36 year old woman with pituitary mass

Sharon H. Chou, MD

Endorama

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History of Past Illness

- 29 year old woman who experienced a sudden loss of peripheral vision and dizziness for 15 minutes, followed by numbness in the hands and headache.
  - Only followed by Ob-Gyn.
  - Referred to Neurology and Primary Care.
  - Work up was negative except for a “pituitary microadenoma.”
    - Just under 1 cm in maximum diameter.
    - No evidence of suprasellar extension or cavernous sinus invasion.
    - Some bowing of the diaphragma sellae.
  - Referred to Endocrinology.
  - Episode was attributed to initiation of transdermal birth control and never recurred.

Past Medical History

- Past Medical History
  - Hyperlipidemia
  - Anxiety/Depression
  - Migraines
  - Obstructive sleep apnea
  - Herniated disc with chronic back pain
- Medications:
  - Lipitor 10 mg QHS
  - Lexapro 20 mg QHS
  - Allegra-D QAM
  - Topamax 100 mg QHS
  - Imitrex 100 mg prn migraines
- Allergies:
  - Hydrocodone (headache)

Past Medical History

- Family History:
  - Father with CAD.
  - Mother with HTN.
  - Maternal grandmother with breast cancer.
  - Brother (39 yo) with hyperlipidemia.
  - Daughter with learning disability, concern for autism.
  - No family history of pituitary disorders, pancreatic tumors, thyroid disease, or parathyroid disease.
- Social History:
  - Married with 2 children.
  - Works as a part-time teacher's aide.
  - No history of tobacco use.
  - One glass of wine per month.
  - No recreational drug use.

ROS

- Most concerned about fatigue in the past year, stable.
- Also concerned about her weight, joined Weight Watchers a couple of months prior and had lost 5 pounds.
- Headaches approximately 3 to 4 times a week, associated with her menstrual cycle.
- No visual changes or loss of vision.
- No galactorrhea.
- Regular menses.
- Occasional heat intolerance.
- Increased stress and anxiety related to the uncertainty of her pituitary issue as well as her husband recently losing his job.
- Polydipsia over several months, drinking ~64 ounces of water per day. No polyuria. Occasional episodes of nocturia 1 to 2 times per week.

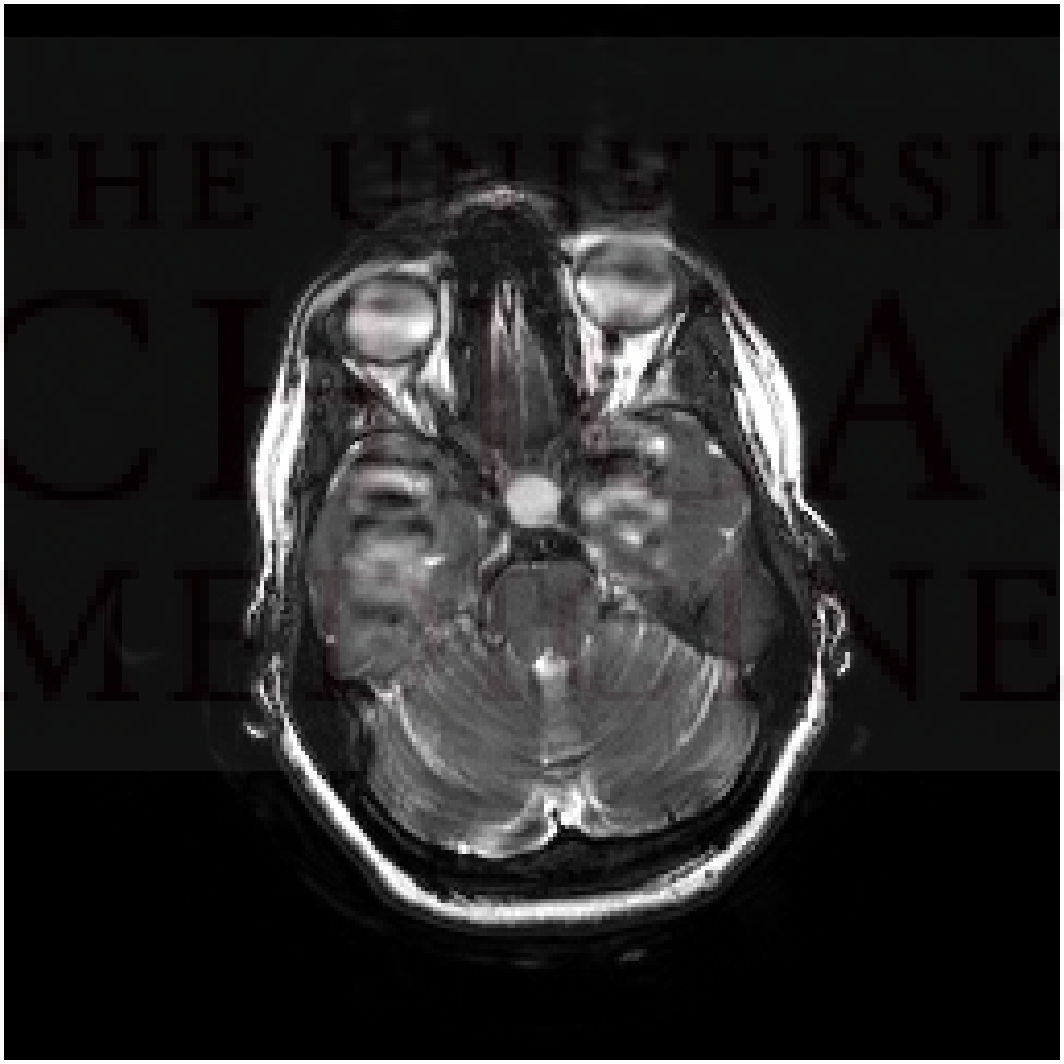
Physical Exam

- VITAL SIGNS: Blood pressure 116/76, pulse 81, weight 166 pounds, height 5’5’’, BMI 27.6 kg/m^2.
- GENERAL: She is a pleasant woman in no acute distress.
- HEENT: Normocephalic. No dysmorphic facial features. Extraocular movements were intact. There was no exophthalmus. Visual fields tested by confrontation were normal. Cranial nerves were intact. Oropharynx was pink and moist without visible lesions.
- NECK: The thyroid was not enlarged. There were no palpable thyroid nodules.
- LUNGS: Clear to auscultation bilaterally.
- HEART: Regular rate and rhythm without murmurs, rubs, or gallops.
- ABDOMEN: Soft, scaphoid, nontender, nondistended. She had normal muscle strength and tone on musculoskeletal exam.
- DERMATOLOGIC: Her skin was warm and dry.
- NEUROLOGIC: Deep tendon reflexes at the biceps and patellar locations were normal and equal.
- PSYCHIATRIC: Mood was mildly anxious.

Labs (OSH)

- TSH 1.4 mIU/mL (0.4 to 4.5), free T4 1 ng/dL (0.9-1.7), T3 91 ng/dL (80-195)
- LH 5.1 mIU/mL (1-11, 85), FSH 5.3 mIU/mL (1.7-19), estradiol of 184 pg/mL (30-400)
- 8:41AM cortisol 4.8 mcg/dL (6.8-26), ACTH 11 pg/mL (<52).
- 24-hour urine free cortisol 11.8 ug/day (<45), with a total urine volume of 2.5 liters.
- Growth hormone 0.2 ng/mL (0.03-10), IGF-1 237 ng/mL (49-292).
- Prolactin 7.9 ng/mL (4.8-23.3)
- Na 139, urinalysis specific gravity 1.023
- Visual fields negative.
- Repeat tests:
  - TSH of 0.1 mIU/mL
  - 8:42 AM cortisol 6.5 mcg/dL
- Repeat TFTs:
  - TSH 0.49 mIU/L (0.4-4.5)
  - Free T4 1.0 ng/dL(0.8-1.8)
- Insulin tolerance testing or a CRH stimulation test
  - ACTH stimulation test: 8→22

MRI pituitary: T2-weighted image



Interval History

- Serial MRIs:
  - 2006-2010: enlargement by 3 mm with bowing of the diaphragma sella superiorly
  - 2010-2011: stable
  - December 2011-May 2012: definite growth of the pituitary adenoma with further compression of the apparent normal pituitary anteriorly and superiorly, further suprasellar extension, and now abuts and slightly deforms the anterior chiasm.
- Visual fields normal in July 2012.
- S/sxs:
  - Occasional lightheadedness, sometimes with standing, that occur a couple of times a week, stable in frequency.
  - Denies any nausea, vomiting, abdominal pain.
  - Had gained 35-40 lbs since 2005 and subsequently lost 20 lbs in the last 4 months with Weight Watchers.
  - Denies any vision problems, galactorrhea, growth in hands/feet.
  - Denies tremors, palpitations, bowel changes, skin/hair changes. Reports chronic stable cold intolerance. Anxiety/depression stable on Lexapro.
  - Regular menses overall, missed 1 period.

History of Present Illness

- Underwent transsphenoid surgery
  - Operative report:
    - Extremely thinned out anterior sellar wall.
    - Cyst under moderate high pressure.
      - Milky-cheese white contents
      - Egressed spontaneously at high pressure
    - Spontaneous egress of clear fluid consistent with cerebrospinal fluid upon exploration of the cyst cavity.
    - No other visible pathology around the cyst wall.
    - Consistent with a Rathke's pouch.
  - No specimen could be sent for pathology
- Perioperative management:
  - Dexamethasone 6 mg IV BID→4 mg IV BID

Labs

- Preop labs

138 107 9 / 3.5 23 0.8 — 114

Ca 9.3

Total protein 7.6, alb 4.7
Tbili 0.5, alk phos 61
AST 19, ALT 34

14.2 / 7.7 248 / 43.1

- Post op labs

140 111 9 / 3.6 22 0.6 — 128

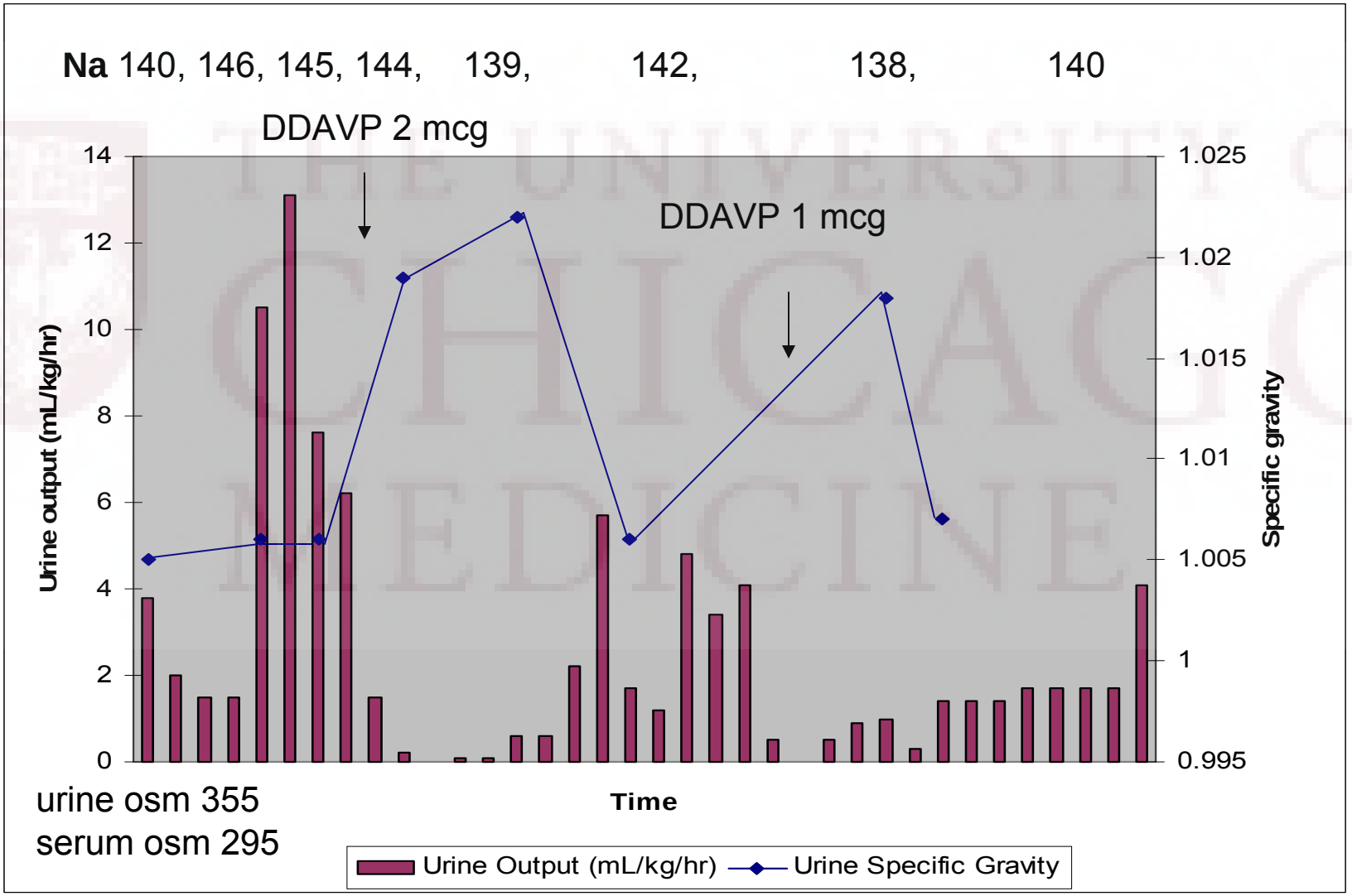
Ca 8.3

Total protein 7.6, alb 4.7
Tbili 0.5, alk phos 61
AST 19, ALT 34

13.1 / 16.0 261 / 38.8

Na and UOP trend

Na 140, 146, 145, 144, 139, 142, 138, 140



urine osm 355
serum osm 295

Assessment and Plan

- 36-year-old female with a pituitary lesion since 2005 with no definitive evidence of gross endocrinopathy but persistent growth who underwent transsphenoidal surgery, found to have a fluid filled cyst.
  - Diabetes insipidus:
    - Monitor UOP and Na.
    - Would recommend DDAVP x1 (not standing) as needed.
    - Drink to thirst.
  - Adrenal axis:
    - Unable to assess cortisol function in the setting of perioperative dexamethasone.
    - Recommend discharge regimen of hydrocortisone 20 mg QAM and 10 mg QPM.
  - Thyroid axis: Prior labs suggested mild secondary hypothyroidism.
    - Check TFTs: TSH 0.62, free T4 1.81
    - Started on levothyroxine 50 mcg daily, then discontinued.
  - Gonadal axis: Menses regular.
  - Hyperglycemia: Fasting blood sugar of 143 on dexamethasone. History of overweight and dyslipidemia.
    - Check HgbA1c: 5.3%.

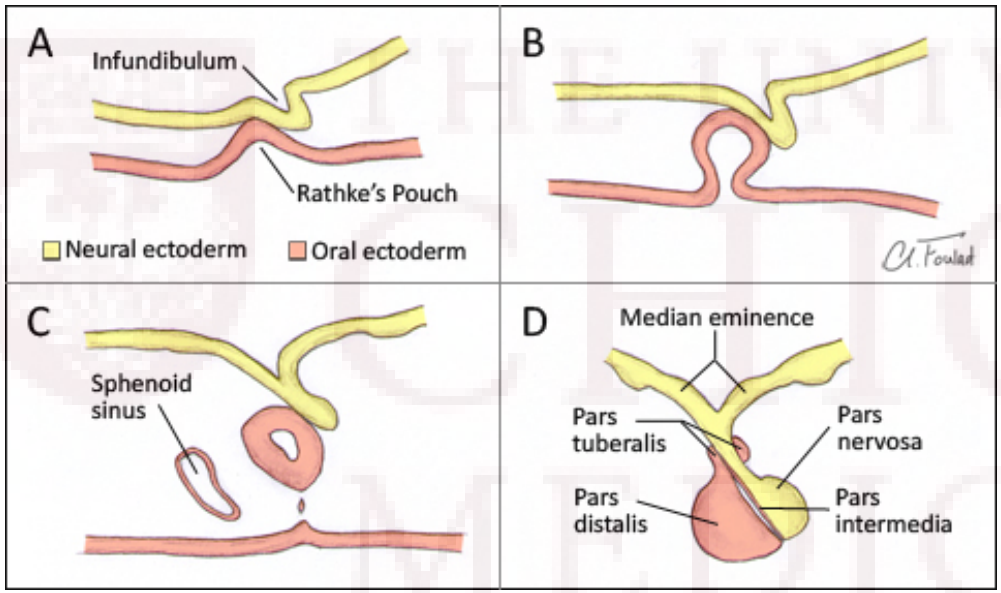
Follow up

- Discharged on POD #5
- Discharged on:
  - Hydrocortisone 20/10
  - Desmopressin 0.1 mg po prn
- Endocrine follow up on 10/22/12

Objectives

- Review Rathke's cleft cysts
  - Presenting symptoms
  - Postoperative management
  - Differences compared to pituitary adenomas
- Review steroid management peri-pituitary surgery

Rathke's cleft cyst



- Benign
- Common: 12-33% in routine autopsies
- Usually 1-2 cm, case reported up to 5 cm
- Intrasellar, up to 60% with suprasellar extension
- Symptomatic cases are rare: 5-15% of all surgically resected sellar lesions
- Female:male ratio up to 3 for presence and associated apoplexy.

http://emedicine.medscape.com/article/1899167-overview

Clin Endocrinol (Oxf). 2012 Feb;76(2):151-60.

Rathke's cleft cyst

- Small, asympomatic RCC do not require surgery.
  - In a series of nonoperated presumed RCCs, 26-94% did not progress during follow up periods up to 9 years.
- Symptomatic RCC is an indication for surgery.
  - Associated with compression of adjacent structures.
  - Goal of surgery is to drain cyst content and remove as much of the capsule as possible.
  - May spontaneous involute, described in 9/29 patients.
    - Headache resolved in 5/7 patients.

Table 1. Manifestations at presentation in patients with Rathke's cleft cysts

References	No of patients	Headache (%)	Visual disturbances (%)	Pituitary hormone dysfunction (%) (one or more axes affected)
Trifanescu *et al.*[49]	33	67	58	58
Xie *et al.*[65]	23	65	39	26
Wait *et al.*[24]	73	75	39	49
Madhok *et al.*[17]	35	81	–	19
Nishioka *et al.*[22]	46	59	35	24
Nishioka *et al.*[9]	37	49	38	24
Aho *et al.*[26]	118	–	49	66
Benveniste *et al.*[5]	62	71	20	55
Kim *et al.*[8]	53	81	47	–
Kasperbauer *et al.*[56]	29	55	–	66
Isono *et al.*[15]	15	33	33	60
Shin *et al.*[10]	26	65	38	81
Mukherjee *et al.*[4]	12	50	75	25 (panhypopituitarim)
Eguchi *et al.*[6]	19	–	47	47
Ross *et al.*[23]	43	44	12	
Volker *et al.*[19]	155	49	56	39

Clin Endocrinol (Oxf). 2012 Feb;76(2):151-60.

Rathke's cleft cyst

- Trifanescu et al. cohort of 33 patients:

	At presentation
FSH/LH deficiency[a]	60% (18/30)
ACTH deficiency	36% (10/28)
TSH deficiency	36% (11/29)
On desmopressin	18% (5/27)
Hyperprolactinaemia	31% (9/27)

- Compared with nonfunctioning pituitary adenomas, 122 cases:
  - Gonadal (67%) > thyroid (39%) > adrenal axis (24%)
  - Hyperprolactinemia: 46-68%

Eur J Endocrinol. 2011 Jul;165(1):33-7.
Clin Endocrinol (Oxf). 2012 Aug 13. doi: 10.1111/cen.12009.

Rathke's cleft cyst

- Trifanescu et al. cohort of 33 patients:

	At presentation	Post-operatively	Last assessment
FSH/LH deficiency[a]	60% (18/30)	52% (14/27)	50% (15/30)
ACTH deficiency	36% (10/28)	43% (13/30)	42% (13/31)
TSH deficiency	36% (11/29)	43% (12/28)	47% (14/30)
On desmopressin	18% (5/27)	39% (13/33)	39% (13/33)
Hyperprolactinaemia	31% (9/27)		

- Recovery of anterior pituitary hormone deficits is not common.
  - Compared to non-functioning pituitary macroadenomas: 39% recovered in 93 cases.
  - Poor endocrine prognosis for Rathke's cleft cysts is probably related to pituitary damage attributed to chronic pressure by the cyst, chronic inflammation following cyst rupture, or effects of surgery.
- New postoperative conditions:
  - Anterior hormone pituitary deficits: 4-30%
    - Similar to non-functioning pituitary macroadenomas: 25%
  - Diabetes insipidus: 2-67%
    - Higher risk with intraoperative CSF leak.

Clin Endocrinol (Oxf). 2012 Feb;76(2):151-60.
Eur J Endocrinol. 2011 Jul;165(1):33-7.
Clin Endocrinol (Oxf). 2012 Aug 13. doi: 10.1111/cen.12009.
J Neurosurg. 2005 Sep;103(3):448-54.

Rathke's cleft cyst: relapse

- Relapse:
  - Range between 0-33%.
  - Most occur within 5-6 years.
  - Risk factors: squamous metaplasia in the cyst wall, cyst size, presence of inflammation, enhancement of the lesion on MRI, use of abdominal fat and/or fascial graft for closure, and intraoperative CSF leak.
- Trifanescu et al. cohort of 33 patients
  - At the 2 year follow up, relapse free rate was 88%. At 4 years, the rate was 52%.

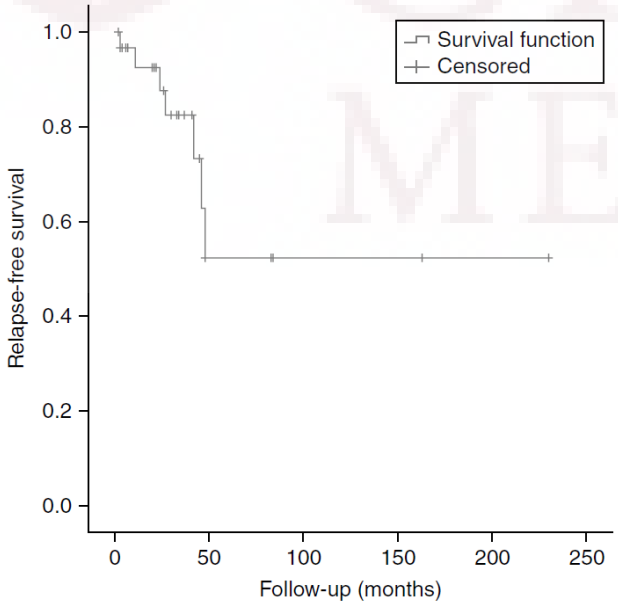


Table 3 Pituitary function at presentation and at the last assessment in patients with relapse (data are presented as the number of patients and the relevant percentages).

	At presentation	Last assessment
FSH/LH deficiency[a]	67% (4/6)	83% (5/6)
ACTH deficiency	50% (3/6)	57% (4/7)
TSH deficiency	50% (3/6)	57% (4/7)
On desmopressin	50% (3/6)	71% (5/7)

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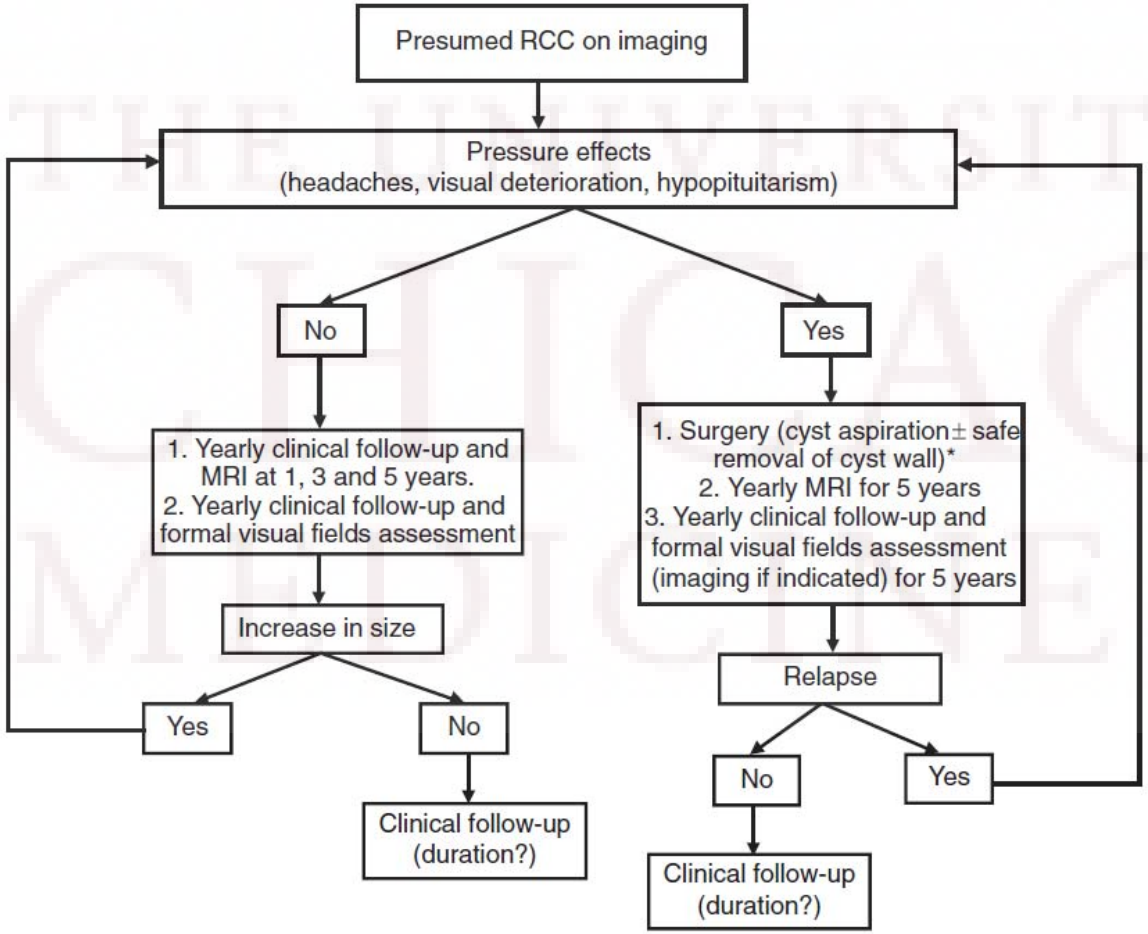
Management Algorithm



* In case of multiple relapses external irradiation may be considered

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Do all patients undergoing TSS need stress dose steroids?

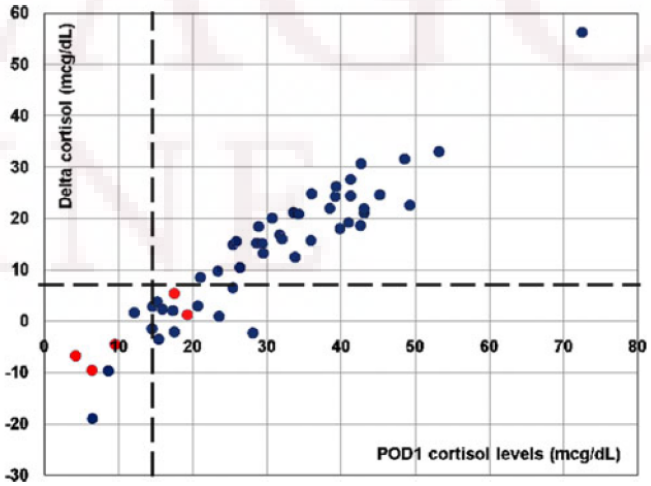
- Marko et al. at Cleveland Clinic prospectively studied 83 consecutive patients who underwent TSS for pituitary adenoma.
  - 77% had early postoperative AM cortisol levels ≥15.
    - 52/64 (81%) had sufficient response to CST at 1-3 mo follow up visit.
    - 12 had insufficient response to CST
      - 9 had normal response to ITT or MTT.
      - 1 had insufficient response and was started on steroid supplementation
      - 2 refused further testing.
    - Overall, 1.6% demonstrated HPA dysfunction.
  - 23% had early postoperative AM cortisol levels <15
    - 15 patients had normal CST results at follow up; 4 had abnormal results.
  - ROC: cutoff values of ≥ 15.0 or even as low as ≥ 12.0 µg/dl

J Neurosurg. 2009 Sep;111(3):540-4.

Do all patients undergoing TSS need stress dose steroids?

- Zada et al. at BWH retrospectively reviewed 52 patients who underwent TSS for pituitary lesions.
  - "Postoperative stress response, "
    or Δ cortisol index =
    POD 1 AM cortisol – preop AM cortisol
    - Mean preop cortisol level: 16.5
    - Mean POD1: 29.2
  - Δ cortisol index: -19.0 to +56.2 (mean +12.7)
  - 5 patients had early postop (POD 1-3) hypocortisolemia.
    - Mean Δ cortisol of -2.8 compared to +14.4 in patients without evidence of AI
    - Only 1 patient needed steroids >6 weeks.
  - Of the 48 patients sent home without, none develop postop AI.

Test	Sensitivity (%)	Specificity (%)
POD1 cortisol level <15 μg/dL	60	89
Δ cortisol index less than +6.0 μg/dL	100	74
Δ cortisol index less than +1.5 μg/dL	80	85



Zada et al. Pituitary. 2012 Aug 23. [Epub ahead of print]

Is the cort stim reliable?

- Klose et al. retrospectively studied 110 patients after transsphenoidal adenomectomy.
  - Cort stim (250 ug) was performed at 1 week and 1, 3, 6, and 12 months postop.
    - 32 developed secondary AI: 7 had a positive test after 1 week, 16 after 1 month, and 9 after 3 months.
    - None developed AI after 3 months.
    - Predicted by postoperative DI (OR=4.0, p=0.03)
  - Cort stim may be unreliable in the immediate postoperative setting (<3 mo).

Klose et al. Clin Endocrinol (Oxf). 2005 Nov;63(5):499-505.

Is the cort stim reliable?

- Dokmetas et al. propsectively studied 19 patients after transsphenoidal surgery.
  - ITT and 1 ug and 250 ug cort stim test were performed between POD 4-11 and repeated at the 3rd month.
  - Early postop period: only ITT and 1 ug stim test correlated.
    - 6 patients had subnormal ITT: 2 patient had normal response to 1 ug test, 5 patients had normal response to 250 ug test
  - Late postop period: all patients had normal HPA axis
  - Authors conclude that HPA axis dysfunction shown by ACTH stimulation tests and the ITT in early postoperative period may be normalized within 3 months after surgery and these dynamic tests may not be useful early after pituitary surgery.

J Clin Endocrinol Metab. 2000 Oct;85(10):3713-9.

References

- Caputo et al. Clin Endocrinol (Oxf). 2012 Aug 13. doi: 10.1111/cen.12009. [Epub ahead of print]
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- Nemergut et al. J Neurosurg. 2005 Sep;103(3):448-54.
- Marko et al. J Neurosurg. 2009 Sep;111(3):540-4.
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    - Overall, 1.6% demonstrated HPA dysfunction.
  - 23% had early postoperative AM cortisol levels <15
    - 15 patients had normal CST results at follow up; 4 had abnormal results.
  - ROC: cutoff values of ≥ 15.0 or even as low as ≥ 12.0 µg/dl
- McLaughlin et al. in Santa Monica studied 207 patients with pituitary adenoma or Rathke's cleft cyst
  - Only treated if cortisol level ≤4.
  - 9 patients had early post operative hypocortisolemia; 5 were weaned off
  - 3/130 patients with "normal" cortisol levels later required steroids
  - Concluded sensitivity of 96%, specificity of 57%, and positive predictive value of 98%

J Neurosurg. 2009 Sep;111(3):540-4.
World Neurosurg. 2012 Aug 14.