18 yo F w/Chiari malformation (s/p decompression), pseudotumor (s/p shunt) w/worsening hypotension

Jess Hwang

9/12/13

HPI

- Admitted 7/2013 Adm for HA, nausea/vomiting. Ophtho exam: no optic disc swelling, VF normal. LP shunt revision performed.
- HA are mainly frontal but in the last 2 years have also been located in the occipital region.
- Worse in AM, with stormy weather, when bearing down, with sitting up for >2h

- Has been on dilaudid q4h chronically at home. Started on Methadone on 7/17.

Headache history

- Age 4– Chiari surgery (synthetic patch graft)
- 4/2011 Cleveland Clinic for HA
  - LP opening pressure 27.5 cm→improved symptoms after drainage and starting diamox
- 4/2012 Chiari decompression (replacement w/autograft)
- 5/2012 readm with HA, nausea/vomiting with worsening photophobia. She requeted an LP– opening pressure 23 cm H2O. Started on Diamox.
- 6/2012 Ophtho- disc edema→orbital pseudotumor
- 6/2012 Lumbar drain placed→removed
- 7/2012 LP shunt insertion, revised in 1/2013.

HPI

- Intermittent episodes of acute word-finding difficulties, blurry vision after being upright for a while.
- BP range 80/50-100/50 since admission. Often requiring IVF for maintenance.
- Diagnosed with POTS a few years ago and has been on Florinef 0.1 mg BID.
- 8/5 consult for hypotension, hypocortisolemia

Endocrine ROS

- LMP was a 3 days before consultation.
- +menorrhahgia
- No galactorrhea, no peripheral vision problems
- No polyuria, no polydypsia
- +constipation, +nausea
- +fatigue, +dizziness, +depression
- Has been on 2% hydrocortisone cream BID for 2 wks for PICC line irritation

More history

PMH

- Chiari type 1 (s/p decompression 1999)
- Migraine (since 8 yo)
- Platelet abnormality
- Menometrorrhagia
- MTHFR mutation (heterozygous)
- Postural orthostatic tachycardic syndrome (POTS)- (since 14 yo)- sees cards in OH
- Premature 36 wks
- Seizures
- Reflux- sees GI in OH, has had multiple EGDs and has required PPI BID

FHx

- Mother- hypothyroidism
- No known pituitary/adrenal problems

SHx

- Senior in highschool
- Lives with mom/dad/sister 4.5 hours away in Michigan

Home meds

Prozac 25 mg daily
Nexium 40 mg BID
Flexeril 10 mg daily prn
Zofran 8 mg q8h prn
Desmopressin 2 sprays q12h (prn menorrhagia)
Topamax 125 mg BID
Valium
Vitamin E daily
CoQ 10 200 mg BID
Thiamine 100 mg BID

Miralax
Pericolace
Dilaudid
Florinef 0.1 mg BID
Midodrine 5 mg BID
Propanolol LA 60 mg daily
Pyridostigmine 60 mg 5x/d
Adderall daily
Riboflavin 200 mg BID
Selenium 50 mcg daily
L-carnitine 330 mg BID
Lipoic acid 100 mg daily

Physical Exam

Vitals: 36.2, HR 84, RR 14, BP 105/62, O2 sat 100 RA (+orthostatic vitals)

Gen: chronically ill appearing

HEENT: PERRL. EOMI. VF grossly normal on confrontation. Extreme pallor.

Neck: no thyromegaly or nodules.

Heart: RRR.

Resp: no distress. CTAB.

GI: soft, NT/ND.

Ext: no edema.

Neuro: A+Ox3, napping before and after exam.

Psych: flat affect

Labs

MCV 73

135	106	7
5.7	21	0.5

85

8.2

2.0

5.3

9.3

6.3 393

6.9	4.8
0.3	72
11	9

25-OH vit D 16
Iron 19 mcg/dL (RR 40-160)
TIBC 429 mcg/dL (RR 230-430)
% saturation 4.4 (14-50)
Ferritin 6 ng/mL (RR 10-220)
CRP 4 mg/L (RR <5)
Pregnancy test neg

Endo work-up

- 8/3 8AM cortisol 0.5
- Cosyntropin stim

8AM	30 min	60 min
ACTH 9.9 Cortisol < 0.4	Cortisol 4.7	Cortisol 6.9

- Prolactin 89.55 ng/mL (RR 4.8-23.3)
- IGF1 249 ng/mL (RR 163-584)
- FSH 2.9/LH 3.2/Estradiol 28 (day 5 of her cycle- early follicular phase)
- TSH 1.31 FT4 0.74, TT3 121, rT3 134 (160-353), Tg Ab +/TPO Ab +
- Adrenal Ab neg

7/4 6:30AM cortisol = 6.8
7/4 TSH 0.41, FT4 1.10

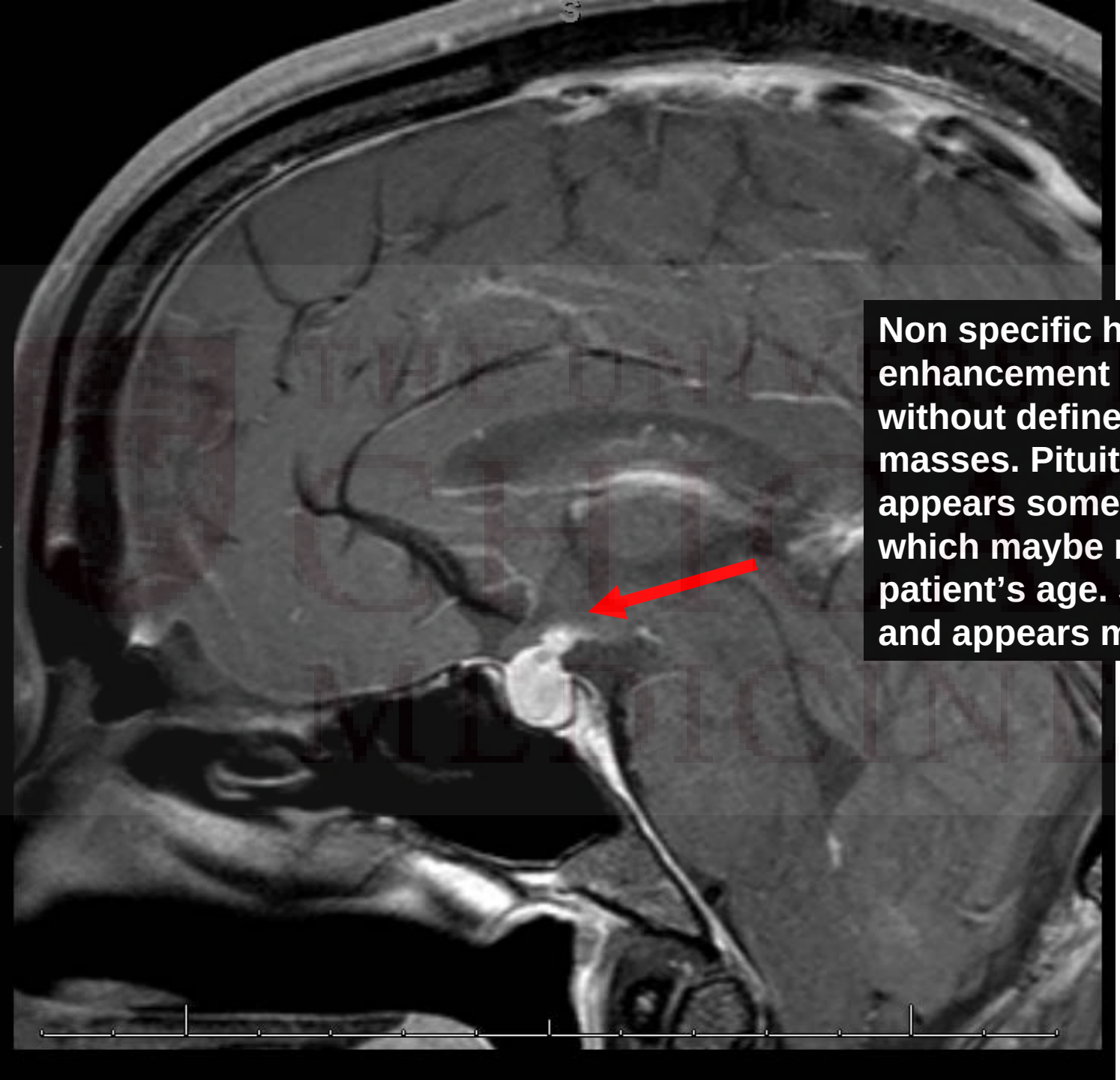
Steroid history

- 4/23-5/2/2012 High-dose decadron/taper
- 6 months ago recalls taking a few doses of Prednisone for ?pneumonia
- Hydrocortisone 2% cream BID during this admission for PICC line irritation

Other tests

- 3/2013 CSF WBC 10 (Lymph 89%, Mono 11%), protein 47 (RR 15-45), glu 62 (50-70)
- 7/3/2013 CSF WBC 2 (Lymph 86%), protein 58, glucose 71

- Pelvic US: normal uterus, endometrium. Normal ovaries.



Non specific heterogeneous enhancement of pituitary gland without defined pituitary masses. Pituitary gland appears somewhat prominent which maybe normal for patient's age. Stalk is thickened and appears mildly nodular.

DDx of Thickened Pituitary Stalk

- Neoplasms of the stalk- craniopharyngioma, germ cell tumor, metastatic disease (lymphoma), Langerhans histiocytosis
- Inflammatory: lymphocytic hypophysitis, sarcoidosis, histiocytosis, hypophysitis (lymphocytic, granulomatous, necrotizing)
- Infection: bacterial, viral, fungal
- Chronic opioid use (per our radiologists)

Byrne TN. MGH Neuroendocrine Clinical Center Bulletin. Spring 2008;14(1):1-3.

Biopsy+ lymphocytic hypophysitis

Clinical Questions

- Epidemiology/Presentation/Management of lymphocytic hypophysitis (LH)
- Presumptive diagnosis of LH without biopsy
- Natural history of LH

Epidemiology of LH

- Prevalence = 5 per million
- As of 2008, there are 500 patients described
- M:F ratio ranges from 4-6:1
- Peak incidence is 4th decade of life
- In 211 women with LH between 15-45 years of age, LH presented during late pregnancy or early post-partum in 69%

Caturegli P. Autoimmun Rev 2008 Sept;7(8):631-637.

Typical presentation of LH

- Categories of symptoms
  - 58% Headache, visual disturbances
  - 44% Hypopituitarism
  - 31% Polyuria/polydypsia
  - 18% Hyperprolactinemia

Caturegli P. Autoimmun Rev 2008 Sept;7(8):631-637.

Typical presentation of LH

Symptoms	Frequency, %
Endocrine dysfunction	80
Adrenal insufficiency	65
Hypothyroidism	60
Growth hormone deficiency	54
Hypogonadism	40
Hyperprolactinemia	30
Diabetes insipidus	15

N = 145. Multiple hormone deficiencies are found in 75%

Molitch ME. Lymphocytic Hypophysitis. Horm Res 2007;68(5):145-150.

Work-up

- Definitive diagnosis = biopsy
  - Biopsy is only considered if alternative treatments with significant adverse effects (high-dose steroids, immunosuppressive agents, pituitary radiation) are being considered.
- Antigen-specific antibody assays are not sensitive/specific, nor are they readily available

MRI findings

- Generally the gland is symmetrically enlarged
- Intense/homogeneous post-gad enhancement
- Loss of posterior pituitary bright spot
- Dura adjacent to the mass shows marked contrast enhancement– dural tail
- Thickened but undisplaced stalk

Molitch ME. Lymphocytic Hypophysitis. Horm Res 2007;68(5):145-150.

Medical Management of LH

- High-dose steroids
  - Variable response
- Other immunosuppressive agents: azathioprine, methotrexate
- Supportive management= hormone replacement

Medical Management of LH

Medical therapy	Patients treated	Before medical therapy			After medical therapy		
		Hypopit	Diabetes insipidus	Pituitary mass	Improvement of hypopit	Improvement of diabetes insipidus	Improvement of pituitary mass
Glucocorticoids oral	23	13	11	23	6 (46%)	2 (18%)	20 (87%)
Glucocorticoids iv	16	13	9	16	7 (54%)	6 (66%)	12 (75%)
Azathioprine	5	5	2	5	1 (20%)	1 (50%)	5 (100%)
Total	44	31	22	44	14 (45%)	9 (41%)	37 (84%)

N = 44 cases, follow-up only available in 37 patients
Pituitary size reduced in 84%
Anterior pituitary function improved in 45%
Posterior pituitary function improved in 41%

Lupi I. J Endocrinol. Invest. 2011;34:e245-e252.

Presumptive clinical diagnosis

- History of gestational/post-partum hypopituitarism (esp if no hypotension)
- Contrast-enhancing sellar mass with typical features
- Pattern of pituitary hormone deficiency (ACTH > TSH > FSH/LH) vs adenomas (GH > LH/FSH > ACTH = TSH)
- Relatively rapid development of hypopituitarism
- Pattern of symptoms out of proportion to MRI findings

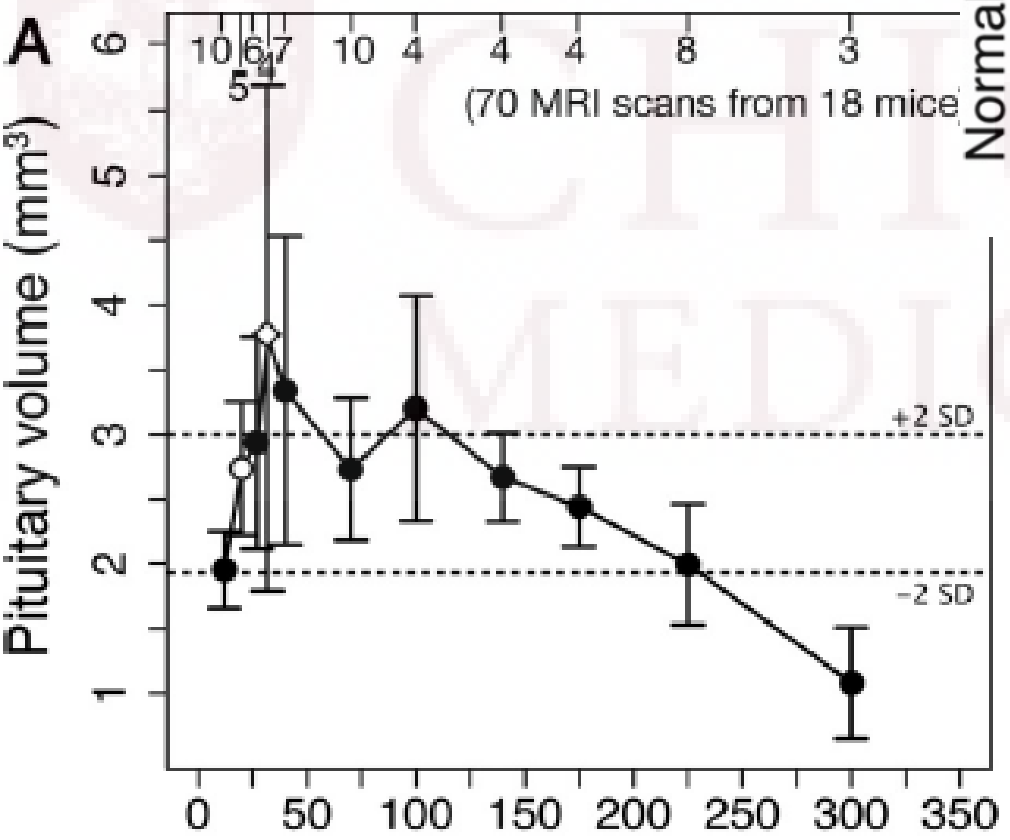
Molitch ME. Lymphocytic Hypophysitis. Horm Res 2007;68(5):145-150.

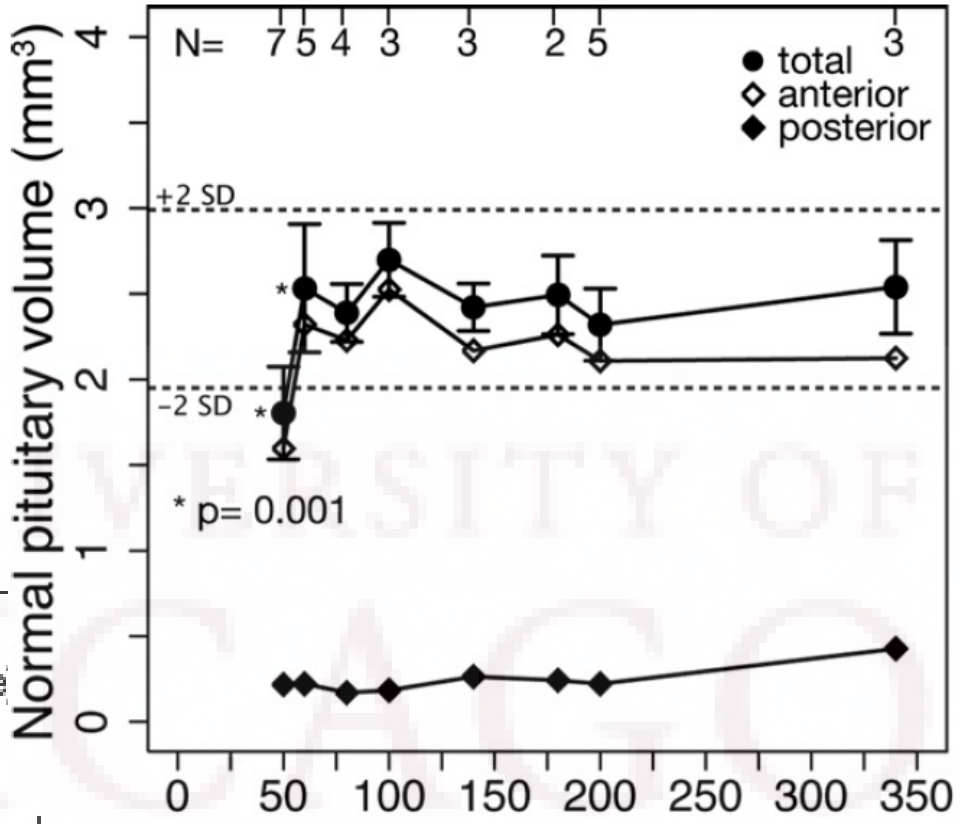
Natural history of LH

- Aim: define course of hypophysitis
- Cohort: 33 F mice (18 immunized with pituitary proteins, 15 controls)
- Results: immunized mice showed significant expansion of pituitary volume during early phase. Volume decreased gradually in 78% cases and reached empty sella values by day 300.

Lupi I. Endocrinology 2011;152(11):4190-4198.

18 post-immunization mice





Non immunized mice

Back to our patient

- Repeat Prolactin 65.58 ng/mL (RR 4.8-23.3)
  - Dilution: no hook effect
- Discharged home on:
  - HC 40/20→taper after 1 week to 20/10
  - LT4 50 mcg daily→rechecking labs in a month
  - Iron, Vitamin D replacement

- Plan for repeat MRI pituitary
- Will also check celiac, vit B12, folic acid, immunoglobulin levels
- Follow-up with NUS, Endo

Take Home Points

- Presumptive clinical diagnosis includes symptoms, pattern of hormone deficiency, MRI findings.
- Possible improvement in hypopituitarism reportedly 40-50% with high dose steroids
- MRI improvement is 80% with high dose steroids but this could be the natural course of disease

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