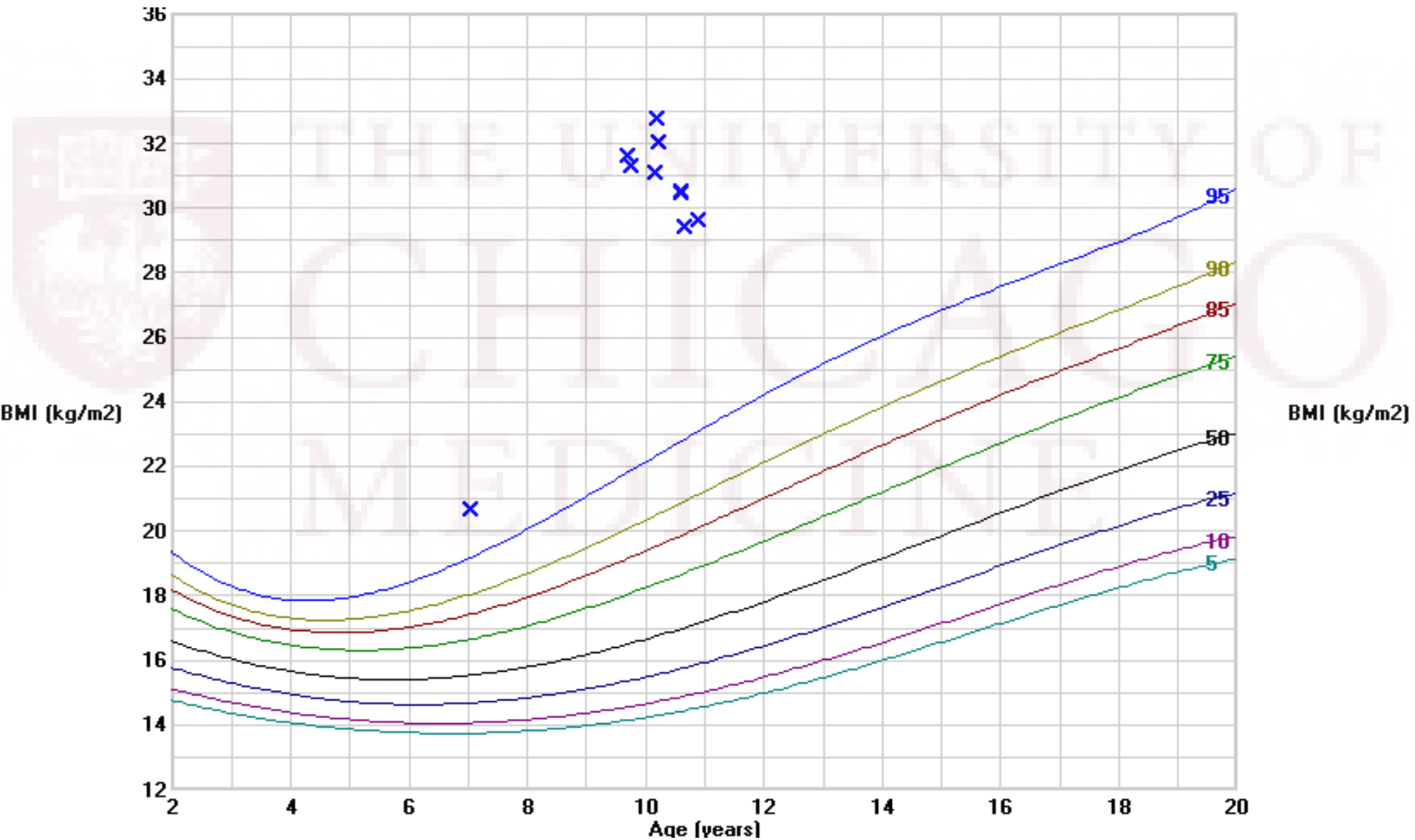




Growth chart



BMI chart



Labs

141	106	11	81
3.5	20	0.7	
			9.5

7.5	4.6	A1c 5.0%
0.2	151	HDL 39
29	56	LDL 170
		TG 69
		IGF-1 361 (88-452)
		TSH 1.64
		FT4 1.24

Work-up

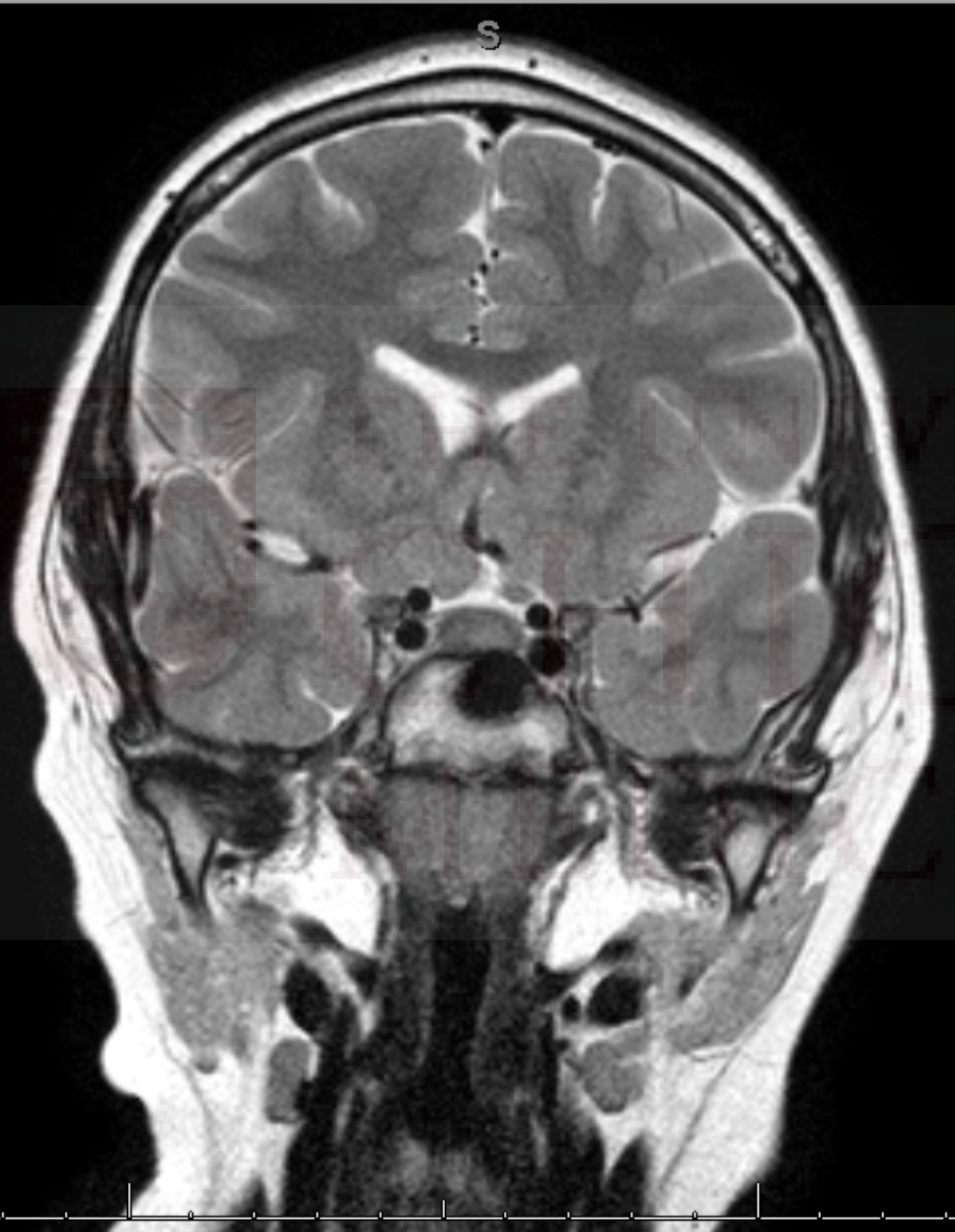
- Midnight Salivary Cortisol (RR <100)
 - 137, 105, 99
- Urine Free Cortisol 53 mcg/24h (2.6-37)
 - Vol 1.5L, UCr = 1410 mg
- Urine Free Cortisol 76 mcg/24h (2.6-37)
 - Vol 1.3L, UCr = 1000 mg
- 8AM ACTH 56.8 (RR <52)
- 8AM Cortisol 17.6 mcg/dL (6.8-26)

LDDST → CRH stim

LDDST: 0.5 mg dexamethasone q6h for 48h
Dexamethasone level 271 ng/dL (RR < 20)

Time (min)	-15	0	15	30	45	60	90	120
ACTH	34.9	31.0	68.7	62.4	59.2	58.9	63.4	71.6
Cortisol mg/dL	3.4	3.2	9.6	15.5	14.3	15.2	17.2	18.3

↑
IV CRH 1 ug/kg



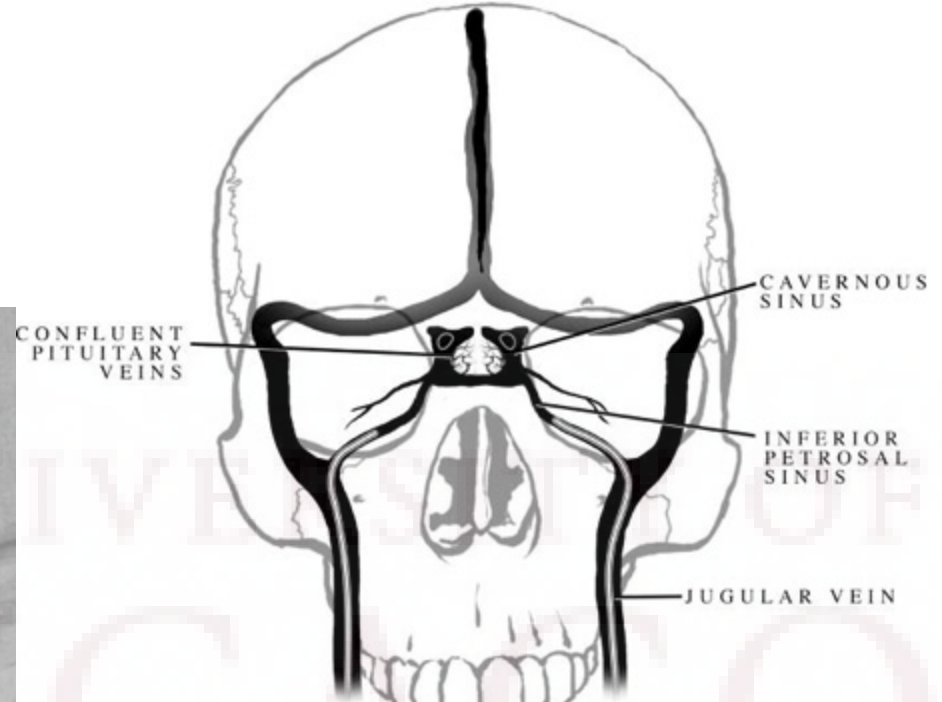
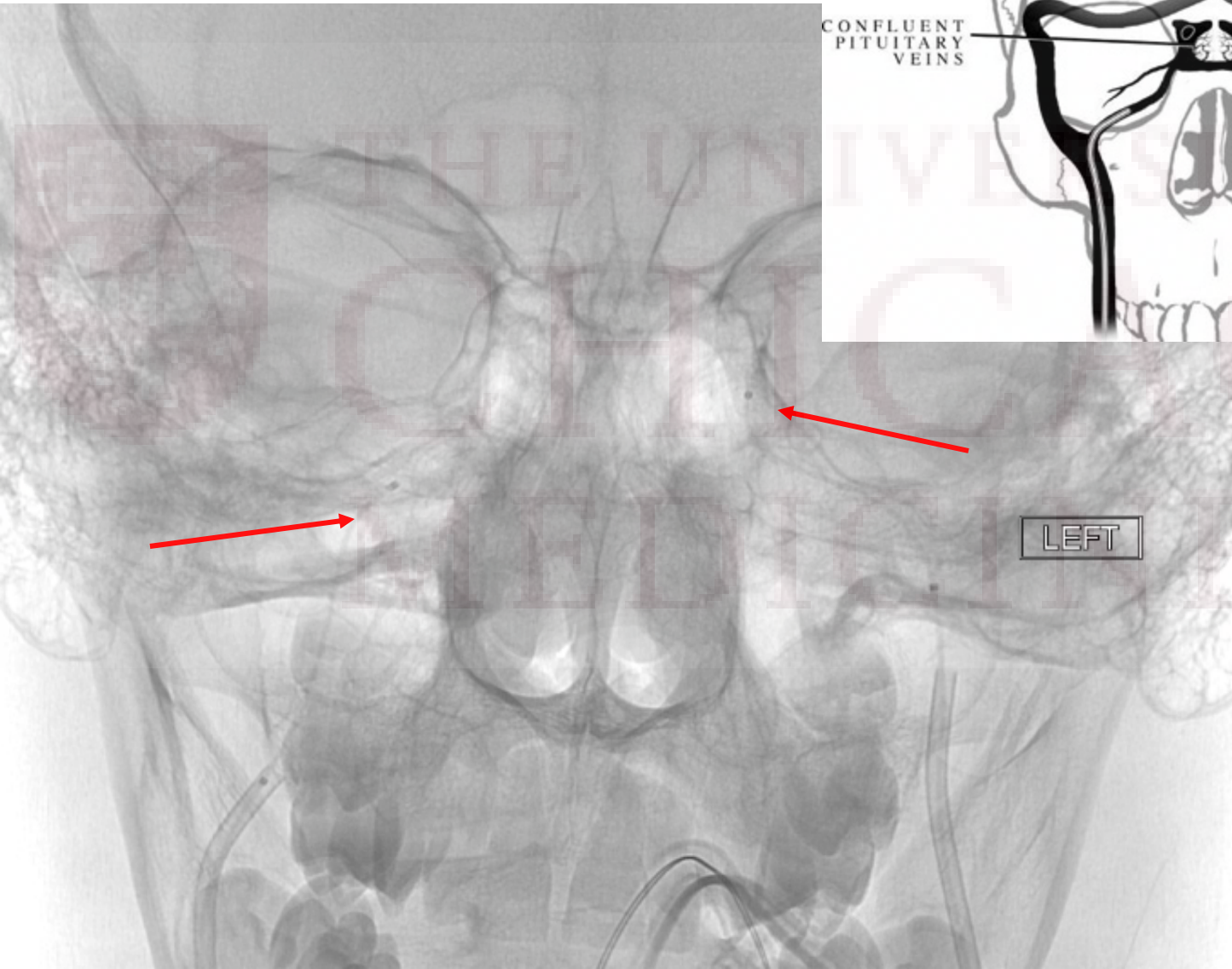
Pituitary gland/stalk are normal without any evidence of abnormal enhancement.

IPSS results

Time (min)	L/P ACTH ratio	R/P ACTH ratio	L/P PRL ratio	R/P PRL ratio
-10	0.8	1.2	0.9	1.0
-5	1.1	1.1	1.0	1.0
0	0.9	1.0	1.0	1.0
2	1.1	1.1	0.9	1.0
5	1.1	0.9	1.0	1.0
10	1.0	1.0	1.0	1.0
15	1.0	0.9	1.0	1.0
30	1.0	0.9	1.0	1.0

Acutal Time (min)	sample	ACTH			Cortisol			Prolactin		
		ACTH L	ACTH R	ACTH P	Cortisol L	Cortisol R	Cortisol P	Prolactin L	Prolactin R	Prolactin P
-10	1	46	68	55	22	23	23	39	41	42
-5	2	74	71	68	23	23	23	40	41	39
0	3	64	67	70	23	23	23	40	40	39
2	4	71	71	67	22	23	23	36	38	39
5	5	112	98	105	23	24	23	37	38	38
10	6	121	122	121	27	26	26	38	38	38
15	7	126	115	132	30	31	29	37	37	38
30	8	123	113	124	34	35	33	33	34	34

IPSS



Clinical questions?

- Pediatric Cushings- unique aspects
- Relationship between pseudotumor and Cushings Disease
- Management of pediatric CD w/neg MRI

Pediatric Cushings

- JCEM 2013, prospective observational
- 200 Cushing's Disease patients
- Mean age sx = 10.6 ± 3.7 yrs
- Mean interval (sx to surg) = 3.3 ± 2.1 yrs
- Early remission rate 195 of 200 (98%)
- Factors affecting surgical outcomes in CD
 - Identifying adenoma in surgery
 - +immunohistochemistry for ACTH
 - Non-invasive adenoma

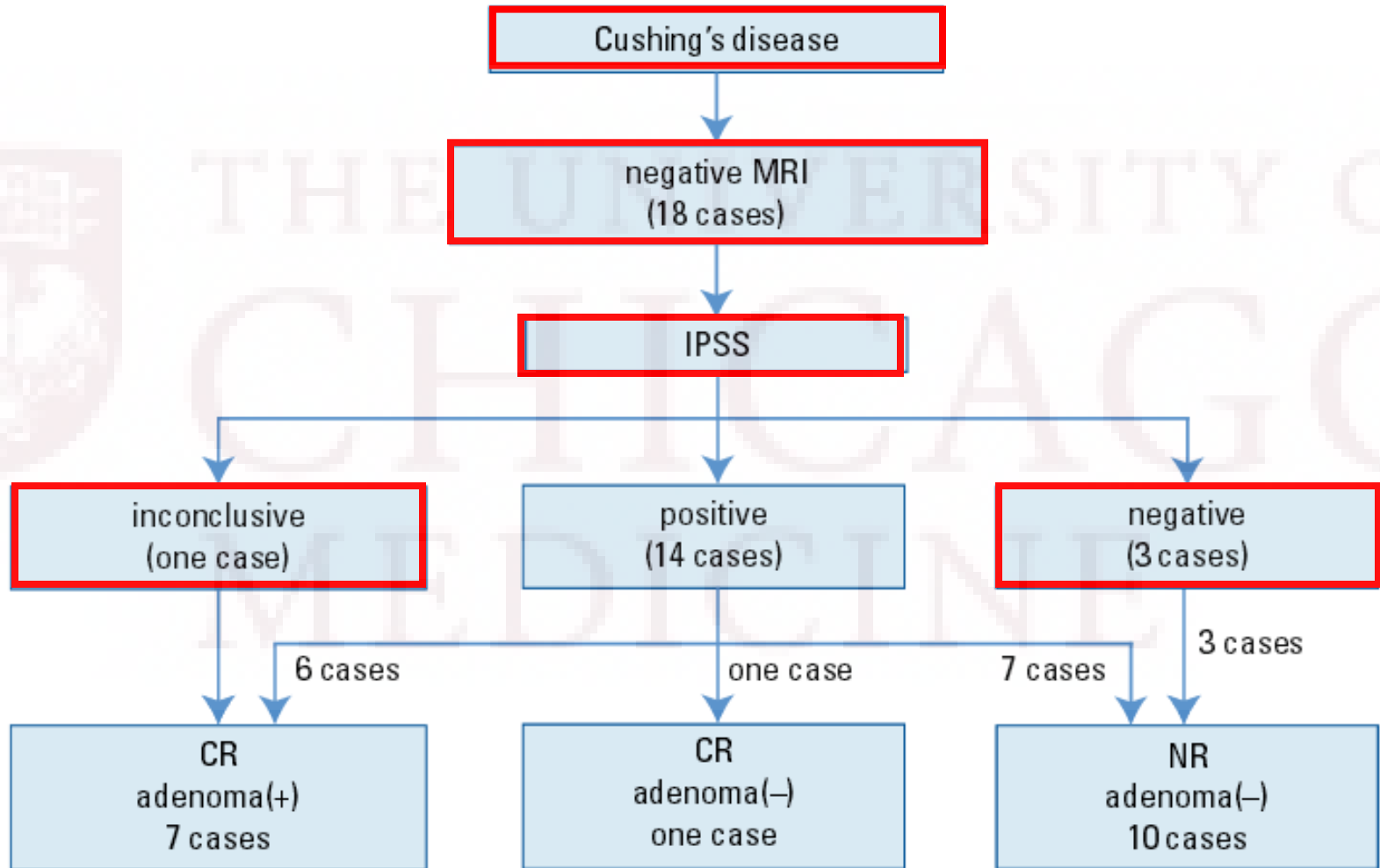
Pediatric Cushings

Presenting Signs and Symptoms	Prepubertal Patients (n = 91)	Postpubertal Patients (n = 109)
Rapid weight gain	88 (97)	98 (90)
Obesity ^a	81 (89)	59 (54)
Dorsal cervical or supraclavicular fat pad	58 (64)	79 (72)
Moon facies	56 (62)	70 (64)
Decreased linear growth ^b	77 (85)	48 (44)
Central obesity	57 (63)	66 (61)
Hirsutism	47 (52)	65 (60)
Abdominal striae ^b	39 (43)	70 (64)
Fatigue	43 (47)	52 (48)
Acne	44 (48)	50 (46)
Amenorrhea (primary or secondary) ^c	NA	49 (72)
Headaches	33 (36)	43 (39)
Hypertension	27 (30)	44 (40)
Acanthosis nigricans	32 (35)	32 (29)
Depression, anxiety, mood swings	22 (24)	39 (36)
Easy bruising ^b	14 (15)	35 (32)
Gynecomastia ^c	8 (15)	9 (22)
Glucose intolerance or diabetes	2 (2)	11 (10)
Alopecia	3 (3)	8 (7)
Bone fractures	3 (3)	4 (4)
Nephrolithiasis	1 (1)	6 (6)

TSS in CD w/neg MRI

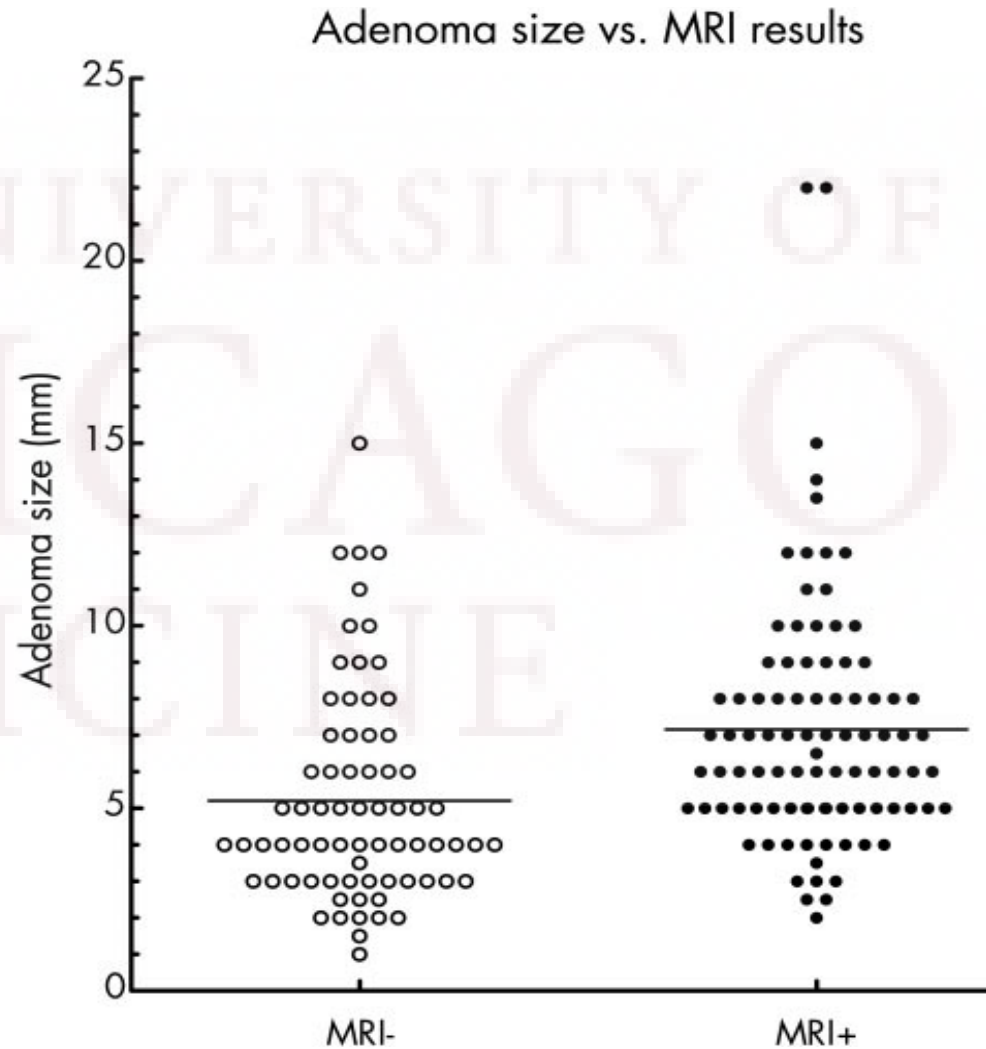
- Objective: Retrospective analysis of outcomes of TSS w/ biochemical CD and no visible adenoma on MRI
- 106 MRI+ and 18 MRI-
- Remission rate: 44% MRI- vs 94% MRI+
 - 0% in MRI- and IPSS-

TSS in CD w/neg MRI



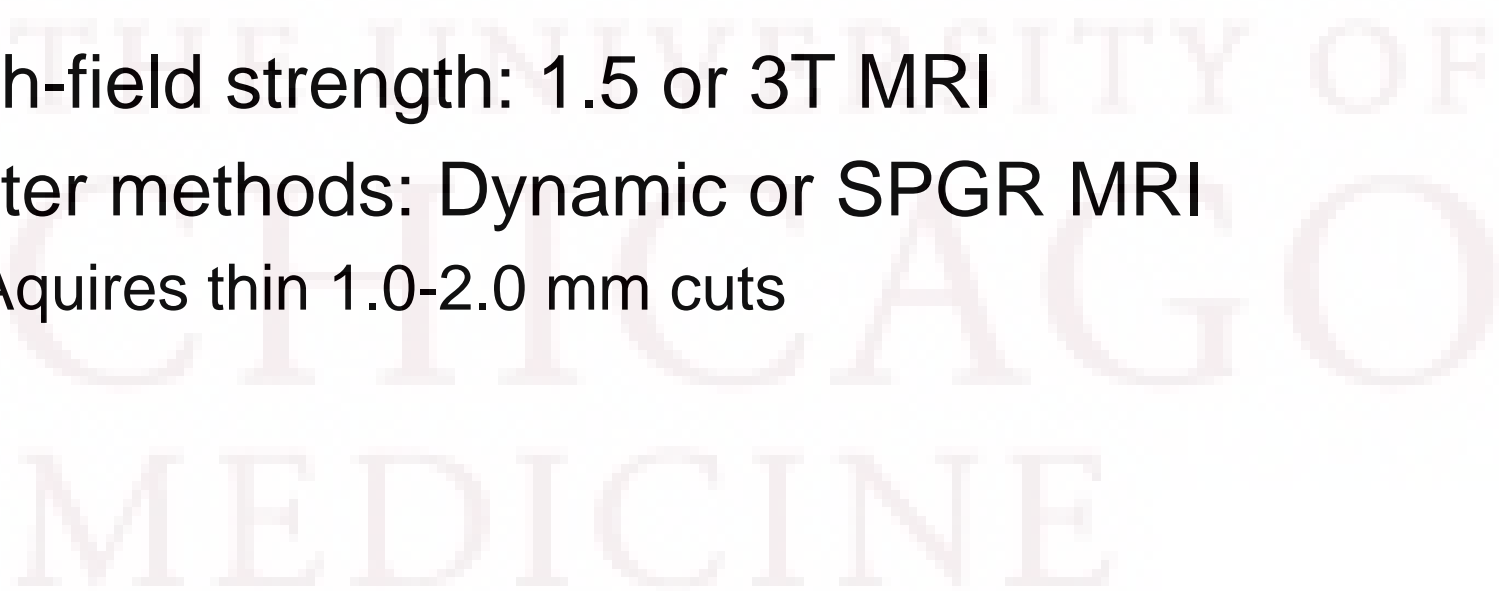
Variables

- Neg MRI
 - Characteristics of tumor
 - Field strength
 - Technique
 - Method of analysis



Modifications to MRI

- Modifications to MRI
 - High-field strength: 1.5 or 3T MRI
 - Better methods: Dynamic or SPGR MRI
 - Acquires thin 1.0-2.0 mm cuts



Pseudotumor and Cushings

Reference	Case: age (yr) and sex	Treatment for hypercortisolism	Cortisol replacement	Time from treatment to PC onset
Newman et al (6)	18 M	Metyrapone and aminoglutethimide	None	†
Martin et al (7)	29 F	Transsphenoidal surgery	HC, 30 mg/day	4 wk
Fischer & Anast (8)	17 M	Transsphenoidal surgery	For 3 wk	7 wk
Weissman et al (9)	7 F	Transsphenoidal surgery	None	3 wk
Griffith et al (10)	55 F	Metyrapone, 1,500 mg/day	HC, 30 mg/day	3 wk
Parfitt et al (11)	11 F	Transsphenoidal surgery	HC, 20 mg/day for 12 wk	14 wk
Current report	44 F	Total adrenalectomy	HC, 60 mg/day	2 wk

*HC = hydrocortisone; NA = not applicable; PC = pseudotumor cerebri.

†PC was present before treatment for hypercortisolism.

*CSF absorption in dogs on steroids and after steroid withdrawal**

Experiment No.	Group 1 (Control)	Group 2 (On Steroids)	Group 3 (After Steroid Withdrawal)
1	43.8	42.3	39.5
2	55.2	28.4	21.7
3	26.8	25.9	18.8
4	37.8	14.0	22.3
5	46.4	34.0	16.1
6	46.3	43.2	12.1
mean	42.7	31.3	21.7
SD	9.6	11.0	9.5
p	—	NS	<0.01

*Resistance to CSF absorption in dogs on steroids and after steroid withdrawal**

Experiment No.	Group 1 (Control)	Group 2 (On Steroids)	Group 3 (After Steroid Withdrawal)
1	28	34	84
2	46	48	42
3	48	36	80
4	38	31	65
5	56	58	94
6	40	34	65
mean	42.7	40.2	71.7
SD	9.6	10.6	18.4
p	—	NS	<0.01

Steroid withdrawal is associated:

1. Reduction in CSF absorption
2. Increased resistance to CSF flow

Back to our patient

- Discussed case with his neurosurgeon Dr Frim and with Dr Stratakis (NIH) who recommended
 - CT chest (negative for ectopic source)
 - Chromogranin A (normal limits)
 - MRI abd/pelv
- Repeat MRI pituitary scheduled 8/26

Take Home Points

- Pediatric CD most common chief complaint: rapid weight gain and decreased linear growth
- Treatment in MRI neg, IPSS neg cases is controversial
- Pseudotumor cerebri can complicate the recovery of Cushing's Disease patients post-treatment

References

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