Cases from the California Center for Pituitary Disorders at UCSF

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Case One: Clinical Presentation

- **HPI:**
  - 35 y.o. woman
  - Headaches
  - N/V, photophobia, anorexia x 3 days
  - Delivered Daughter 14 months ago:
    - Fatigue, Nausea
    - Lost pregnancy weight
    - No resumption of menses
    - Night-time polydipsia

- **Past Medical History:**
  - 1. Pars Planitis & Iritis 2 months ago
Case One: Initial Labs & Studies

- Na 141, BG 91, USpGr 1.011
- Cortisol 0.6 mcg/dL
- ACTH 1 pg/mL (7 - 51)
- TSH 0.45 mcU/mL
- FT4 0.14 ng/dL
- LH 0.1 & FSH 1.1 mIU/mL
- Estradiol <20 pg/mL
- Prolactin 0.5 ng/mL
- IGF-1 23 & GH 0.1 ng/mL
Case One: Differential Diagnosis

- Pituitary Macroadenoma
- Metastatic Disease
- Sheehan’s Syndrome
- Pituitary apoplexy
- Postpartum Lymphocytic Hypophysitis

Which of these is most likely?
Case One: Diagnosis

- Postpartum Lymphocytic Hypophysitis:
  - Standard hormone replacement
  - If no regression, then high-dose steroids
    - Dex 4 mg q6 hrs
    - Prednisone 35 BID
    - F/u MRI in 4 weeks

Following 10 Days of Dexamethasone
Overview of Hypophysitis

TABLE 1. Suggested Classification Scheme: Inflammatory and Infectious Hypophysitis

- **Primary**
  - Granulomatous
  - Lymphocytic Autoimmune Hypophysitis (AIH)
    - Lymphocytic Infratubular Neurohypophysitis (LINH)
    - Lymphocytic Panhypophysitis (LPH)

- **Secondary**
  - Infectious
    - Tuberculosis, Bacterial, Fungal, Viral
  - Non Infectious
    - Wegener's Granulomatosis
    - Sarcoidosis, Crohn's, Takayasu's, Ruptured Cyst, Histiocytosis

Clinical Features of Hypophysitis

- 1) Pituitary Lesion in a Woman Around the Time of Pregnancy
- 2) Rapidly Progressive Pituitary Lesion
- 3) Pituitary function discordant with the size of the lesion

Most common manifestations:
Hypopituitarism (63%), mass effects (56%),

Cheung CC et al 2001 J Clin Endocrinol Metab 86:1048-1053
Hypophysitis: Diagnostic Studies

- High Degree of Suspicion
  - 1 case: 9 million
  - 1% of all surgical pituitary specimens

- CT/MRI Features
  - Symmetrical & intense enhancement
  - No erosion on the sellar floor
  - No stalk displacement

- Anterior Pituitary Hormone Evaluation
Hypophysitis: Pathophysiology

- **Histology**
  - Lymphoplasmacytic infiltrate
  - Destruction of underlying parenchyma

- **Autoimmune etiology**
  - 25% with previous h/o autoimmune disease
  - Anti-pituitary antibodies

Caturegli P et al 2005 *Endocrine Reviews* 26: 599-614
Hypophysitis: Management

MEDICAL MANAGEMENT W/SEQUENTIAL MRI’s

- Glucocorticoid Therapy
- Surgical Resection
  - If Radiographic and/or Clinical Progression
- Observation
  - Spontaneous recovery with resolution of pituitary mass has been described
Case 1: Follow up Imaging

3 mos later: Partial Empty Sella

One year later: Further Regression
Autoimmune Hypophysitis: Take-Home Points

1) Female, recent or current pregnancy, History of autoimmune disorder

2) MRI Characteristics: bright and homogeneous

3) Trial of Steroid Therapy with Sequential MRI’s monitoring and Evaluation of Anterior Pituitary Hormones
Case Two: Clinical Presentation

- **HPI:**
  - 51 y.o. woman
  - Pituitary Tumor discovered during w/u for syncopal episode at work
  - Daily HA, weight gain, nausea, hot flashes, poor exercise tolerance, and difficulty w/ concentration
  - No galactorrhea, s/p hysterectomy
  - Reports increase in ring size

- **PmHx:**
  - 1. s/p TKR
  - 2. s/p hysterectomy

- **Meds:**
  - Prevacid & Premarin

- **Family History:**
  - Several sisters with thyroid disease.
Case Two: Initial Labs and Studies

LH 64.2 mIU/mL
FSH 90.7 mIU/mL
Prolactin 8.5 ng/mL
Estradiol 35 pg/mL
TSH 2.42 mcU/mL
FT4 0.95 ng/dL
ACTH 5 pg/mL
Cort-stim 11.5 to 21.3 mcg/dL
IGF-1 116 ng/mL
Case Two: Differential Diagnosis

- Non-functioning Pituitary Macroadenoma
- Gonadotroph Adenoma
- Hypophysitis
- Gonadotroph Hyperplasia

What is the most likely diagnosis?
Pituitary Hyperplasia: Pathophysiology

- Settings: Pregnancy, Hypothyroidism, Klinefelter Syndrome, GHRH Excess

- Hypothesis:
  Intrinsic (Genetic) Pituitary Cell Defects → Lack of Negative Feedback → Cell Stimulation
Pituitary Hyperplasia: Clinical Presentation and Diagnosis

- Asymptomatic
- Incidental finding on Imaging (height >9 mm)
- If applicable, distinguish from TSH-producing adenoma:
  - If biopsied...morphology preserved.
  - No visual field deficits.
Physiologic Pituitary Hypertrophy

Chanson P 2001 J Clin Endocrinol Metab 86:3009-3015
Pituitary Hyperplasia: Management

- Avoid unnecessary repeated hormonal evaluations and neurosurgical consultation
- Hormone replacement, if indicated:
  - Tx goal is relief of symptoms
  - May confirm diagnosis with serial MRI imaging
Case Two: Follow up

Over the next year
- Persistent symptoms of estrogen deficiency
- Estradiol increased to 2 mg daily
- MRI performed and unchanged
- LH in the 50’s and FSH of 80
- Re-eval of Pituitary Function Normal
Case Two: Follow up

- And then over the next year:
  - Replacement switched to transdermal estrogen
  - FSH 48 and Estradiol 25 on OSH labs
Case Two: Serial MRI Studies
Case Two: Take Home Points

- Consider Physiologic Hyperplasia of the Pituitary Gland
  - Clinical setting
  - Laboratories consistent with primary endocrine organ failure
  - Absence of Mass Effect Symptoms
  - Characteristic MRI findings

- Confirm with symptomatic relief following hormone replacement and resolution of MRI findings
Case Three: Clinical Presentation

- **HPI:**
  - 27 y.o. woman
  - Increased thirst and urination
  - Secondary amenorrhea x 3 months, increased somnolence, cold intolerance, anorexia & weight loss

- **Past Med Hx:**
  - MVA 3 months ago with closed head injury…in coma for 1 month
  - Depression/panic d/o
  - Seizure d/o
Diagnostic Studies

- Thyroxine 3.5 µg/dL
- TSH 4.2 µIU/mL
- FSH 1.0 mIU/mL
- Estradiol <20 pg/mL
- Stimulated GH 1.1 ng/mL
- 9 AM cortisol 0.6 µg/dL
- Prolactin 46.3 ng/mL
- Na 145 with Uspgr 1.003
Hypopituitarism Following Traumatic Brain Injury

- **Epidemiology**
  - TBI 250 per 100,000/year
  - Autopsy studies reveal pituitary necrosis in 1/3rd of patients with fatal head injury

- **Incidence of Hypopituitarism**
  - 28-35% Exhibit 1 Hormonal Deficiency (GH)
  - 6% demonstrate multiple deficiencies

Agha A. et al 2004 *J Clin Endocrinol Metab* 89:4929-4936
Aimaretti G et al 2004 *Clin Endocrinol* 61: 320-326
Elovic EP 2003 *J Head Trauma Rehabil* 18: 541-543
TBI Induced Hypopituitarism

● Pathophysiology:
  – Anterior Lobe Necrosis
  – Posterior Lobe Hemorrhage
  – Stalk Laceration
  – Vascular injury to the Hypothalamus

● Recommendations
  – Initial Hospital Visit: Hormonal testing if clinical indicated (AI, DI)
  – Re-evaluate at 3 months and 12 months post (r/o GHD after institution of other hormonal therapies)
Case Three: Take Home Points

- Include history of Traumatic Brain Injury in the ROS during an evaluation for suspected Hypopituitarism

- GHD most common in setting of remote Traumatic Brain Injury
Case Four: Clinical Presentation

- 85 yo WF…mother-in-law of a patient
- CC: visit to allergist 8 yrs ago for difficulty breathing thru nose
- HPI
  - Antihistamines…failed
  - RTC in 3 weeks…XRAY performed in office
  - Lead to Head CT…and eventually to head MRI/MRA
- No Medications and no significant PmHx
Case 4: Post-Contrast T1 MRI
Case 4: Follow up

- Asymptomatic in regards to pituitary hormone deficiencies
- Underwent ENT surgery of her sinuses without complication
  - Breathing improved
  - Occasional nosebleeds
- Surgical pathology consistent with pituitary adenoma, “negative for malignancy”
Pituitary Carcinoma: Diagnosis

DEFINED BY THE PRESENCE OF METASTASES

- @140 published cases; 0.2% pituitary tumors
- Most are hormonally active (ACTH, Prolactin)
- Initially present as invasive macroadenomas..early recurrence following initial surgery with repeated operations for rapid local growth
- Two subtypes:
  - Invasive adenoma with multiple recurrences and eventual mets. Prolonged survival.
  - Early malignant behavior with a much shorter survival.
Pituitary Carcinoma: Diagnosis

- No reliable MRI characteristics with the exception of invasion
- Somewhat useful in findings mets:
  - PET
  - Octreoscan

Kaltsas G. et al 2005 J Clin Endocrinol Metab 3089-3099
Criteria for Pituitary Carcinoma

TABLE 1. Criteria needed to be fulfilled for the classification of pituitary carcinomas

- The primary tumor must be identified as a pituitary tumor by histology.
- An alternative primary tumor has to be excluded.
- Discontinuous spread in the form of single or multiple nodular subarachnoid metastatic deposits occasionally invasive of underlying brain or overlying dura.
- Single or multiple systemic deposits broadly similar to and grossly indistinguishable from metastases of carcinomas arising in other organs.
- The structural features or marker expressions of the metastases should correspond or be similar to those of the pituitary tumor.

Kaltsas G. et al 2005 J Clin Endocrinol Metab 3089-3099
Pituitary Carcinoma: Pathophysiology

- Adenoma → Carcinoma
- Intracellular and Extracellular (VEGF, MMP’s) events
- Histological Parameters:
  - High mitotic activity
  - p53 positivity
  - Increased microvascular density
  - Ki-67(%) LI usually > 10%

Scheithaumer B et al 2005 Neurosurgery 56: 1066-1074
Pituitary Carcinoma: Management

- **Surgery**
  - Rarely curative, relieves mass effect symptoms, recurrence the rule and quickly occurs

- **Radiotherapy**
  - Temporary partial control of primary as well as bony and visceral mets

- **Chemotherapy**
  - Observational data indicating patients with extra-CNS mets have prolonged survival if received chemotherapy.

- **Medication**
  - DA unsuccessful. Variable experiences with SS analogs.
Case 4: Take Home Points

- A high index of suspicion for a pituitary carcinoma when relevant features are present may result in more aggressive therapy and therefore an improved prognosis.

- Rule out a metastatic tumor elsewhere before making the diagnosis of a pituitary carcinoma.

- Obtain Ki-67% LI and p53 immunostaining on surgical pathology from an aggressive pituitary tumor...to guide choice of post-op radiotherapy and influence aggressive follow-up.