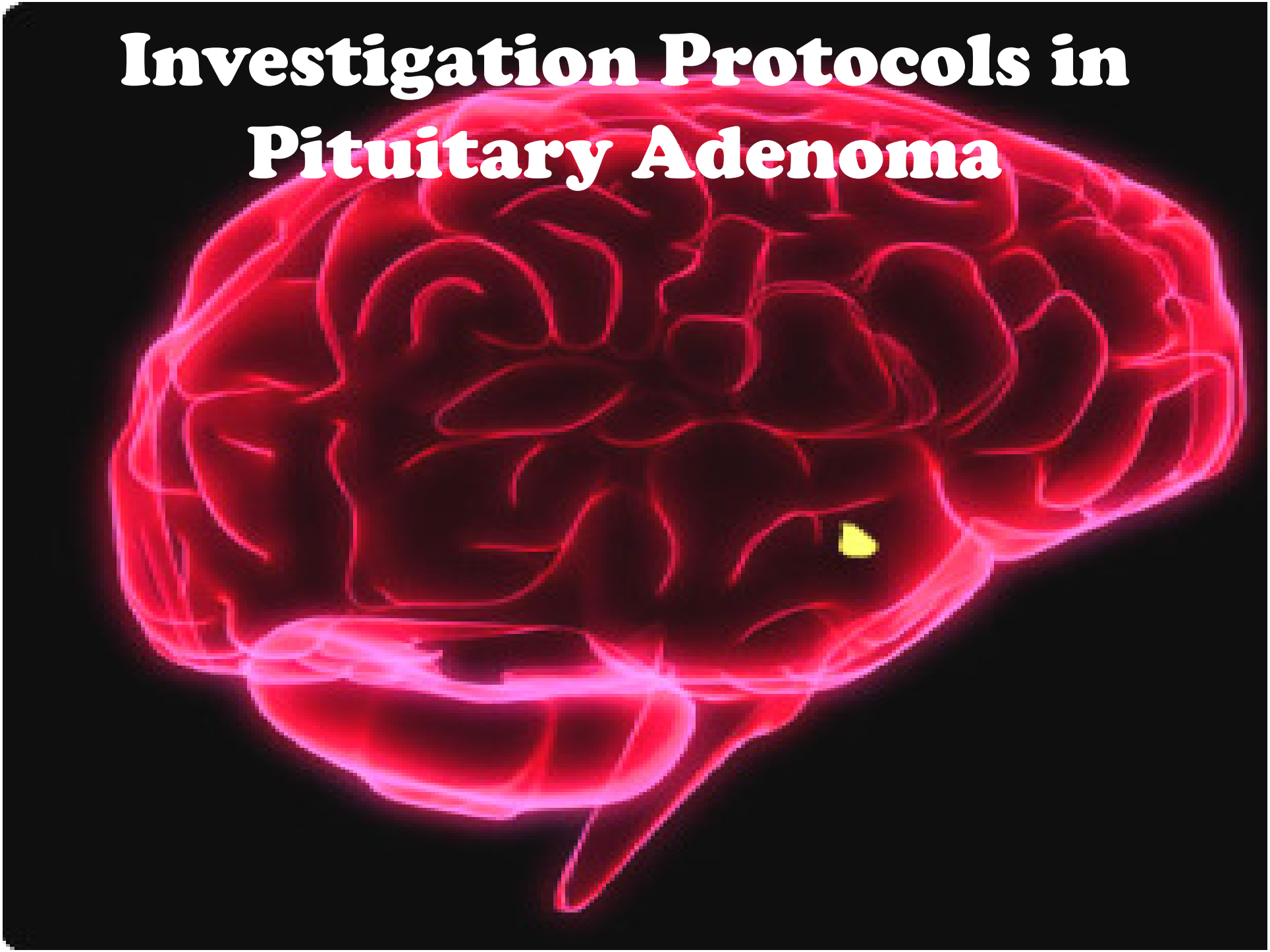
Investigation Protocols in Pituitary Adenoma



Pituitary gland: Originates from Rathke's pouch

Lying within dimensions of 7 x 9 x 11 mm

All of 0.6 gms

Cell type	hormone	Clinical syndrome
Somatotroph	Growth Hormone	Acromeg/gigan
Lactotroph	Prolactin	Amen/galactor
Somato/Lact	Gh+prl	Acro+hyperprl
		Acro+hyperprl
		Amen/Gal/Acro
Corticotroph	Acth/Pomc/B-LPH/MSH	Cushings,nelson
Gonadotroph	FSH,LH,A- Sub Unit	Hypopituitarism
Thyrotroph	TSH, A-sub Unit	Hyperthyroid/ Hypopituitarism
NULL Cell	None	Hypopituitarism

Pituitary Adenoma

15-20 % of all primary brain tumors

Incidental finding in 5-20%

Broadly divided

(a) Functional

(b) Non functional

History

Physical examination

Neuro-ophthalmology: Acuity, field, fundus and movements

Pituitary and target hormones in basal and dynamic states

Radiology
- X-Rays
- MRI
- NCCT/CECT
- Routine blood investigation

Presentation

HYPER SECRETION (most common):

PRL, GH, ACTH and TSH (rarely) produce clinical syndromes

HYPO SECRETION:

Affected in sequence- Gonadotrophs -> Thyrotrophs ->
Somatotroph -> Corticotroph

Presentation

Mass effect

- Headache
- Vision loss
- Hypothalamic compression
- 3rd ventricular extension
- Cavernous sinus extension
- Lateral growth

Apoplexy

Incidental finding

Investigations

X-Rays:

Widening of sella

Destruction of sellar floor

Erosion of posterior clinoids

If secretary- bony changes like that seen in Acromegaly

CT Findings

(1) A focal low-density area in the pituitary gland

(2) Increased gland size (>9 to 10 mm)

(3) Calcification (rare ~ 5%)

(4) Apoplexy- hyper density

T1- Slightly hypo intense compared to normal pituitary tissue

T2- The lesion is slightly hyper intense

(This combination is seen in 75% cases)

Cavernous sinus extension

Three signs to look for:

1. Is there more than 50% encirclement of the carotid artery?
2. Is there lateral displacement of the lateral wall of the cavernous sinus compared to the opposite side?
3. Is there an increased amount of tissue interposed between the carotid artery and the lateral wall of the cavernous sinus?

Prolactinomas

Normal < 20 ng/mL (in absence of pregnancy/ lactation)

< 200 ng/mL - Require careful interpretation

Caused by variety of intrasellar lesions, systemic disorders and drugs (CPZ, haloperidol, metoclopramide, verapamil, cimetidine)

Prolactinomas

Particular attention should be paid to excluding hypothyroidism, CRF and cirrhosis. Hypothyroidism may be a/w pituitary enlargement d/t thyrotroph hyperplasia, mimicking a tumour

Practical rule : PRL levels > 200 ng/mL diagnostic

PRL > 1000 ng/mL indicates : invasive adenoma

Prolactinomas

Hook effect or prozone phenomenon:

Very high levels of PRL interfere with the assay and produce low readings. Occurs because there is not enough anitbody to bind to antigenic (prolactin)

To overcome the hook effect, the serum sample is diluted and then PRL assayed

To accurately estimate PRL in patients with large pituitary tumours, PRL should be assayed in 1:100, 1:200 or even higher dilutions

GH secreting adenomas

Clinical phenotype is characteristic, but GH excess must be documented

Endocrine criteria :

1. Elevation of serum IGF-1 levels: First step
2. OGTT- nadir GH suppression after administration of glucose is considered the "gold standard"

inability to suppress serum GH to less than 1 ng/mL after glucose administration is considered the diagnostic criterion for acromegaly

3. Elevated basal GH level (>5 ng/mL)

AACE Acromegaly Guidelines 2011

GH secreting adenomas

Somatotroph adenomas are a well-known component of the MEN-1 syndrome (pituitary, parathyroid, and pancreatic islet cell tumors), and the endocrine evaluation should be directed at identifying or excluding this condition

Cushing's Disease

ACTH- dependent Cushing's Syndrome (80%)

Pituitary lesion (85%)

- Corticotroph adenoma
- Corticotroph carcinoma (rare)
- Primary corticotroph hyperplasia (rare)

Ectopic ACTH lesions (15%)

- SCLC Lung
- Carcinoid tumor
- Islet cell tumor
- Medullary thyroid cancer
- Pheochromocytoma

Other rare tumors

- Ectopic CRH producing lesions

Cushing's Disease

***ACTH- Independent Cushing's Syndrome* (20%)**

Adrenal adenoma
Adrenal carcinoma
Nodular adrenal hyperplasia (rare)
Exogenous steroids

Cushing's Disease

Step 1: Establishing Hypercortisolemia (screening test)

A. 24-hour urine free cortisol (First-choice method)

B. 11 PM salivary cortisol levels

C. Low-dose dexamethasone (1 to 4 mg) suppression test-use routinely to verify hypercortisolemia

- 1-mg overnight DST (Dexa @ 11 PM -> S.Cortisol @ 8 AM)
- Longer low-dose DST (2 mg/d for 48 h)

[Random serum cortisol or plasma ACTH levels not recommended (Endocrine Society Clinical Practice Guideline, 2008)]

Cushing's Disease

Step 2: Differentiating ACTH–Dependent from ACTH–Independent Causes

Plasma ACTH levels

Levels suppressed in primary adrenal diseases but elevated in corticotroph adenomas, ectopic ACTH syndrome, and CRH-producing tumors. Corticotroph adenomas produce moderate elevations of ACTH (80 to 200 pg/mL), whereas marked elevations are typical of ectopic ACTH-producing lesions (>200 pg/mL)

Cushing's Disease

Step 3: Differentiating Cushing's Disease from Ectopic Adrenocorticotropic Hormone States

High-dose Dexamethasone test:

Dexamethasone 2 mg every 6 hours over a 48-hour period and measurement of urinary cortisol or 17-hydroxycorticosteroids

50% reduction in urinary steroid excretion is taken as appropriate suppressive response and strongly suggests a corticotroph adenoma; ectopic ACTH-producing lesions resist suppression

Cushing's Disease

Alternative:

A single 8-mg dose of dexamethasone is given at 11 PM, and plasma cortisol levels are measured in the morning. A 50% reduction in the plasma cortisol level indicates a normal suppressive response

Cushing's Disease

CRH stimulation test :

Rationale- patients with corticotroph adenomas have an exaggerated response to CRH stimulation, resulting in a prompt, dramatic, and measurable increase in ACTH and cortisol levels

Positive response - 50% increase in plasma ACTH levels or a 20% increase in plasma cortisol levels above baseline

[As a rule, this response should be absent with ectopic ACTH-producing lesions]

Cushing's Disease

In less straightforward cases bilateral inferior petrosal sinus (IPS) sampling can be a helpful means of confirming or excluding a pituitary source of ACTH excess.

In patients with corticotroph adenomas, the basal central-to-peripheral ACTH concentration gradient is almost always greater than 2. In patients with ectopic ACTH-producing lesions, this gradient is less than 1.7. The diagnostic accuracy of this procedure has been further increased by measuring ACTH levels during CRH stimulation

Cushing's Disease

IPS sampling can determine on which side of the pituitary gland the adenoma is located.

When the ACTH concentration in one IPS exceeds that of the other by a factor of more than 1.5, the adenoma is likely situated on the side having the higher ACTH concentration

This information can facilitate the intraoperative identification of adenomas that are too small to be seen radiologically

TSH secreting adenoma

Key endocrinological feature of these tumors is the presence of detectable TSH levels in the presence of high levels of circulating thyroid hormones

80% of thyrotroph adenomas, the glycoprotein hormone α-subunit is produced in measurable excess. An α-subunit–to–TSH ratio that exceeds 1 provides additional evidence of a thyrotroph adenoma

THANK YOU