Perioperative management of the pituitary patient: The endocrine perspective

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Cnflicts of Interest/ Disclosures

- None to report

A Tale of Two Tumors

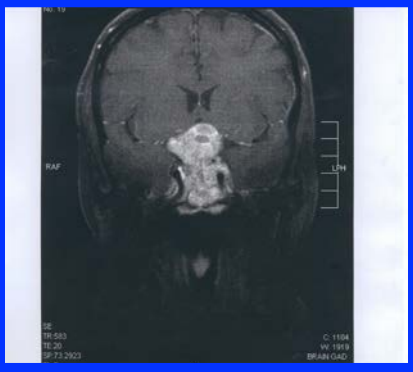
Objectives

By the end of this talk, you should understand:

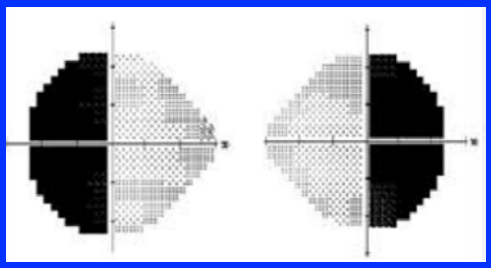
1. Indications for surgery for the pituitary adenoma.
2. Perioperative management of HPA axis.
3. Postoperative water balance disturbances.
4. How to assess postoperatively for:
   - Hormonal cures
   - Hormonal deficiencies

Case 1

- Ms DR 44 year old female
- PMH:
  - Breast reduction
  - Oral contraception X 25 years
- Bitemporal hemianopsia
- Prolactin 200 μg/L



Visual field defect



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Does she need surgery?

Hook effect

- Comtois Ann Intern Med 1993
  - "very high levels of antigen (prolactin) can impair the radioimmunometric assay" (not enough antigen has two antibodies bound to it)
- Prolactin 100-200 ng/dl undiluted
- Large (5 cm) tumors, males
- Respond to dopamine agonists (DA)
  - St Jean E Clin Endocrinol 1996

Serially diluted prolactin...

- 13, 072 μg/L

- 8 AM cortisol 415 nmol/L
- GH < 0.1 μg/L
- LH 0.3
- FSH 1.5
- IGF-1 49 μg/L
- TSH 3.77 mU/L
- free T4 7.9 pmol/L

How effective are DA in the treatment of macroprolactinomas with mass effect?

Study	Visual fields normalized	Visual fields better	Tumor shrinkage
Verhedst JCEM 99	70%		67%
Corsello Clin Endo 2003			90%
Shimon Eur J Endo 2007	33%	57%	

How effective is surgery in the treatment of nonfunctional adenomas with mass effect?

- Surgical series (Marazuela) for non-functional tumors:
- Pre-op: 60% had visual field defect
  - 3/3 remained blind
  - 28% regained normal sight
  - 67% variable improvement

Case 2: Ms SP

- 25 year old administrator
- Started "looking different" 4-5 years ago
- Many features of acromegaly

Case continued...

- Investigations:
  - GH: 25 μg/L
    - Glucose suppression test: GH ↑37.8 μg/L
  - IGF-1 974 μg/L
  - Baseline pituitary function tests:
    - **FSH 1.1**
    - **LH 0.1**
    - **8 AM cortisol 127**
    - **ACTH 8**
    - **prolactin 17.9**
    - **TSH 1.13**
    - **free T4 8**

Visual field testing

- Normal

Does she need surgery?

- What would the goals of surgery be?

Does she need surgery? YES

- What would the goals of surgery be?
  - Cure acromegaly
    - 70% cure microadenomas, non-invasive macroadenomas
    - much lower if invasive
  - Restore pituitary function?

Hypopituitarism: Hormonal response to surgery

- Marazuela J Endocrinol Invest 1994
- Arafah JCEM 1986
- Webb JCEM 1999

% of patients with hormonal deficiencies pre-and post-selective adenectomy

Study	↓LH/ FSH Pre	↓LH/ FSH Post	↓T4 Pre	↓T4 Post	↓cortisol Pre	↓cortisol Post
Mara-zuela	70%	50%	23%	20%	20%	10%
Arafah	96%	30%	81%	34%	62%	38%

"Half improve, half stay the same"; who gets worse?

Postoperative pituitary function

- Webb JCEM 1999
- 234 patients
  - 93 (40%) had preoperative deficit
- Postop:
  - 52 (22%) had a new deficit (3-4% in other studies)
  - Of those with preop deficit:
    - 45 (48%) recovered 1-3 deficiencies

Predictors of recovery of function

- Normal or mildly elevated prolactin preoperatively
- Rise in TSH after TRH administration
  - Arafah JCEM 1986

Why?

How will we prepare her for surgery?

1. Indications for surgery for the pituitary adenoma

- Mass effect
- Hypersecretion
  - Acromegaly (if curable or if mass effect)
  - Cushing's disease
  - ↑TSH
- Hypopituitarism

Indications for surgery for the pituitary adenoma

- Mass effect
- Hypersecretion
- Hypopituitarism

Prolactinoma is the exception!!!

How will we prepare her for surgery?

- Hormonal deficiencies?
  - 8 AM cortisol 127 (repeated)
- Metabolic/cardiac complications of acromegaly?

2. Perioperative management of HPA axis.

- Intraoperative steroids for all?
- If not, for whom is it safe to withhold therapy?
- How should we assess for the need for postoperative steroids?

Do we want to give our patient GC coverage?

- Preoperatively?
- Intraoperatively?
- Post-op: Do we need to reassess its need?

Intraoperative steroids for all?

- Some centres give glucocorticoid (GC) coverage to all patients undergoing transsphenoidal surgery
  - Jane JA Neurosurg 2002 , Dumont AS J Intensive Care Med 2005
- Concern: the tumor/surgery would blunt the normal rise in GC required to handle the stress of surgery

Evaluation of the HPA axis immediately after pituitary adenectomy: Is perioperative steroid therapy necessary? Hout WM JCEM 1988

- Assessed patients pre-op with ITT or metyrapone tests of HPA axis function
- Followed 83 patients (normal HPA) with no GC coverage
- Cortisol levels:
  - 6 hr: 1110 nmol/L
  - Day 4-7: 450 nmol/L
- 2/83 developed postoperative hypoadrenalism

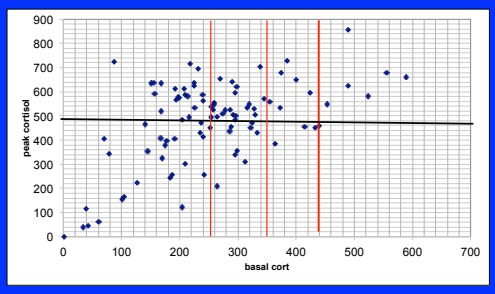
For whom is it safe to withhold therapy?

- Some groups use basal cortisol and cortrosyn stimulation test
- Is just basal good enough?

Using basal 8 AM cortisol to decide on the need for intraoperative GC

- Hout: 5 patients with pre-op hypoadrenalism: basal cortisol ranged from 14-215 nmol/L
- Pavord SR Clin Endocrinol 1992
  - Reviewed 232 ITT from 1980's
  - Needed basal cortisol > 400 nmol/L to exclude hypoadrenalism
- Jones SL Clin Endocrinol 1994
  - reviewed 161 ITT done in 1991
  - needed a basal cortisol of >500 nmol/L to exclude hypoadrenalism

SMH ITT 2006-2010 Goldberg



Using basal 8 AM cortisol to decide on the need for intraoperative GC

- Basal cortisol 350-500: < 4% fail ITT, most of these have peak cortisol close to 500 nmol/L.
- Is basal cortisol > 250 nmol/L highly predictive of normal ITT?
  - Inder JCEM 2002

Need for perioperative GC coverage

- None given unless preoperative early morning cortisol was < 112 nmol/L
- (Postop GC Rx was given for morning cortisol < 112 nmol/L
  - Sensitivity 96%, specificity 57%, PPV 98%)
  - McLaughlin World Neurosurg 2013
- Nothing happened to 9 patients with preoperative early morning cortisol < 220 who did not receive GC Rx
  - DeTomassi Acta Neurosurg Wien 2012

Assessing the need for postop steroids:

Inder JCEM 2002 & Jayasena Clin Chem 2009:

Measure 8 AM plasma cortisol

- Day 1-3: if on no GC coverage
- Day 3-5: with GC coverage, >24 hours after last dose

Replacement based on 8 AM cortisol level:

- < 100 nmol/L: give GC (diagnosis made)
- 100-250 nmol/L: give GC, do ITT
- 250-399 nmol/L: ITT at 4-6 weeks
- >400 nmol/L: no further testing (normal HPA)

When should the ITT be done?

- First week (day 5-8) is valid
  - Auchus Clin Endocrinol 1997
- Need to wait until 1-3 months post op (early dysfunction can normalize later)
  - Dökmetaş JCEM 2000

3. Postoperative water balance disturbances.

- DI
- SIADH

DI

- How common is it?
- What are the patterns of DI?
- How should we recognize and treat it?
- What advice should we give our patients on discharge?

DI: Incidence and pattern

- Incidence: 0.5-25% of cases postop
- Seckl BMJ 1989
  - Reviewed 1571 postop patients
  - Day 3: 17%; Day 7: 6%

DI: Incidence and pattern

- Incidence: 0.5-25% of cases postop
- Seckl BMJ 1989
  - Reviewed 1571 postop patients
  - Day 3: 17%; Day 7: 6%
- Patterns:
  - Transient (Days 1,2 postop)
  - Permanent
  - Triphasic:
    - ↓ ADH day 1,2 ("nerve shock")
    - ↑ ADH day 1-14 (release of preformed ADH)
    - ↓ ADH day: once reserves gone

DI: Diagnosis

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- Negative fluid balance
  - rule out redistribution of OR fluids
- Plasma Na+ elevated
  - rule out "polydipsia" (appropriate secretion of excess water)

DI: Therapy

- DDAVP 1 μg sc prn
  - Later 60-120 ug oral melt or 10 μg intranasal qhs
  - Titrate to sleep through the night
  - Add A.M. dose prn to maintain reasonable day time urine output
- Watch fluid intake
- Watch plasma sodium/correct prn
- Reassess need 2 weeks later

SIADH

- Incidence
- Etiology
- How to recognize and treat it

SIADH

- Incidence
  - Plasma [Na^+] < 135: 25-40% of patients
  - Symptomatic hyponatremia: 7-9%
- Etiology
  - day 5-10 postop
  - female, premenopausal
- How to recognize and treat it
  - R/O: hypoadrenalism, hypothyroidism, cerebral salt wasting
  - Fluid restriction +/- salt

SIADH

Janhangiri J Neurosurg 2013

- Reviewed 1045 pituitary surgeries
- Postop hyponatremia
  - after 165 operations (16%)
  - Average 4 days after surgery (range 0-28 days)
  - 20% were symptomatic
- Only preop hypopituitarism predicted postoperative hyponatremia
- The mean correction rates:

No treatment (n = 112): 0.4 mEq/L/hr
Free water restriction (n = 24): 0.5 mEq/L/hr
Salt tablets (n = 14) = 0.7 mEq/L/hr
3% saline (n = 20) = 0.3 mEq/L/hr
IV vasopressin receptor antagonist Vaprisol (n = 22) = 0.7 mEq/L/hr
Oral vasopressin receptor antagonist tolvaptan (n = 9) = 1.2 mEq/L/hr (p = 0.002, ANOVA).

SUMMARY: Role of endocrinologist

- Preop:
  - ?role for medical therapy
    - prolactinoma
    - R/O hook effect
  - assess for hormonal excess/deficiency
  - assess for metabolic/cardiovascular complications (if Cushing's, acromegaly, panhypopit)
  - decide for need for intraoperative GC

Intraoperatively GC coverage

- Ordered for transsphenoidal selective adenectomy:
- Hydrocortisone 50 mg iv q 8 hr if basal 8 AM cortisol is < 220 nmol/L

How to assess postop for Hormonal cure

Excess hormone	When to test	Test to use
Prolactinoma	Day 1	Prolactin< 10
Acromegaly	Day 7 Months 3-12	GH< 1 on OGST IGF-1
Cushing's	Q 6 hr	Cortisol off GC
	8 AM day 3	Cortisol 24 hr after GC < 157*

↓↓ 8 AM cortisol (<100 nmol/l) = highly predictive of remission

AbdelMannan Rev Endo Metab Disorders 2010

Krikorian Neurosurg Focus 2007

How to assess postoperatively for Hormonal deficiencies

Hormone	When
Prolactin	Week 1,4: marker for pituitary destruction
Cortisol	Q 12 hr
T4	Day 7
Sex hormones	1-2 month: history, testosterone/estradiol
GH	ITT (4-6 weeks)
ADH	Daily Ins/outs, plasma Na Watch for delayed SIADH

Conclusions

We have reviewed:

1. Indications for surgery for the pituitary adenoma (and who can be treated medically).
2. Perioperative management of HPA axis.
3. Postoperative water balance disturbances.
4. How to assess postoperatively for:
   - Hormonal cures
   - Hormonal deficiencies