



36 year old woman with
pituitary mass

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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

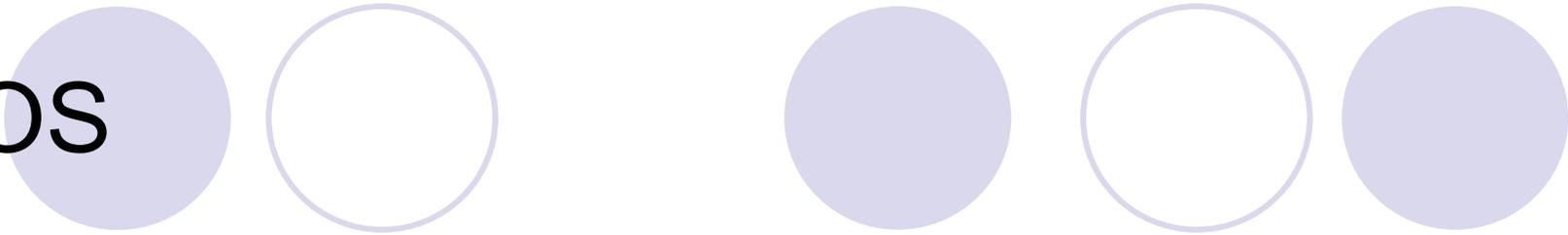
- Family History:

- 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.

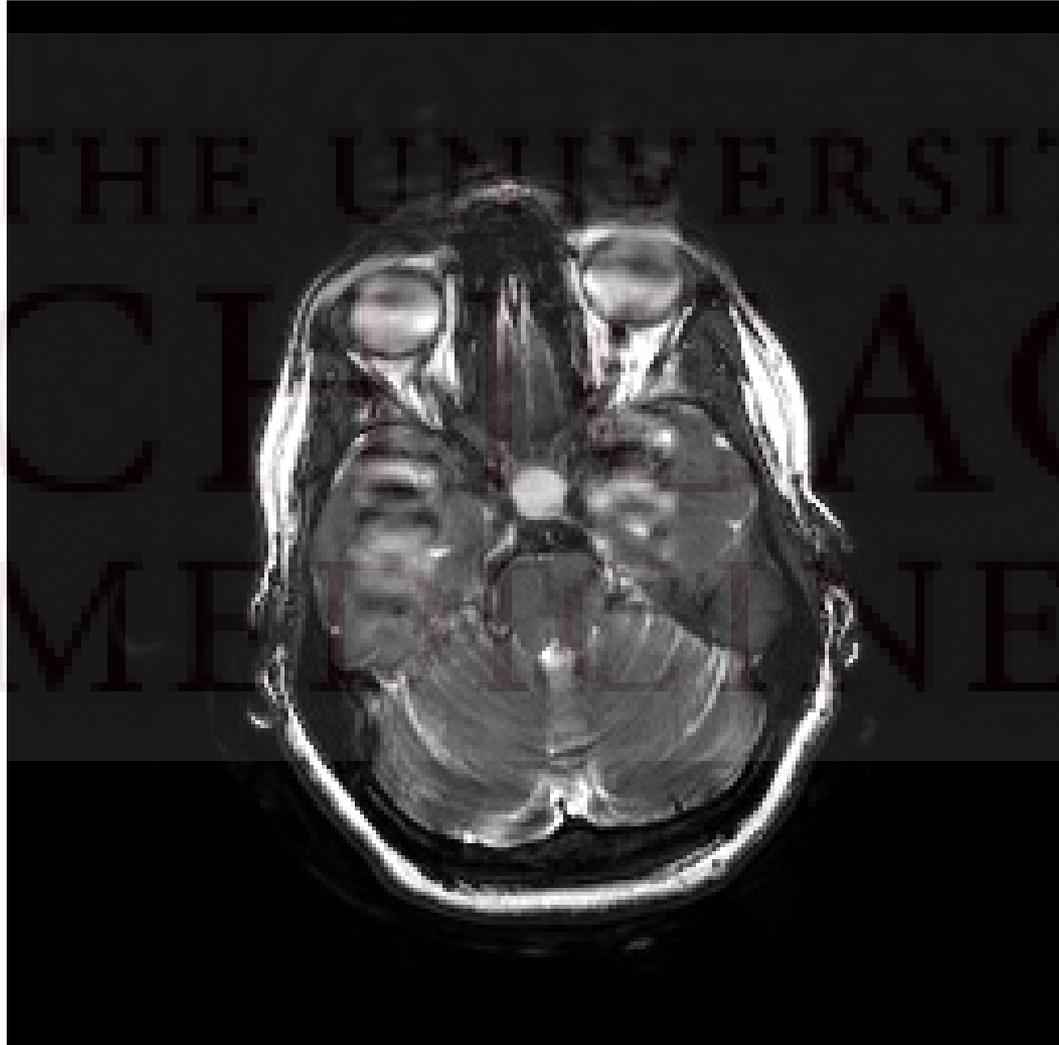
Physical Exam

- VITAL SIGNS: Blood pressure 116/76, pulse 81, weight 166 pounds, height 5'5", BMI 27.6 kg/m².
- 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

$\frac{138 \ 107 \ 9}{3.5 \ 23 \ 0.8} \left\{ \begin{array}{l} 114 \\ 114 \end{array} \right.$
Ca 9.3

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

~~$\frac{14.2}{7.7 \ 248} \left\{ \begin{array}{l} 43.1 \\ 43.1 \end{array} \right.$~~

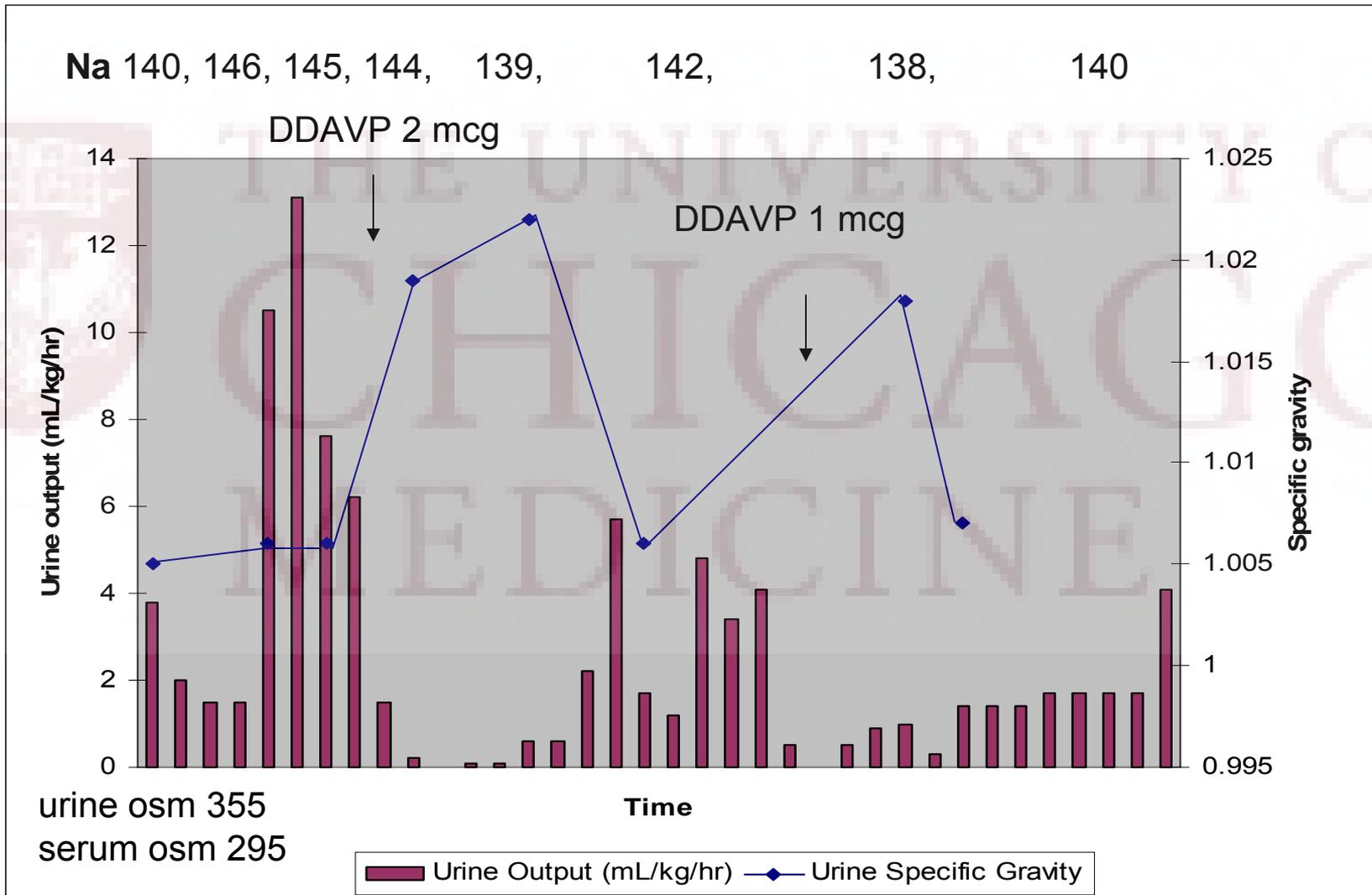
● Post op labs

$\frac{140 \ 111 \ 9}{3.6 \ 22 \ 0.6} \left\{ \begin{array}{l} 128 \\ 128 \end{array} \right.$
Ca 8.3

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

~~$\frac{13.1}{16.0 \ 261} \left\{ \begin{array}{l} 38.8 \\ 38.8 \end{array} \right.$~~

Na and UOP trend



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%.

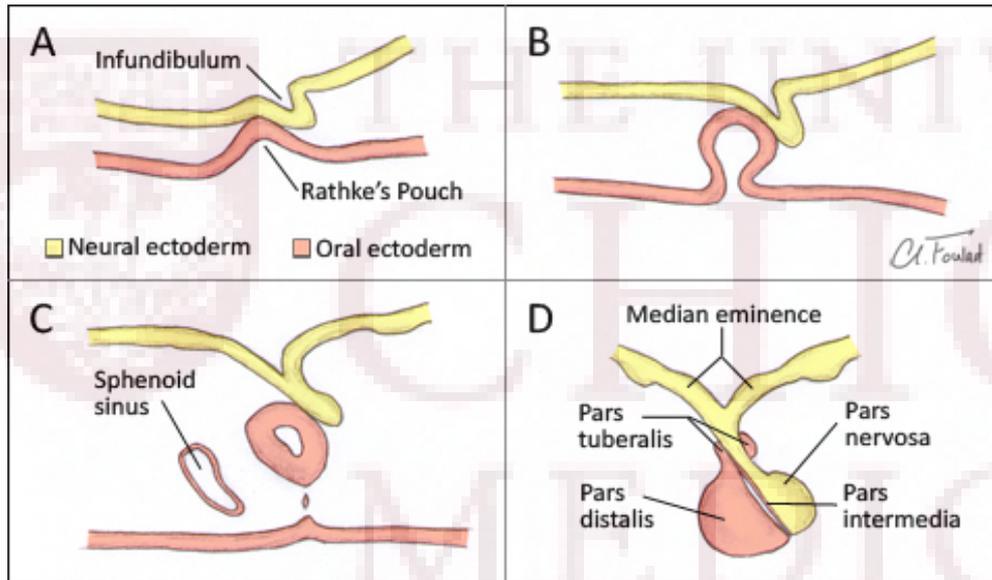
Follow up

- 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

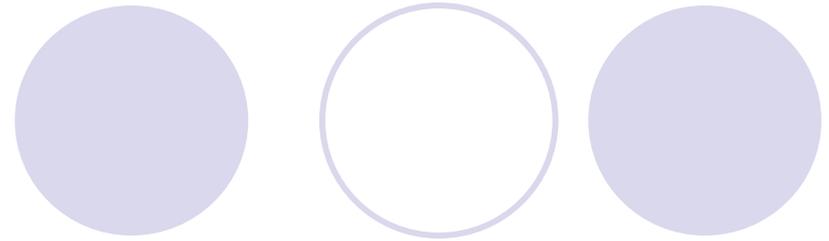


- Benign
- Common: 12-33% in routine autopsies
- Usually 1-2 cm, case reported up to 5 cm
- Intrasellar, up to 60% with suprasellar extension
- Symptomatic cases are rare: 5-15% of all surgically resected sellar lesions
- Female:male ratio up to 3 for presence and associated apoplexy.

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

[Clin Endocrinol \(Oxf\)](#). 2012 Feb;76(2):151-60.

Rathke's cleft cyst



- Small, asymptomatic 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 spontaneously 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 <i>et al.</i> ⁴⁹	33	67	58	58
Xie <i>et al.</i> ⁶⁵	23	65	39	26
Wait <i>et al.</i> ²⁴	73	75	39	49
Madhok <i>et al.</i> ¹⁷	35	81	–	19
Nishioka <i>et al.</i> ²²	46	59	35	24
Nishioka <i>et al.</i> ⁹	37	49	38	24
Aho <i>et al.</i> ²⁶	118	–	49	66
Benveniste <i>et al.</i> ⁵	62	71	20	55
Kim <i>et al.</i> ⁸	53	81	47	–
Kasperbauer <i>et al.</i> ⁵⁶	29	55	–	66
Isono <i>et al.</i> ¹⁵	15	33	33	60
Shin <i>et al.</i> ¹⁰	26	65	38	81
Mukherjee <i>et al.</i> ⁴	12	50	75	25 (panhypopituitarism)
Eguchi <i>et al.</i> ⁶	19	–	47	47
Ross <i>et al.</i> ²³	43	44	12	
Volker <i>et al.</i> ¹⁹	155	49	56	39

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%

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%.

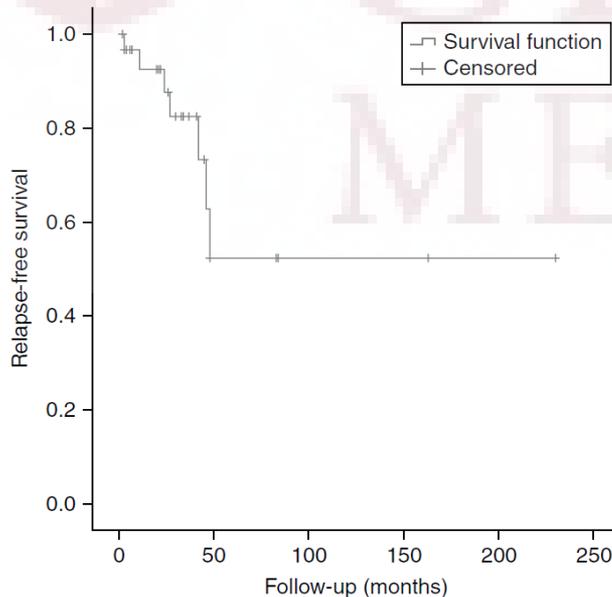
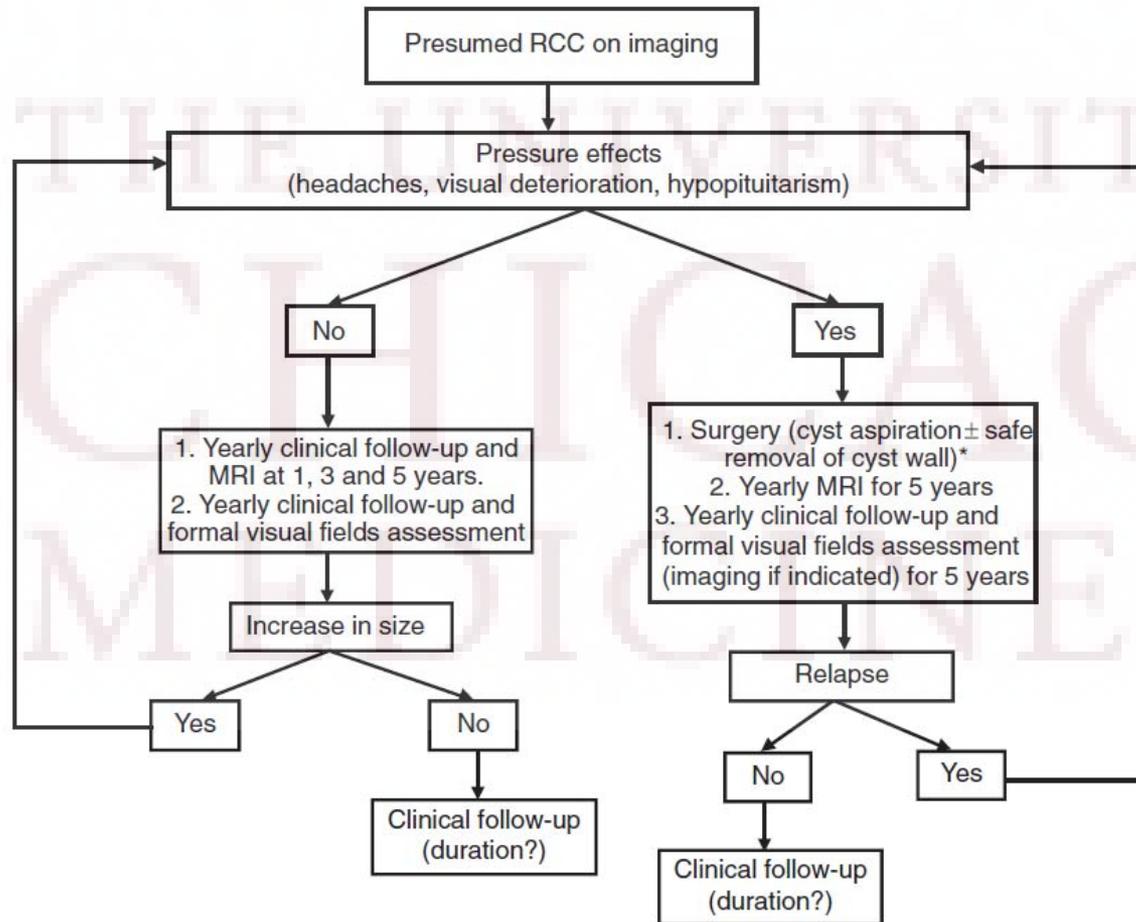


Table 3 Pituitary function at presentation and at the last assessment in patients with relapse (data are presented as the number of patients and the relevant percentages).

	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)

Management Algorithm



* In case of multiple relapses external irradiation may be considered

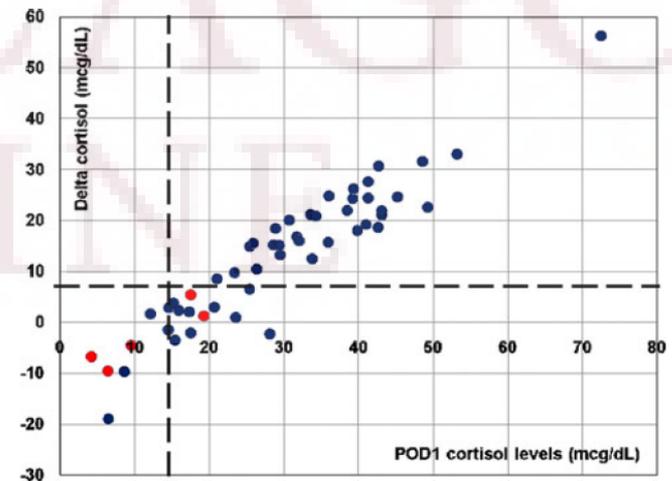
Do all patients undergoing TSS need stress dose steroids?

- 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 $\mu\text{g}/\text{dl}$

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 $\mu\text{g/dL}$	60	89
Δ cortisol index less than +6.0 $\mu\text{g/dL}$	100	74
Δ cortisol index less than +1.5 $\mu\text{g/dL}$	80	85



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).

Is the cort stim reliable?

- Dokmetas et al. prospectively 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.

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.
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- McLaughlin et al. [World Neurosurg](#). 2012 Aug 14.
- Trifanescu et al. [Clin Endocrinol \(Oxf\)](#). 2012 Feb;76(2):151-60.
- Trifanescu et al. [Eur J Endocrinol](#). 2011 Jul;165(1):33-7.
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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 $\mu\text{g}/\text{dl}$
- 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%