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Guidelines for Perioperative Management of Pituitary Adenomas

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Perioperative management plays a critical role in the treatment of pituitary adenomas requiring surgery. In this brief review, general guidelines were given for perioperative managements of the prolactin, growth hormone, ACTH producing adenomas as well as the endocrine inactive adenoma. Perioperative steriod supplement, postoperative diabetes insipidus monitoring and other endocrine evaluation were also included.

The management of pituitary adenomas is best carried out by a multidisciplinary approach, in which a team consists of at least endocrinologist, neuroradiologist and neurosurgeon working together in the diagnostic and treatment planning of the patients. However, this ideal situation may not exist in some hospitals and the neurosurgeons may have to manage these patients most of the time by themselves. In this unfortunate setting, the knowledge of neuroendocrinology will be crucial to ensure that these patients receive adequate and relevant perioperative evaluation and management. In this review, guidelines for the perioperative management of patients with the commonly found pituitary adenomas were given based on the routine practice at the Toranomon Hospital, which is a referral center for pituitary surgery in Tokyo.

PERIOPERATIVE MANAGEMENT

In modern neuroendocrinology, the preoperative patient evaluation is not only for diagnostic purpose but will also play a great role in the surgical decision making, postoperative adjunctive treatment planning in cases of incomplete tumor removal or supplement therapy for important hormone deficits.[1-3]

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In general, a complete dynamic evaluation of pituitary function is performed in every case to document the response profiles of the hypersecreted hormones as well as the functional reserve of the normal gland. This usually includes the measurements of various basal hormone levels followed by certain provocative tests.[2-9] Because it is now known that the endocrine inactive adenoma may secrete some hormones or hormone subunits,[10,11] it will become more common to include the assays of these substances in this group of patients.

The present state of the art in neuroimaging plays a significant role in the definition of pituitary tumors especially in micro and picoadenomas. Direct coronal CT, plain and enhanced T1-W MRI in coronal as well as sagittal sequences could reach the diagnosis in most of the cases.[3,11,12] For smaller lesions, dynamic MRI is added to the routine investigation. Polytomography, though does not assist in the diagnosis, is still performed to aid surgical planning.[1] Angiography is rarely needed nowadays to exclude the possibility of aneurysm.[1] In such situation, the non-invasive MRA may be sufficient to provide the final answer.

All patients with macroadenomas also undergo opthalmological evaluation[13] and those with abnormal findings are reassessed postoperatively within the same admission period.

Table 1 Guide for abbreviations.

ACTH	= Adrenocorticotropic hormone
CRH	= Corticotropin releasing hormone
FSH	= Follicle stimulating hormone
GH	= Growth hormone
GRH	= Growth hormone releasing hormone
IGF-1	= Insulin like growth factor 1 (somatomedin C)
LH	= Luteinizing hormone
LHRH	= Luteinizing hormone releasing hormone
OHCS	= Hydroxycorticosteroid
PRL	= Prolactin
T3/T4	= Thyroid hormones
TRH	= Thyrotropin releasing hormone
TSH	= Thyroid stimulating hormone

Perioperative steriod management is routine for every patient and is tappering off within a week. Then, the pituitary-adrenal axis is reassessed to determine long term management. Prophylactic antibiotics is given prior to surgery and continued for 3 day postoperatively. Monitoring for diabetes insipidus (DI) is started in the operating room and is continued for 4 to 5 days after the operation. In general, about 50 per cent of patients may develop mild transient DI which is self-limiting and does not require the administration of vasopressin.

The nasal tubes and/or nasal packing are remained in place for 3 to 4 days. In extreme cases, this packing may be kept for 7 days. Occasional suction of the nasopharyngeal secretion may be needed but usually no special medication is required.

Patients with uneventful course are discharged in 10-14 days postoperatively after the function of the pituitary-adrenal axis is ascertained. The more complete endocrine evaluation relevent to individual specific problem is usually performed at the later follow up in 2-3 weeks.

PREOPERATIVE EVALUATION

Workups for Prolactin Secreting Adenoma

Neuroimaging

- CT direct coronal.
- MRI coronal and sagittal;

microadenoma adds Dynamic MRI coronal section.

- Tomogram sphenoid sinus, coronal and sagittal.

Routine laboratory tests

Endocrine laboratory tests

A. Basal plasma hormone levels.

PRL, TSH;

GH, ACTH, LH, FSH;

T3, T4, cortisol;

estrogen, progesterone for female and testosterone for male.

B. Provocative tests.

- Bromocriptine suppression test (Parlodel 2.5 mg PO); preadministration plasma PRL, postadministration samples at 1,

2, 4, 6, 12 and 24 hours.

- TRH stimulation test (TRH 500 micrograms IV); preadministration plasma PRL, TSH, postadministration samples at 30, 60, 90 and 120 minutes.

- LHRH stimulation test (LHRH 100 micrograms IV); preadministration plasma LH, FSH, postadministration samples at 30, 60, 90 and 120 minutes.

Workups for Growth Hormone Secreting Adenoma

Neuroimaging

The same as in prolactin producing adenoma, and plain films of hands (for cauliflower-like tufting), feet (for heel pad thickness; more than 20 mm is abnormal), spine (for kyphosis and scoliosis).

Routine laboratory tests

Endocrine laboratory tests

A. Basal plasma hormone levels.

Fasting morning level of GH, IGF1, somatomedin C;

PRL, TSH or alpha subunit;

ACTH, LH, FSH;

T3, T4, cortisol;

estrogen, progesterone for female and testosterone for male

B. Glucose tolerance test (75 g glucose PO);

C. Provocative tests.

- Oral glucose test (75 g glucose PO); preadministration plasma GH, glucose and insulin, postadministration samples at 30, 60, 90, 120 minutes. (Non-suppressibility of GH levels)

- TRH stimulation test (TRH 500 micrograms IV); preadministration plasma GH, TSh, PRL, postadministration samples at 30, 60, 90 and 120 minutes.

- Bromocriptine suppression test (Parodel 2.5 mg PO); preadministration plasma GH, (PRL), postadministration samples at 1, 2, 4, 6, 12 and 24 hours.

- GRH stimulation test (GRH 100 micrograms IV); preadministration plasma GH, postadministration samples at 30, 60, 90 and 120 minues.

- CRH stimulation test (CRH 100 micrograms IV); preadministration plasma ACTH, cortisol, (GH), postadministration samples at 30, 60, 90 and 120 minutes.

- Somatostain suppression test (somatostatin 100 micrograms SC); preadministration plasma GH postadministration samples at 30, 60, 90 and 120 minutes.

- LHRH stimulation test (LHRH 100 micrograms IV); preadministration plasma GH, LH, TSH, postadministration samples at 30, 60, 90 and 120 minutes.

Workups for ACTH Secreting Adenoma

Nouroimaging

The same as in prolactin producing adenoma.

Routine laboratory tests

Endocrine laboratory tests

A. Basal plasma hormone levels.

Fasting morning level of ACTH, cortisol; GH, IGF1, PRL, TSH, LH, FSH; estrogen, progesterone for female and testrosterone for male.

B. Urine hormone levels.

24 hour 17 OHCS (above 10 mg/24 hours or 7 mg/g creatinine excretion);

24 hr free cortisol (above 100 micrograms/24 hours).

C. Biological rhythm evaluation.

Plasma ACTH and cortisol at 8, 11, 16 and 24 hours.

D. Provocative tests.

- Dexamethasone suppression test.

**Overnight screening test:* To confirm the diagnosis of Cushing's syndrome (Dexamethasone 1 mg PO at midnight); preadministration plasma cortisol (at 8.00 hour, morning before), postadministration sample (at 8.00 hour, next morning; above 5 micrograms/dl).

**Standard low dose test:* To confirm the diagnosis of Cushing's syndrome (Dexamethasone 0.5 mg PO every 6 hours for 2 days); preadministration 24 hour urinary 17 OHCS, free cortisol, postadministration 24 hour urinary 17 OHCS, free cortisol; not suppressible in definite Cushing's syndrome.

**Standard high dose test:* More likely to be suppressible in Cusing's disease than in ectopic ACTH syndrome or adrenal neoplasm

(Dexamethasone 2 mg PO every 6 hours for 2 days); preadministration 24 hour uninary 17 OHCS, free cortisol, postadministration 24 hour urinary 17 OHCS, free cortisol; above 50% decrease is considered as suppressible.

**Overnight high dose test:* Modified test, similar to standard high dose test (single high dose Dexamethasone 8 mg PO at night); preadministration plasma cortisol (morning before), postadministration plasma cortisol (next morning); above 50% decrease is considered as suppressible.

- *CRH stimulation test (bovine CRH 1 microgram / kg IV);* preadministration plasma ACTH, cortisol, postadministration samples at 15, 30, 60, 90 and 120 minutes (ACTH, cortisol increase above 50% and 20% are considered as positive tests).

E. Simultaneous bilateral inferior petrosal and cavernous sinus samplings are used in cases of negative or questionable imaging tests.[12,13]

Superselective catheterization is employed. The central to peripheral gradient above 2:1 is usually considered as positive test.

Workups for Endocrine Inactive Adenoma

Neuroimaging

The same as in prolactin producing adenoma.

Routine laboratory tests

Endocrine laboratory tests

A. Basal plasma hormone levels.

PRL, TSH, GH, ACTH, LH, FSH;
FSH, TSH alpha subunits;
T3, T4, cortisol;
estrogen, progesterone for female and testosterone for male.

B. Urine hormone levels.

24 hour OHCS and contisol.

C. Provocative tests.

- Combined TRH, LHRH and GRH, CRH stimulation test; preadministration serum TSH, LH, GH, PRL, FSH, ACTH postadministration samples at 15, 30, 60, 120 minutes.

Opthalmological evaluation

Visual acuity, visual field studies are performed in every case.[13] Patients with abnormal preoperative tests are reevaluated a few days after the surgery.

PERIOPERATIVE STEROID REGIMEN

Steroid is given routinely for patients undergoing pituitary surgery. The following is the general regimen.

Before operation

If hypocortisolism is suspected;
Day -2 : 100 mg Hydrocortisone IM, OD.
Day -1 : Same.
In every case;
Day 0 : 100 mg Hydrocortisone IM

During operation

100 mg Hydrocortisone DIV

After operation

Day 1 : 100 mg Hydrocortisone IM, OD
Day 2 : Same
Day 3 : 50 mg Hydrocortisone IM, OD
Day 4 : Same
Day 5 : 30 mg Cortisol acetate PO, OD
Day 6 : Same
Day 7 : Same
Day 8 : Steriod off
Day 6 : Evaluation (24 hour urinary 17 OHCS, free cortisol).
If normal: Steroid off.

DIABETES INSIPIDUS (DI)

Monitoring and Management

Diabetes insipidus may occur if the posterior pituitary lobe or pituitary stalk is retracted or injured during the operation. The following is the routine observation and management regimen.

When DI is definite (from intraoperative situation).

A. Urine volume monitoring.

- Foley's catheter placement.
- Hourly urine recording.

B. Vasopressin preparation and administration.

- Vasopressin 2-5 units SC every 5-6 hours; or
- Vasopressin 10 units in NSS 200 ml (0.05 unit/ml), IV.

C. Dosage.

- Urine volume above 200 ml/hr, vasopressin solution 1 ml IV.
- Urine volume above 500 ml/hr, vasopressin solution 2 ml IV.
- Urine volume below 60 ml/hr, vasopressin solution off.

D. Fluid supplement.

- Urine volume is not excessively high; PO supplement.
- Urine volume is high; IV supplement in the form of 5% DW.

Routine monitoring

A. Bedside observation.

- Urine output and specific gravity every 1 hour.
- Questioning for the feeling of thirst.

B. Vasopressin preoperative and administration.

- Subcutaneous injection (SC).

C. Dosage.

- Urine volume above 400 ml/hr, vasopressin 2-5 units SC.

D. Fluid supplement.

- Urine volume is not excessively hight; PO supplement.
- Urine volume is high; use IV supplement and start the IV pitressin regimen.

CEREBROSPINAL FLUID RHINORRHEA

If CSF leakage is seen intraoperatively, all effort should be given to careful sellar packing with muscle plus fascia and fibrin glue, followed by sellar floor reconstruction with bone, cartilage or ceremic plate and fibrin glue.

Post-operative CSF rhinorrhea can lead to meningitis and therefore should be treated aggressively. Once CSF leakage has been confirmed, management should begin with bed rest, elevation of head to 30 degrees followed by placement of lumbar drain with intermittent CSF drainage for 3-5 days. In most cases, the CSF rhinorrhea should stop after these measures. If the leakage still persists, surgical exploration and direct closure of leak may be indicated.

POSTOPERATIVE EVALUATION

Endocrine Evaluation

Prolactin secreting adenoma

A. Basal plasma PRL levels.

B. Dynamic studies.

This is useful for the identification of high risk for recurrence.

Growth hormone secreting adenoma

A. Basal plasma GH levels.

(Fasting morning level of less than 5 ng/ml)

B. Oral glucose test.

(GH decrease to 2 ng/ml or less after 75 g glucose PO)

C. IGF I levels.

ACTH secreting adenoma

A. Basal plasma cortisol levels.

(Morning cortisol of less than 1 microgram/dl)

B. 24 hour urinary free cortisol.

(Less than 10 micrograms/24 hours)

Endocrine inactive adenoma

A. Plasma tumor marker levels.

(FSH, glycoprotein hormone alpha subunits, etc.)

Imaging Evaluation

Plain CT scan to check for intracranial complication after the first post-operative day. Intermediate and long term follow up imagings are not included in this paper.

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