

NEUROENDOCRINE & PITUITARY TUMOR CLINICAL CENTER (NEPTCC) BULLETIN

CASE RECORDS OF THE MGH NEPTCC

A PITUITARY MASS PRESENTING WITH VISUAL LOSS DURING PREGNANCY

-BROOKE SWEARINGEN, M.D.

A 30-year-old nulliparous woman presented to MGH at 34 weeks gestation with headaches and visual loss. She was referred by her ophthalmologist, who documented a bitemporal field defect with a dense left central scotoma. The visual loss was progressive, and had worsened in the week prior to presentation. She had developed headaches three months prior to admission. The pregnancy was otherwise uncomplicated. Menses were normal before her pregnancy, and she had no history of galactorrhea, polyuria/polydipsia or other endocrine symptoms. Medical history was notable for a deep venous thrombosis three years ago, and she was being treated with low molecular weight heparin during the pregnancy. She had a history of primary hypothyroidism and had been maintained on 100 µg of thyroxine daily for the past five years. She was otherwise healthy.

On exam, she did not appear acromegalic or Cushingoid. There was a dense left central and superior temporal defect, and a subtle right superior temporal defect. Acuity was 20/30 on the right and 20/800 on the left.

Endocrine testing revealed a 5am cortisol low at 2.3 ug/dl, prolactin 33 ng/ml (normal <20), TSH 0.09 uIU/ml (normal 0.4-5.0), T4 7.8 ug/dl (normal 4.5-10.9), free T4 low at 0.7 ng/ml (normal 0.9-1.8). She was begun on steroid replacement with hydrocortisone and her thyroxine dose was increased.

A noncontrast (because of the pregnancy) MRI was performed. This demonstrated a 2.3 cm mass arising from the sella, extending into the suprasellar cistern, with significant chiasm compression. There was T1 hyperintensity within the central portion of the mass suggestive of hemorrhage. (Figure 1)

The presumptive diagnosis was pituitary adenoma with hemorrhage, perhaps related to her heparin requirement, leading to visual loss. She was seen by the high risk obstetrics service and the low molecular weight heparin was

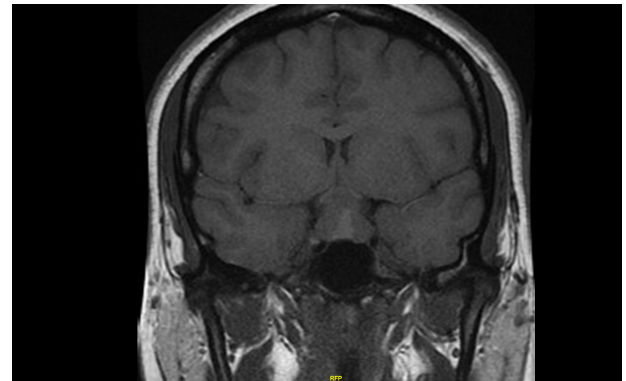


FIGURE 1. Preop non-contrast MRI shows a large sellar mass with central T1 bright signal

discontinued prior to planned surgery. Transsphenoidal exploration was performed after discontinuation of anticoagulation. At operation, a densely fibrotic mass was found and biopsied. The T1 hyperintensity seen on her preoperative MRI proved to be high-protein fluid within a Rathke's cleft cyst. Frozen section pathologic analysis showed fibrotic anterior pituitary with a dense inflammatory infiltrate composed predominantly of lymphocytes, consistent with lymphocytic hypophysitis.

Postoperatively, her vision initially improved to 20/25 on the right and 20/50 on the left, with a smaller central scotoma. She was maintained on 20 mg of prednisone daily. Transient diabetes insipidus developed, which resolved spontaneously after a few days. At 2.5 weeks post biopsy, (35.5 weeks gestation), she reported worsening vision on the left despite steroid treatment, and return of the resolved visual defect on the right. The prednisone dose was increased to 60 mg daily. She was admitted for induction of labor, which was unsuccessful at 48 hours, and she therefore underwent cesarean section, with delivery of a healthy boy. Postpartum, a contrast-enhanced MRI was obtained (Figure 2) which showed the large densely enhancing sellar mass with persistent chiasm compression. The high dose prednisone was continued.

VISIT OUR WEBSITE AT:
MASSGENERAL.ORG/NEUROENDOCRINE

On post delivery day one, her vision had begun to improve, with acuity improved to 20/30 on the left and 20/20 on the right, and a smaller scotoma. The prednisone was tapered to 40 mg daily. By two weeks post delivery, formal neuro-ophthalmologic exam documented 20/15 vision bilaterally with full visual fields. A follow-up MRI was obtained which showed dramatic shrinkage in the inflammatory mass, without chiasmal compression. (Figure 3)

Discussion. The differential diagnosis and management of pituitary disorders during pregnancy is complex. Possibilities in this case included a previously unrecognized nonfunctioning pituitary adenoma, with hemorrhage related to the anticoagulation, leading to rapid expansion and visual loss, enlargement of a previously unrecognized macro prolactinoma, or an inflammatory mass. A prolactinoma was considered unlikely, given the history of normal menses, absence of galactorrhea, and minimally elevated prolactin level on hormone testing, and we suspected hemorrhage into a previously existing tumor. Given the rapid progression and severity of presentation, a biopsy and possible resection was felt to be indicated. Pathology showed a dense inflammatory infiltrate composed predominantly of CD3 positive lymphocytes with scattered histiocytes and eosinophils, consistent with hypophysitis.

Hypophysitis can occur in a number of variants, including adenohypophysitis or infundibulohypophysitis. It is rare, with an incidence of one in 9 million person-years. It is most common in peri-partum women, but has been found in men, non-pregnant women and the elderly. A number of pathologic

subtypes exist including lymphocytic, granulomatous, xanthomatous and IgG4. A subtype associated with the use of ipilimumab in the treatment of metastatic melanoma has been recently described. Symptoms typically include headaches and visual loss from the enlarging mass, as well as endocrine symptoms from hypopituitarism. As an autoimmune disorder, it is often associated with the presence of anti-pituitary antibodies and other autoimmune disease. Imaging typically demonstrates homogeneous enhancement in an enlarged pituitary, without a focal mass lesion. Indications for therapy vary with the severity of presentation; classic hypopituitarism without mass effect can be treated with replacement only. With symptomatic mass effect, definitive diagnosis and possible transsphenoidal debulking may be necessary, followed by immunosuppressive treatment with high-dose glucocorticoids and/or azathioprine. In our case, there was initial improvement with high-dose prednisone after biopsy, but dramatic improvement occurred only after delivery, with resolution of mass effect and improvement in vision.

REFERENCES

1. Carmichael, JD. *Curr Opin Endocrinol Diabetes Obes.* 2012; 19:314-21.
2. Faje AT, et al. *J Clin Endocrinol Metab.* 2014; 99:4078-85.
3. Glezer A, Bronstein MD. *Endocrine.* 2012; 42:74-9.

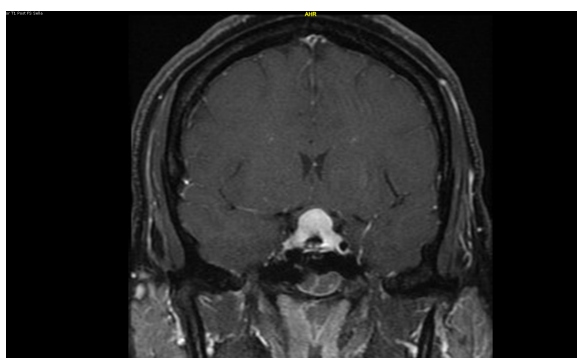


FIGURE 2. Contrast MRI after delivery shows a homogeneously enhancing mass with persistent chiasm compression

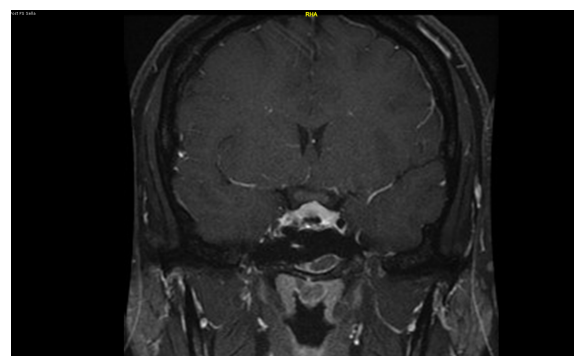


FIGURE 3. Contrast enhanced MRI 2 weeks after delivery and treatment with high-dose prednisone. There is dramatic decrease in the size of the mass with relief of chiasm compression.



CONGRATULATIONS MR. LOMAX!

Rodney Lomax, the Patient Service Coordinator in the Neuroendocrine and Pituitary Tumor Center, has been awarded the "MGH 2015 Pamela J. Ellis Award." This award honors those Hospital employees who exhibit exceptional qualities in their work. Mr. Lomax is totally dedicated to the complex pituitary patients seen in the Center. Many patients come from other states and countries and often need appointments with the neurosurgeon, radiation oncologist or neuroophthalmologist. Recognizing the difficulty of traveling to Boston for many days, Mr. Lomax works closely with all of those offices to coordinate appointments and ensure a smooth visit.

REGISTER NOW!

MASSACHUSETTS GENERAL HOSPITAL AND
HARVARD MEDICAL SCHOOL CME PRESENT:
CLINICAL ENDOCRINOLOGY: 2016

March 20 – March 24, 2016
THE FAIRMONT COPLEY PLAZA, BOSTON, MA

For over four decades this course has provided practicing endocrinologists and other healthcare providers with a comprehensive review and update of recent literature in clinical endocrinology. The faculty consists of staff endocrinologists at the Massachusetts General Hospital and Harvard Medical School as well as nationally-renowned guest lecturers, all selected for their teaching and clinical skills. A comprehensive syllabus is provided.

FOR ADDITIONAL INFORMATION CONTACT:

Harvard Medical School Department of Continuing Education
By Mail: Harvard MED-CME, P.O. Box 825, Boston, MA 02117-0825
By Telephone: 617-384-8600

REGISTER NOW AT WWW.HMSCMEREISTRATION.ORG/CLINICALENDOCRINOLOGY2016

RESEARCH STUDIES AVAILABLE

Patients may qualify for research studies in the Neuroendocrine Clinical Center. We are currently accepting the following categories of patients for screening to determine study eligibility. Depending on the study, subjects may receive free testing, medication and/or stipends.

-The Neuroendocrine Clinical Center is involved in many different research studies. Types of studies and enrollment status changes frequently, so please call our office (617-726-3870) or check our webpage (massgeneral.org/neuroendocrine) for more information about potential studies which may not be listed here.

SUBJECTS	STUDIES	CONTACT 617-726-3870
Adults with Growth Hormone Deficiency	<ul style="list-style-type: none">• Long acting GH replacement study• Assessing bone microarchitecture	Beverly MK Biller, MD Karen Pulaski Liebert, RN Nicholas Tritos, MD
Adults with Cushing's Disease	<ul style="list-style-type: none">• Treatment study assessing the effect of an investigational medication on cortisol levels	Beverly MK Biller, MD Karen Pulaski Liebert, RN
Adults with active or treated acromegaly	<ul style="list-style-type: none">• Quality of life• Cross-sectional bone density study• Assessing bone microarchitecture	Karen K Miller, MD Pouneh Fazeli, MD Karen Pulaski Liebert, RN Nicholas Tritos, MD
Men with hypopituitarism	<ul style="list-style-type: none">• Characterization of oxytocin deficiency	Elizabeth Lawson, MD



THE NEUROENDOCRINE CLINICAL CENTER WELCOMES DR. SUMAN SRINIVASA

Dr. Srinivasa earned her medical degree at the University of Illinois at Chicago, completed her residency training at New York University School of Medicine and fellowship in endocrinology at the Massachusetts General Hospital. At MGH, Dr. Srinivasa sees patients with pituitary and neuroendocrine disorders, as well as patients with HIV-related endocrinopathies and metabolic disorders. In addition, Dr. Srinivasa is also involved with consulting on inpatients, teaching and conducting clinical research studies.

PATIENTS' FREQUENTLY ASKED QUESTIONS (FAQS)

ABOUT TRANSSPHEOIDAL SURGERY FOR ACROMEGALY, CUSHING'S DISEASE, NON-FUNCTIONING PITUITARY ADENOMAS AND OTHER PITUITARY ABNORMALITIES

-MICHELLE GUREL, BSN, RN AND KAREN JP LIEBERT, BSN, RN

WHAT IS TRANSSPHEOIDAL PITUITARY SURGERY?

This is a neurosurgical procedure typically used to remove pituitary tumors. It is important that the operation be done by someone who is expert in the procedure, performing it on a regular basis, as this provides the best chance to remove the tumor while leaving the normal pituitary gland in place. The pituitary gland is located at the base of the brain and behind the bridge of the nose. The easiest access to the pituitary region is via a transsphenoidal approach. With this approach, an operative microscope or endoscope and surgical instruments are inserted in the nasal cavity (or less commonly, under the upper lip and through the upper gum) and a small incision is made in the bone behind the nasal cavity. Behind this opening is an air cavity, called the sphenoid sinus. The surgical tools are passed through the sphenoid sinus to an area directly behind the sphenoid sinus into the bony cavity of the sella turcica. The pituitary gland is located within the sella turcica.

HOW LONG DOES THE OPERATION TAKE?

The procedure itself usually takes about three hours. Following surgery, patients will usually spend about two to three hours in the recovery room and are then admitted to the hospital floor. There is usually no need to stay in an Intensive Care Unit. Most patients are discharged from the hospital one or two days following surgery. In certain circumstances, such as in a patient with another medical condition, or if there is a complication, the stay may be longer.

HOW WILL I FEEL RIGHT AFTER THE SURGERY?

The most frequent symptoms after surgery are a sinus headache, nasal congestion and mild fatigue, which will gradually improve over a few weeks

COMMON QUESTIONS ABOUT SYMPTOMS AFTER TRANSSPHEOIDAL SURGERY ARE:

WHAT DO I NEED TO KNOW ABOUT HEADACHES & NECK PAIN AFTER TSS?

It is normal to experience headaches after pituitary surgery. If headaches worsen or are unrelieved by over-the-counter pain medication, you should notify your physician/neurosurgeon. If your neck feels stiff and is painful, you should notify your physician/neurosurgeon immediately.

WHAT IF I NEED TO SNEEZE/COUGH AFTER TSS?

If you need to sneeze or cough during the first week or two after surgery, you should stay relaxed and let it happen. Don't hold your breath or pinch your nose. Avoid things that make you sneeze like dust, animal dander, and cigarette smoke. You should gently clear your nose initially. After three days, you can gently blow your nose.

WILL I HAVE SINUS CONGESTION?

Sinus congestion is normal and may persist for up to 3 to 4 weeks after pituitary surgery. Nasal decongestants can be used anytime and saline is okay after the first week. If you think you have a sinus infection, you should notify your physician/neurosurgeon.

WHAT IF I EXPERIENCE NASAL DRAINAGE?

It is normal to have mucous or drainage that is dark red-brown or maroon in color. However, clear fluid, like water dripping from a faucet, or a lot of bright red blood, is not normal and you should notify your physician/neurosurgeon immediately.

WHAT SHOULD I KNOW ABOUT NOSE BLEEDS?

Spotting of red blood, or bloody mucous, from the nose is normal. Brisk bleeding from the nose rarely occurs. The most common cause of a nose bleed is from a small vessel in the nose (not bleeding from the tumor or brain). As with all nose bleeds, apply gentle pressure to stop the bleeding. If this does not control the bleeding, then go to your local emergency room and ask them to notify your physician/neurosurgeon.

WHAT SHOULD I DO IF I HAVE A FEVER?

If the fever is higher than 101°F, double the dose of steroids (prednisone/hydrocortisone), if you are taking this type of medication, until the fever subsides. If during the first two weeks after surgery, the fever goes above 101°F, notify your physician/neurosurgeon.

CAN I DO BENDING & LIFTING OR WORK-OUT/EXERCISE?

During the first two weeks, avoid bending and do not lift more than 20 pounds. After four weeks, most patients can return to strenuous exercise.

-SEE SPECIFIC ACTIVITIES ON THE NEXT PAGE-

WHEN WILL I BE ABLE TO ?

DRIVE, FLY,
WALK, GOLF,
SEXUAL ACTIVITY

ANYTIME
-NO RESTRICTION-

RETURN TO WORK
(GENERALLY, CONSULT PHYSICIAN)
SWIM, JOG

TWO WEEKS

GO ON AMUSEMENT PARK RIDES
(LIKE A ROLLER COASTER)
EXERCISE VIGOROUSLY

FOUR WEEKS

FAQS SPECIFIC TO TRANSSPHENOIDAL SURGERY FOR CUSHING'S DISEASE

WHAT WILL IMPROVE IF I AM IN REMISSION AFTER TSS?

In most patients, the physical and emotional problems associated with Cushing's disease improve and may resolve over the one to two years after remission.

IS THERE ANYTHING I CAN DO TO HELP WITH WEIGHT LOSS IF I AM IN REMISSION AFTER TSS?

Eating a healthy, well-balanced diet, limiting portion size and/or calories will help you lose weight once your cortisol levels are controlled. Lowering the steroid (prednisone/hydrocortisone) replacement dose according to your endocrinologist's instructions will also help. A gradually increasing program of exercise can contribute to weight loss, stamina and muscle strength.

HOW SOON WILL I FEEL BETTER AFTER TSS PUTS ME IN REMISSION FROM CUSHING'S DISEASE?

At first, patients may feel worse, rather than better, because the fall in cortisol can be associated with aches and fatigue. It is important to work closely with your endocrinologist to adjust your steroid (prednisone/hydrocortisone) dose so that you can be on the lowest dose that is safe for you (higher doses than you need can delay the recovery).

WHAT IS THE CHANCE OF THE CUSHING'S DISEASE COMING BACK?

Most patients do not experience a recurrence of Cushing's disease, but it is important to know that this can eventually happen in about 10-25% of patients.

A recurrence may develop as early as six or 12 months after TSS, but can also take place after more than 25 years. For this reason, it is essential to remain under the care of an endocrinologist. You should see an endocrinologist soon after having transsphenoidal surgery and for routine follow-up visits on a regular basis. You should discuss with your endocrinologist any concerns that the Cushing's disease might be returning.

WHAT IF I EXPERIENCE A RECURRENCE OF CUSHING'S DISEASE?

There are many good treatments available for patients who have a recurrence, including surgery, a number of medications and radiation (often given along with medication). Talk with your endocrinologist if you experience a recurrence.

WHAT IF MY CORTISOL LEVELS REMAIN ELEVATED AFTER SURGERY?

It is very important that cortisol levels be controlled to prevent the long-term complications of Cushing's disease. If this is not possible with surgery alone, further treatment is needed. There are many treatments available for patients who are not in remission after TSS. Talk with your endocrinologist about these options to find the one that is right for you.

FAQS SPECIFIC TO TRANSSPHENOIDAL SURGERY FOR ACROMEGALY

WILL THE CHANGES IN MY BODY RETURN TO THE WAY THEY WERE BEFORE I HAD ACROMEGALY?

While bony changes will not return to normal, soft tissue swelling in the face, hands and feet can improve significantly. Rings and shoes may become loose and facial changes may diminish.

HOW QUICKLY MIGHT I SEE CHANGES IN MY BODY AFTER TSS?

Some patients experience very rapid improvement in soft tissue swelling as the levels of growth hormone fall after surgery, and may feel their rings and shoes getting looser within days. In other patients, the improvement may be more gradual.

COULD THERE BE IMPROVEMENT IN MEDICAL CONDITIONS SUCH AS DIABETES AND HYPERTENSION (HIGH BLOOD PRESSURE) AFTER TSS?

When growth hormone is lowered/controlled, medical conditions, such as diabetes and hypertension, may improve and even resolve. In some patients with diabetes, blood sugar may fall quickly, so that it is important to talk with the doctor treating your diabetes to learn whether a reduction in any medications is advised. Similarly, in patients with high blood pressure, a reduction in medications may be needed if blood pressure improves. Be sure to discuss this with the doctor who prescribes your blood pressure medications.

WHAT IF MY GROWTH HORMONE LEVELS REMAIN ELEVATED AFTER SURGERY?

It is very important that growth hormone levels, and the hormone called insulin-like growth hormone (IGF-I) be controlled, to prevent the long-term complications of acromegaly. If this is not possible with surgery alone, further treatment is needed. There are several types of medications available to treat acromegaly if a patient is not cured by surgery. Somatostatin analogs and a GH receptor antagonist (both given by injection) are the most commonly used medications. In mild cases, a dopamine agonist, which is given in pill form, may be tried. Sometimes these medications are used in combination. Discuss the many treatment options with your endocrinologist.

Massachusetts General Hospital
Zero Emerson Place, Suite 112
Boston, Massachusetts 02114

Non-Profit Org
U.S. Postage
PAID
Massachusetts
General Hospital

SUPERVISING STAFF

Endocrinology:

Anne Klibanski, MD
Chief, Neuroendocrine Unit
Beverly MK Biller, MD
Steven K Grinspoon, MD
Alex Faje, MD
Pouneh K Fazeli, MD
Elizabeth A Lawson, MD
Janet Lo, MD
Karen K Miller, MD
Lisa B Nachtigall, MD
Suman Srinivasa, MD
Nicholas A Tritos, MD, DSc
Markella V Zanni, MD

Neurology:

Thomas N Byrne, MD

Neurosurgery:

Robert L Martuza, MD
Chief, Neurosurgical Service
Brooke Swearingen, MD
Nicholas T Zervas, MD

Radiation Oncology:

Jay S Loeffler, MD
Chief, Radiation Oncology
Helen A Shih, MD

Psychiatry:

Gregory L Fricchione, MD
Ana Ivkovic, MD

Pediatric Endocrinology:

Madhusmita Misra, MD, MPH
Takara L Stanley, MD

ANNE KLIBANSKI, MD – ENDOCRINE SOCIETY OUTSTANDING MENTOR AWARD



This annual award recognizes a career commitment to mentoring and a significant positive impact on mentees' education and career. Dr. Klibanski has mentored more than 50 trainees, many whom have gone on to leadership roles at Harvard and other top institutions. As the first woman promoted to full Professor of Medicine at Harvard from Massachusetts General Hospital, Dr. Klibanski recognized the barriers women face for career advancement. She established and now oversees institutional offices for career development and mentoring for women faculty, researchers and clinicians as the Director of the Center for Faculty Development at Massachusetts General Hospital. Dr. Klibanski is the Chief of the Neuroendocrine Unit at Massachusetts General Hospital and the Chief Academic Officer at Partners Healthcare in Boston, MA. She is the Laurie Carrol Guthart Professor of Medicine at Harvard Medical School.

SERVICES AVAILABLE AT THE NEPTCC

Facilities

The Center is located on the 1st floor (Suite 112) of Zero Emerson Place at the Massachusetts General Hospital. A test center is available for complete outpatient diagnostic testing, including ACTH (Cortrosyn) stimulation; insulin tolerance; CRH stimulation; oral glucose tolerance and growth hormone stimulation testing. Testing for Cushing's syndrome can also be arranged, including bilateral inferior petrosal sinus ACTH sampling for patients with ACTH-dependent Cushing's syndrome.

Neuroendocrine and Pituitary Tumor Clinical Conference

A weekly interdisciplinary conference is held to discuss all new patients referred to the Center and to review patient management issues. It is a multidisciplinary conference, attended by members of the Neuroendocrine, Neurology, Neurosurgery, Psychiatry and Radiation Oncology services. Physicians are welcome to attend and present cases.

Physicians' Pituitary Information Service (PPIS)

Physicians with questions about pituitary disorders may contact the PPIS at (617) 726-3965 within the Boston area or toll free at (888) 429-6863, or e-mail to pituitary.info@partners.org.

Scheduling

Outpatient clinical consultations can be arranged by calling the Neuroendocrine and Pituitary Tumor Clinical Center Office at (617) 726-7948.

The MGH NEPTCC Bulletin was supported in part by unrestricted educational grants from Chiasma and Cortendo. Other financial relationships may exist between these companies and The Massachusetts General Hospital.

NEWS OF NOTE:



Anne Klibanski, M.D., Nicholas T. Zervas, M.D. and Agnes Schonbrunn, PhD in the Historic Ether Dome for the 16th Annual Nicholas T. Zervas, MD Lectureship at the Massachusetts General Hospital on Tuesday, May 19, 2015. Dr. Schonbrunn is a Professor in the Department of Integrative Biology and Pharmacology Medical School, The University of Texas Health Science Center at Houston. She spoke on "Somatostatin Receptors as Therapeutic Targets: The promise, the limitations, and the opportunities".



MASSACHUSETTS
GENERAL HOSPITAL