53 year-old female with polyuria

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Endorama

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HPI

- 53-year-old female with T cell ALL s/p stem cell transplant in June 2010 with PTLD (post-transplant lymphoproliferative disorder) and GVHD (skin) was admitted on 1/26 with:
- decreased po intake 1-2 weeks, with n/v and diarrhea 3 days before admission.
- AKI (Cr 2.3)
- Worsening rash on extremities (GVHD of skin)

HPI continued…

- Reports increased urine output prior to admission
- Since hospitalization, she had polyuria with 6.8 L of urine output noted on 1/28.
- Her sodium was 146 on admission and increased to 158 on 1/29.
- Nephrology was consulted for AKI and hypernatremia

Trend of serum Na

DDAVP Challenge

DDAVP 4 mcg IV

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	Ref. Range	2/1/2012 10:54	2/1/2012 10:57	2/1/2012 12:07	2/1/2012 12:29	2/1/2012 13:18	2/1/2012 13:30	2/1/2012 13:32	2/1/2012 13:37
Osmolality (Untimed)	Latest Range: 500-800 mOsm/kg	122 (L)		126 (L)	204 (L)			285 (L)	309 (L)

Urine volume

0 - DDAVP 4 mcg administered

30 min-300 ml

60 min-60 ml

90 min-50 ml

120 min-30 ml

HPI continued…

- Endo consulted for evaluation on 2/2 per Nephrology since DDAVP challenge was more consistent with central DI
- Denies recent medication changes, NSAIDs, or OTC supplements.
- Did not receive IV contrast
- Complains of thirst
- Denies mental status changes
- Denies head trauma or recent surgery

Past Medical History

- T Cell ALL (Dx in 2009) Matched related donor stem cell transplant in June 2010 with conditioning with Clofarabine, Melphalan, and alemtuzumab.
- -Post Transplant lymphoproliferative disorder s/p Rituxan
- EBV viremia 6/2011
- -GVHD (10/11-developed after prograf tapered off. Improved with steroids but recurred 1/11. Started on prednisone and resumed prograf)
- Hysterectomy with oopherectomy in 2003

Social Hx, Family Hx, and Meds

Social Hx:

- Married, lives with husband
- No smoking, no EtOH, no illicit drug use

Fam Hx:

Mother-died of breast cancer

Father-healthy

Allergies: Iodine

Home Meds:

Prednisone 20 daily
Acyclovir 800 BID
Sirolimus 1 mg q2 days
Penicillin V BID
Bactrim DS BID Sa and Sun
Noxafil 5 mL TID
Prilosec
Posaconazole oral suspension

ROS:

-hard of hearing (over the past year-has had evaluation by ENT)
-denies galactorrhea
-denies h/a or vision problems

Hospital Medications

- acyclovir 800 mg Q24H
- ciprofloxacin 500 mg Q12H
- desmopressin 0.05 mg QHS
- esomeprazole 20 mg QAM
- micafungin (MYCAMINE) IV 50 mg DAILY
- penicillin V potassium 250 mg BID
- prednisone 30 mg DAILY
- sulfamethoxazole-trimethoprim-DS 1 Tab BID

Physical Exam

VS: Height: 170 cm (5' 6.93") Weight: 65.12 kg (143 lb 9 oz) Temp: 36 °C (96.8 °F) Heart Rate/Pulse: 93 , BP: 114/88 mmHg, Resp: 16 SpO2: 96 % on RA

Physical Exam

- Constitutional:NAD
- HENT: wears hearing aids
- Head: Normocephalic and atraumatic.
- Eyes: Conjunctivae are normal.
- Neck: Neck supple.
- Cardiovascular: Normal rate and regular rhythm.
- Pulmonary/Chest: Effort normal and breath sounds normal.
- Abdominal: Soft, Nontender
  Neurological: She is alert and oriented to person, place, and time.
- Skin: Skin is warm and dry. Rash noted consistent with GVHD
  Psychiatric: She has a normal mood and affect. Judgment normal.

Labs

1/26 (labs on admission)

142 | 103 | 27 / 190
3.7 | 25 | 2.3 \

6.4 \ 9.3 /153
/ 28.7\

Labs on day of Endo consult 2/2

137 | 99 | 19 / 127
3.6 | 25 | 1.2 \

10.3 \ 11.2 / 119
/ 32.3 \

1/29 –day of Nephrology consult
Serum sodium -158
Serum Osm- 328 (289-308 mOsm/kg)
Urine Osm- 149 (500-800 mOsm/kg)

Renal Ultrasound on 1/30

RIGHT KIDNEY: The right kidney measures 11.4 cm. No hydronephrosis. Echogenic renal parenchyma compatible with medical renal disease.

LEFT KIDNEY: The left kidney measures 11.7 cm. No hydronephrosis. Echogenic renal parenchyma compatible with medical renal disease.

Serum sodium and uop in response to DDAVP

DDAVP 4 mcg IV challenge

Na	147	150	137	136	144
Date	1/31	2/1	2/2	2/3	2/4
Uop	3.9L	8.1L	3.5L	2.1L	1.8L

DDAVP 0.05 mg po qhs daily

- What other labs would you check?

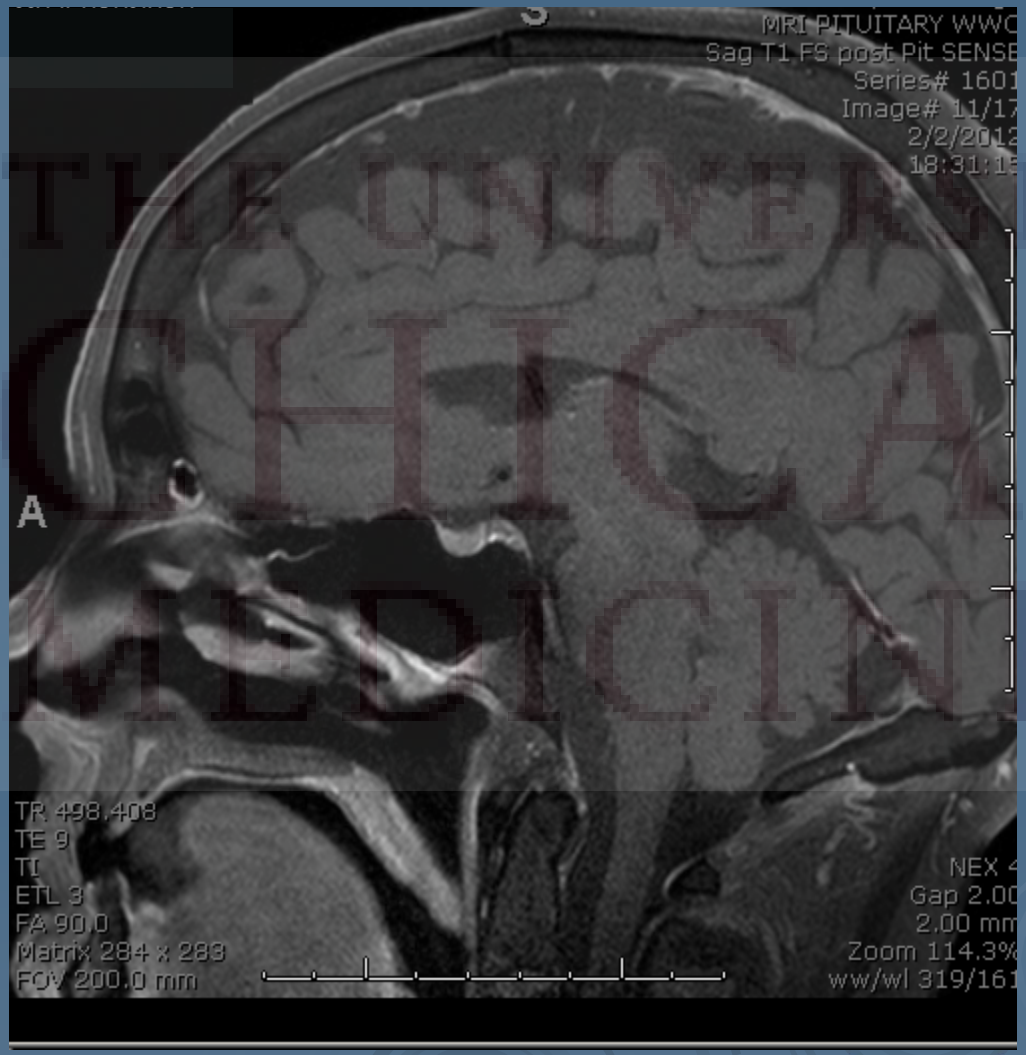
Endo Recs

- Recommend checking pituitary function with a TSH, free T4, FSH, LH, and estradiol.
- Since patient is already on prednisone, we are unable to check the adrenal axis at this time.
- MRI pituitary

Additional Lab Results

- FSH-7.3 miU/ml
- LH-2.6 miU/ml
- Estradiol-<10 (10-400 pg/ml)
- TSH-0.83 (0.3-4 mcU/ml)
- ft4-0.47 (0.9-1.7 ng/dl)
- Prolactin- 52.71 (4.8-23.3 ng/ml)

MRI pituitary



MRI pituitary

- IMPRESSION:
  1. Thickening and enhancement at the base of the infundibulum/hypothalamus but otherwise normal appearance of the pituitary gland.

- This is a nonspecific finding; etiologies include inflammatory, infectious processes and, although less likely secondary to lack of masslike appearance, tumor may also be considered.

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Causes of Central DI

- Idiopathic
- Neurosurgery or Trauma
- Cancer
- Infiltrative Disorders
- Familial and Congenital Disease
  - Familial CDI
  - Wolfram Syndrome
  - Septo-optic Dysplasia
- Hypoxic Encephalopathy
- Post Supraventricular Tachycardia
- Anorexia Nervosa

Lymphocytic hypophysitis

- Rare inflammatory condition affecting the pituitary gland
- Characterized by lymphocytic infiltration and enlargement of the pituitary
- Most reported cases are in women and occur during late pregnancy or in the weeks after childbirth
- Frequent post-partum occurrence and lymphocytic infiltration suggest autoimmune etiology

Lymphocytic Hypophysitis and Typical Imaging Characteristics

- CT and MRI may reveal features of a pituitary mass, mimicking an adenoma
- MRI also shows diffuse and homogenous contrast enhancement of the anterior pituitary, but the enchancement may be delayed or absent in the posterior pituitary area.

Anti-CTLA 4 immunotherapy and lymphocytic hypophysitis

- Hypophysitis and panhypopituitarism may also be a complication of anti-CTLA 4 immunotherapy with ipilimumab or tremelimumab for various cancers
- The clinical and hormonal manifestations appear to be similar to those of idiopathic hypophysitis, but it may be more likely to be transient
- Acquired hypopituitarism and lymphocytic infiltration have also been described in association with an antibody to PIT-1 (POU1F1)

Ipilimumab and hypopituitarism

- In a phase III trial, nine patients treated with ipilimumab (1.8 %) had severe or life-threatening hypopituitarism
- Several of these patients also had other endocrine side effects (hypothyroidism , adrenal insufficiency or hypogonadism).
- An additional 12 patients (2.3 %) had moderate endocrinopathies requiring hormone replacement therapy or other medical intervention.
- The median time to onset of endocrine symptoms was 11 weeks, but in some cases symptoms did not appear until after completion of the initial four courses of therapy.
- Pituitary function should be monitored prior to each dose of ipilimumab and as indicated by clinical signs or symptoms

Hodi FS, O'Day SJ, Urba WJ et. al. Improved survival with ipilimumab in patients with metastatic melanoma. N Eng J Med. 2010 Aug 19;363(8):711-23. Epub 2010 Jun 5.

Endo Recs

- Start Synthroid 50 mcg po daily
- Already on prednisone for GVHD, once tapered will need to be on HC 20/10 mg
- Continue DDAVP 0.05 mg po qhs
- Consider spinal tap to rule out leptomeningeal mets
- Endo f/u as outpatient

Clinical Course

- Patient underwent spinal tap to rule out leptomeningeal metastases.
- Was seen in Onc clinic prior to f/u in Endo- prednisone decreased from 30 mg ->20 mg ->15 mg
- Hypotensive in Endo clinic 50s/40s
- Denies fevers/chills, nausea/vomiting, cough
- Sent to ER immediately for stress dose steroids and for evaluation

Clinical Course

- Started on hydrocortisone 100 mg IV q8, tapered gradually to HC 20/10 mg
- Symptomatic improvement with IV antibiotics for pneumonia
- DDAVP increased to 0.1 mg po qhs since serum sodium increased to 150s despite adequate water intake
- Patient normotensive and serum sodium stable at time of discharge
- Scheduled for Endo f/u as outpatient

Take Home Points

- Lymphocytic Hypophysitis can result in panhypopituitarism.
- Cancer can involve the pituitary/hypothalamic region in the brain and leptomeningeal metastases should be excluded in patients with pre-exisiting cancers and symptoms of new pituitary dysfunction.
- Hypophysitis and panhypopituitarism may also be a complication of anti-CTLA 4 immunotherapy

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