Pituitary Tumors

Last updated: April 12, 2019

PITUITARY ADENOMAS

1. Differential Diagnosis of Sellar and Parasellar Tumors

PITUITARY ADENOMAS

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3. Histology

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2. Treatment
3. Surgery
4. Radiotherapy
5. Chemotherapy

PROGNOSIS

NOSOLOGY OF PITUITARY TUMORS

1) PITUITARY TUMORS are rare variants of PIALACTIC ASTROCYTOMAS.
2) GRANULAR CELL TUMORS (HYALINOMAS, CHONDROMAS) are rare tumors with uncertain cell origin.

Most pituitary tumors are adenomas!
Guidelines on the Management of Patients with No Functioning Pituitary Adenomas (CNS 2016): molecular etiology and epidemiologic risk factors remain incompletely defined.

- pituitary Tumor Suppressor gene alterations:
  1) retinoblastoma gene
  2) multiple endocrine neoplasia type I (MEN-I) gene 11q13 (found in 3-4 %) – inherited pituitary adenoma?
  3) p53 deletions correlates with aggressive behavior.
- pituitary adenomas are not under hypothalamic control
- alternative hypothesis: overstimulation (or deranged signaling) from hypothalamus → inappropriate pituitary growth.
- adenomas grow slowly; initially confined to sella turcica → may grow out of sella and compress / encase / destroy:
  a) optic chiasm
  b) cavernous sinus and internal carotids (lateral extension)
  c) hypothalamus
  d) surrounding bony structures (e.g. sphenoid sinus, clivus)

N.B. locally invasive adenomas nearly always are histologically benign! CNS metastases and, rarely, distant metastases can occur?

- often have small foci of hemorrhage or necrosis, but no mitotic activity.

N.B. pituitary adenomas never have calcifications? (look at CT – if calcium is present, it is craniopharyngioma).


Pituitary adenoma presenting with calcification is relatively rare (5.6%), but should be kept in mind to avoid making a wrong preoperative diagnosis. As not all pituitary adenomas with calcification are hard tumors, preoperative radiological calculation should not affect decision-making regarding surgical indications (tumor resection is usually possible without any complications).

- adenomas lack discrete capsule, but presence of pseudocapsule facilitates surgical separation.

CLASSIFICATION

**SIZE**

- < 1 cm in diameter – MICROADENOMAS
- > 1 cm – MACROADENOMAS

**HORMONAL SECRETION**

- NONSECRETORS, NONFUNCTIONING PITUITARY ADENOMAS (most common pituitary tumors?) – manifest when reach size of MACROADENOMAS – mass effect (normal pituitary tissue destruction, pressure on optic chiasm, etc.)
  - some nonsecretors secrete a subunit of glycoprotein hormones (FSH, LH, TSH) – suggests origin as gonadotrophin.
  - null cell adenomas demonstrate no evidence (clinical or immunohistochemical) of hormone secretion.

- **HORMONE SECRETORS** (frequency: prolactin > GH > ACTH > gonadotropin > TSH) – manifest with specific endocrine syndromes. see p. 2738
  - nonsecretin, product-secretin in men?, gonadotropin-secretin, GH-secretting adenomas manifest late (as MACROADENOMAS)
  - *main symptom – impotence* – men tend to present late for this symptom
  - other adenomas manifest early (still as MICROADENOMAS)
  - some tumors secrete multiple hormones (termed null tumors).
  - normally five pituitary cell types are regionally distributed: lactotrophs and gonadotrophs – widely distributed; corticotroph – peripherally (two lateral wings of gland); thyrotrophs – anecdotally;
  - corticotrophs – central median wedge.

**HISTOLOGY**

- on routine staining:
  - a) chromophilic cells (acidophilic or basophilic)
  - b) chromophobic cells.

N.B. routine staining is meaningless – tumor can be difficult to differentiate from normal tissue or metastatic disease – immunohistochemical staining and electron microscopy are essential!

- typical normal pituitary structure can be lost – adonomas may contain follicular, trabecular, or cystic portions growing as diffuse sheet; cells are arranged in syncytial or sinusoidal pattern; monotonous appearance.
- nuclei with “salt and pepper” chromatin (vs. endocrine chromatin).
- differentiation of hyperplasia from adenoma may be difficult.
- types of undifferentiated cell adenomas:
  1) **MONOMORPHIC (NILL)**
PITUITARY TUMORS

Oncocytoma (s. oxyphil adenoma) - tumor contains buildup of mitochondria.

Adenoma - packed arrangement of cells resembles that of anterior pituitary, together with prominent vascular network:

Microadenoma:

Photograph of MICROADENOMA (0.9 cm in largest diameter): incidental null cell adenoma found postmortem; tumor is well delineated and has compressed residual still functional adenohypophysis in crescent shape.

Macroadenoma:

Figure 26-2. Close-up detail of a pituitary adenoma still attached to brain. Compressed vessels and nerves are apparent above parenchyma.

Figure 26-3. A hypothalamic adenoma displaying a tendency to papillary growth and paxi demarcation from surrounding pituitary substance. Tumor cells are uniform in size and compress adjacent normal gland (above).
EPIDEMIOLOGY

The most common tumor in sella region (except CRANIOPHARYNGIOMAS in childhood)

Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016):

From cancer registries prevalence is:

19-28 cases per 100,000 people

Meta-analysis of autopsy data and radiologic studies in healthy volunteers - pituitary adenomas are
700 times more common than registry data suggests:
pituitary adenomas are found in 14% of autopsies
pituitary adenomas are found in 23% of CT/MRI studies
Mean prevalence of 17%

- 0.005-3% of all intracranial tumors,
- most occur in young adults (peak - 3rd-4th decades); children make 10% of all patients.
- men = women (clinically evident more often in young women); symptomatic prolactinomas and Cushing disease are found more frequently in women.

CLINICAL FEATURES

Most pituitary adenomas can be detected while relatively small (MICROADENOMAS) - located in exquisitely sensitive area.
N.B. nonsecreting microadenomas are asymptomatic!

1. HORMONAL FUNCTION CONTROL

A) hormonal hypersecretion (most commonly prolactin!)
B) destruction of normal gland → hypopituitarism (partial in 37-85% patients with nonsecretory tumors, pan in 6-29% patients with nonsecretory tumors)
N.B. all MACROADENOMAS eventually cause hypopituitarism.

- if hypopituitarism occurs, hormone loss is sequential: GH → gonadotropins → ACTH → TSH

- primary pituitary tumors rarely cause ADH deficiency (except when induced by hypophysectomy); diabetes insipidus is more common in CRANIOPHARYNGIOMAS.

*7% of patients with NFPAs at the time of clinical presentation

2. MASS EFFECT

1) headache occurs in 20% (can be diffuse and nonpulsatile and may be mistaken for daily headaches; more often in females) – due to stretching of diaphragma sellae and adjacent dural structures; ICP is normal!
N.B. nonsecretive headaches may be the only early symptoms, esp. in nonsecreting adenomas!
- it is still debatable if pituitary tumors can cause headaches, but pituitary surgery is associated with headache improvement or resolution in majority of patients (plus, pituitary surgery was not found to cause or worsen headaches)

2) crossing fibers in optic chiasm (superior bitemporal quadrantanopia → full bitemporal hemianopia - chief and earliest finding in most patients!)
- relationship of pituitary and optic chiasm:
  a) chiasm directly above pituitary (80%).
  b) chiasm anteriorly to pituitary (9%)
  c) chiasm behind pituitary (11%).

- further expansion compromises noncrossing fibers - affects lower and finally upper nasal quadrants.
- any pattern of visual loss is possible, e.g.:
  - asymmetrical loss results from chiasm ischemia produced by vessel occlusion.
  - unilateral mass located anterior to postfixed chiasm may produce central scotoma in one eye + upper outer quadrantanopia in contralateral eye (due to von Willebrand’s
3) lateral extension into cavernous sinus → diplopia, ophthalmoplegias, and postgigandromotor Horner syndrome.

4) hypothalamic compression (e.g. hyperprolactinemia*, diabetes insipidus, alterations in consciousness, memory, intake of food and water).  
* if serum prolactin > 90-200 μg/L – prolactinoma is more likely!

5) extension into sphenoid sinus → CSF rhinorrhea (≈ 0.5% cases) - cortical bone separating sella from sphenoid sinus is quite thin in normal individuals!; may occur as prolactinoma shrinks with medical treatment.

6) compression of 3rd ventricle → obstructive hydrocephalus.

7) basal forebrain abnormalities (personality changes, dementia, anosmia).

8) temporal lobe seizures.

pituitary adenomas may enlarge during pregnancy (esp. prolactinomas), sudden hypotension during delivery may cause ischemic stroke (apoplexy).

**Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016)**

1) high resolution MRI (Level II) is recommended as the standard for preoperative assessment but may be supplemented with CT* (Level III) and fluoroscopy (Level III).

*thin-cut CT for sphenoid septal anatomy; CTA for vascular anatomy; dual-energy CT to discriminate between pituitary adenomas and meningiomas with a sensitivity of 90.0% and specificity of 100%

2) while there are promising results suggesting the utility of MR spectroscopy, MR perfusion, PET, and SPECT to evaluate histology and characteristics, there is insufficient evidence to make formal recommendations.

3) while promising results are available pertaining to high-resolution MR and proton density imaging as tools of assessing cavernous sinus invasion, there is insufficient evidence to make a formal recommendation.

4) while promising results are available pertaining to perfusion and gradient echo imaging as tools for assessing tumor vascularity and hemorrhage, there is insufficient evidence to make a formal recommendation.

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**DIAGNOSIS**

N.B. pituitary adenomas almost never have calcifications??

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**SKULL X-RAY**

- limited use.

**MACROADENOMAS** balloon pituitary fossa → asymmetrical floor of pituitary fossa: 
fronotal projection - one side of fossa is deeper than other; 
lateral projection - two more or less parallel lines that create impression of “double floor”.

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**ANATOMY**

- thin-section, direct coronal plane, with bone windows
Dual-energy CT (utilizes high-frequency cycling of high/low voltages to improve the quality of the CT images) can discriminate between pituitary adenomas and meningiomas with a sensitivity of 90.9% and specificity of 100%.

MRI
- gold standard, more sensitive method for tumor identification (esp. 1-mm cuts and magnified views through sella – pituitary protocol – investigation of choice for MACROADENOMAS, detection!!!

Normal Neurohypophysis on T₁-MRI shows increased signal (representing neurosecretory granules in ADH-containing axons).

Normal Adenohypophysis
- isointense with grey matter on all MR sequences
- circumventricular organ without an intact BBB – enhances homogeneously (punctate areas of heterogeneity - local variations in vascularity, microcyst formation, or granularity), strongly and rapidly (within 30 minutes of gadolinium infusion).

Normal pituitary gland size and configuration are highly variable (esp. in women of childbearing age or pubertal girls – normal hypertrophy of gonadotrophs). Note: great care must be exercised in diagnosis of MICROADENOMAS on MRI basis without associated evidence of hormonal abnormality.

- in neonatal period: both anterior and posterior lobes are hypointense and pituitary gland is bulbous in shape.
- during adolescence and puberty there is significant physiological hypertrophy (in girls upper surface is convex, giving gland almost spherical shape on sagittal views - do not mistake for mass).

Schematic diagram of MRI of normal pituitary fossa. pituitary is bordered laterally by cavernous sinus, which contains internal carotid artery and cranial nerves III, IV, V₁, V₂, and VI, optic chiasma lies immediately above pituitary gland.

Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016; discussions and recommendations if any) are highlighted below.

Macroadenomas
- unenhanced MRI is not helpful – only some macroadenomas have different signal intensity to normal gland.
- standard MRI protocol for investigation of macroadenomas - 1-mm thick coronal T₁ spin-echo sequences through pituitary gland before and after IV GADOLINIUM;
  - additional images in sagittal plane are performed in many centers;
  - desirable to perform fat-saturated T₁ sequence (fat-suppressed imaging) - eliminates high signal from fat in clivus and chiasm processes (could be mistaken for enhancement).
- adenomas always enhance less than normal pituitary gland (hypodense area also can represent ischemic stroke in tumor).
- normal pituitary gland is most often displaced superiorly and posteriorly by adenoma; displacement of normal pituitary in other directions can suggest other pathology?
- there is an association between the “bright stalk” and adenoma size:
  - normal pituitary stalk is of relatively low intensity but can be bright when compressed by tumor.
  - stalk compression/deviation or bright stalk are not always associated with elevated prolactin expected effect of stalk effect.
- accuracy can be increased by dynamic pituitary scans (series of rapid images with 10-15 s time intervals for about 3 min following gadolinium IV bolus) – differences in time course of enhancement between adenoma and adjacent normal gland – very useful in detecting microadenomas.

N.B: Microadenomas enhance faster and/or less than normal pituitary tissue!
- other indirect MRI signs:
  1) gland height! (normally < 10 mm)
  2) gland upper margin contour alteration from concave or straight to convex
  3) erosion of sella turcica floor adjacent to hypointensity area

MICROADENOMAS are easily detected - hyperdense mass within enlarged pituitary fossa.
- may miss small MICROADENOMAS (appear as hypodense structures, vs. MACROADENOMAS).
Contrast MRI

Contrast MRI - MACROADENOMA (tumor extends out of sella into hypothalamus):
**MICROADENOMA** - hypodense (arrow) 9 mm in diameter involving right side of pituitary fossa displacing gland and stalk to left:


**MICROADENOMA** (prolactinoma) - hypodense lesion (arrowhead); slight depression of sella floor under tumor:


Dynamic coronal T1-MRI:
A) scan at 90's following injection of gadolinium reveals microadenoma (arrowhead), which has enhanced to lesser degree than surrounding normal pituitary tissue.
B) after 4 min enhancement is similar to rest of gland.

Contrast T1-MRI:
1 cm intrasellar mass; note tumor expansion into sphenoid sinus, extension into suprasellar cistern with partial compression of optic chiasm (arrow):


Prolactin-secreting MICROADENOMA: T1-MRI with contrast - hypodense lesion in left primary; upward convex margin of left lobe of gland, indicating focal expansion (arrow):


MACROADENOMA (contrast T1-MRI) - invasion of left cavernous sinus - tumor (white arrow) surrounds left internal carotid artery and sinus appears expanded; normal enhancement of uninvoluted right cavernous sinus although tumor encroaches under suprasellar portion of right internal carotid artery (black arrowhead):
PITUITARY TUMORS

Hemorrhagic macroadenoma (T1-MRI without contrast) - hypointense intrasellar mass, fluid level within this lesion (arrow). Pituitary fossa has been expanded; surgery revealed hemorrhagic fluid within macroadenoma.

GH-secreting macroadenoma with left cavernous sinus invasion (T1-MRI without contrast) - convex outward margin of left cavernous sinus (arrow); left internal carotid is displaced.

MRI - hemorrhage into tumor (apoplexy):

A) CT with contrast - macroadenoma with suprasellar and parasellar extension.
B) MRI with contrast following bromocriptine therapy shows marked decrease in tumor size such that infundibulum and optic chiasm are decompressed (arrow).

C) MRI - macroadenoma filling sphenoid sinus and extending into 3rd ventricle floor.
D) suprasellar component compressing optic chiasm (arrow).
C) Following gross total resection through extended frontal craniotomy - infundibulum is well decompressed (arrow).
D) no residual tumor, optic chiasm and portion of infundibulum can be clearly seen (arrow).
**Radiolabeled Study**
- Some GH-secreting adenomas (and some prolactinomas) express somatostatin receptors.
- \[^{111}In\] octreotide uptake has place in:
  - a) Evaluation of incomplete tumor resection due to involvement of adjacent structures.
  - b) Identification which patients may respond to octreotide therapy.

**PET Guidelines:**
Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016)

- 18F-FDG PET detects pituitary adenomas with a sensitivity of 94%-100% and a specificity of 85%-100%.
- \[^{11}C\] L-deprenyl PET may facilitate discrimination of meningiomas from adenomas.

**SPECT Guidelines:**
Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016)

- Diagnostic utility remains unclear.
- \[^{123}I\] SPECT using iodinated dopamine D2 receptor antagonist (Iodobenzamide or BHZM) or similar compounds demonstrated that D2 receptors in pituitary adenomas can be visualized using SPECT.
- \[^{111}In\] Technetium-99m-hexakis-2-methoxy-isobutyl-imidazole SPECT can discriminate adenomas from normal pituitary gland.
- \[^{18}F\] FDG PET is actively taken up by adenomas relative to other sellar/suprasellar lesions.
- Radiolabeled somatostatin or dopamine can potentially differentiate hormone producing from nonfunctioning pituitary adenomas and identify patients who would benefit from pharmacotherapy, although the clinical feasibility of this is unclear.

**Angiography:**
1) To exclude aneurysm!!! (pediatric surgical cases described!!!)
2) Surgical planning

**Neuro-Ophthalmological Evaluation**
- Accurate mapping of visual disturbances (important for every patient prior to surgery).
- In addition to formal ophthalmological examination, tests of value include automated static perimetry (as-needed), and optical coherence tomography (OCT).
- Often, patients with obvious chiasmal compression may not be aware of visual loss, discovered only on quantitative ophthalmic assessment.
- Relative position of the chiasm may influence the incidence of visual field deficits, with a decrease in frequency of visual deficits occurring in patients with an anatomically prefixed optic chiasm.

**Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016)**

- Level III Recommendation:
  - Preoperative evaluation by an ophthalmologist is recommended: asymptomatic visual deficits due to the ophthalmologist’s ability to quantitate psychophysical (acuity and visual fields), functional (quantitation of afferent pupillary defect and visual evoked potentials (VEP)), and anatomical (disc appearance and retinal nerve fiber layer (RNFL) thickness) assessment. When paired with postoperative evaluation, documents postoperative change.
  - Automated static perimetry is recommended for early detection of visual field deficits.
  - Visual evoked potentials may be used to assess the optic nerves in cases in which psychophysical areas, such as acuity and visual fields, cannot be assessed.
  - Older patients and patients with longer duration (over 4 months) of vision loss should be counseled regarding the reduced chance of postoperative vision improvement.
  - Formal ophthalmologic examination, looking for optic nerve atrophy or optical coherence tomography (OCT) to measure both retinal nerve fiber layer (RNFL) thickness and the presence of damage to the ganglion cell layer is recommended to assess chances of postoperative vision improvement.
  - Anatomic assessment of the anterior visual pathways with optical coherence tomography documents previous damage, showing evidence of nerve fiber bundle thinning and evidence of ganglion cell dropout with segmental analysis.

**Evaluation of Pituitary Function**
(sensitive radiomimomassay) in all patients!

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<tr>
<th>Hormone</th>
<th>Laboratory Test</th>
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<td>TSH</td>
<td>TSH, free T, T4</td>
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<td>LH/FSH</td>
<td>Male: testosterone, Female: estradiol, progesterone</td>
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<td>ACTH</td>
<td>Morning ACTH</td>
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<td>Decamethasone suppression test</td>
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<td>IGF-1 (reflects GH concentration</td>
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<td>over the preceding 24 hours)</td>
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<td>Prolactin</td>
<td>Prolactin</td>
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N.B. guard against cortisol insufficiency postoperatively.

All endocrine axes + prolactin should be checked in every patient!
High prevalence (37-85%) of hypopituitarism in patients with NFPAs.

- inferior petrosal sinus sampling is used to localize tumors not seen radiographically (e.g. many ACTH-secreting microadenomas are < 5 mm).
- central hypothyroidism is typically confirmed by the thyrotropin releasing hormone stimulation test, in which serum TSH is measured serially post-TRH at 20 and 60 minutes, with a normal response defined as the 20-minute TSH value being higher than the 60-minute TSH value. A flat response is seen in pituitary disease, and delayed response, with the 60-minute value higher than the 20-minute value, is seen in hypothalamic disease.

Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016):

- NFPA may present with hypopituitarism (37-85%, esp. GH deficiency) or pituitary stalk hyperprolactinemia (25-65%, with a mean level of 39 ng/mL, and with a minority of patients exceeding a serum prolactin level of 200 ng/mL).
- level II recommendation: routine endocrine analysis of all anterior pituitary axes + prolactin to assess for hypopituitarism (prolactin and IGF-1 are also valuable to assess for hypersecretion states that might not be clinically suspected).
- no evidence supporting routine biomarker testing (e.g., alpha-subunit or chromogranin A) was available.

Although not widely used, chromogranin A (CGA) has also been assessed as a potential biomarker for NFPAs. In a prospective case-control study by Gussi et al. of 37 patients with NFPAs that had elevations of serum CGA at 576, 143, and 241 ng/mL, respectively. As the authors acknowledge, the low prevalence of CGA elevations in the NFPA population makes its utility as a sensitive biomarker less reliable.

Prolactin

- serum prolactin level is perhaps the most important laboratory level that dictates a given patient’s treatment course – the ability to distinguish between a prolactinoma (for which medical therapy represents first-line therapy in most patients) and an NFPA with hyperprolactinemia caused by the pituitary stalk effect (a surgically treated disease for most patients) is a critical one.
- nonsecreting tumors are commonly associated with slight elevations of serum prolactin (< 150 ng/mL) – STALK SYNDROME (compression of pituitary stalk, interrupting dopaminergic fibers that inhibit prolactin release) must be distinguished from prolactin-secreting tumors because bromocriptine has little or no effect on nonsecretory tumors.

- some studies indicate different thresholds beyond which stalk effect is unlikely: > 94.3 ng/mL, > 85 ng/mL in the absence of renal failure or any prolactin-enhancing drugs, prolactin increment less than 30% following thyrotropin-releasing hormone.
- Be vigilant to prescription/recreational drugs that interfere with normal pituitary function!
- hyperprolactinemia is seen in 25-65% of patients with histologically verified NFPAs, with a mean level of 39 ng/mL, and with a minority of patients exceeding a serum prolactin level of 200 ng/mL.
- be aware of hook effect (e. prozone effect) – type of interference which plagues certain immunoassays and nephelometric assays, resulting in false negatives or inaccurately low results – too much antigen (prolactin) interferes with results (H: diluting blood sample; modern labs do it automatically):

Panel A: Normal sandwich elisa. The capturing antibody is shown in purple, antigen in red and detection antibody in turquoise.
Panel B: Excessive antigen blocks up sites on both capturing and detection antibodies, causing reduced detection level.
Panel C: If blocking antibodies are present (in orange), they compete with detection antibodies for antigen binding. Reduced detection levels results.
response rate), or combination therapy (60% response rate); > 20% patients required surgery as a result of progressive clinical symptoms.

**COMPLICATIONS**

1. Pituitary apoplexy - can be lethal.
2. Permanent visual loss, ophthalmoplegia, and other neurological complications.
3. CSF rhinorrhea – most commonly following favorable response of invasive prolactinomas to initiation of dopamine agonist therapy.

- possible mechanisms - decreased tumor volume (due to intrinsic infarction or hemorrhage), ongoing invasion, ICP increases
- treatment: surgical repair, preferentially via transsphenoidal approach

**TREATMENT**

Only surgical removal can produce cure!

**DIFFERENT STRATEGIES**

**MICROADENOMAS are treated surgically (except maybe prolactinomas)**

- prolactin-secreting - primary treatment is medical with dopamine agonists (role of imaging in hyperprolactinemia is mainly to exclude MICROADENOMA: precise localization of MICROADENOMA is therefore less important - in some centers, imaging is restricted to unenhanced MRI).
- other secreting adenomas are treated surgically - adenoma localization by other means (petrosal venous sampling) is therefore important if MRI is unsuccessful.
- incidental asymptomatic adenomas require no intervention but should be followed periodically (endocrine examinations, visual field examinations, MRI - onset of symptoms or MRI documentation of growth are indications for treatment.

**Goals of treatment differ according to tumor functional activity:**

- nonsecreting tumors - reduction of mass while maintaining pituitary function (although complete surgical resection is desired, radiosenstivity of these tumors invites subtotal surgical debulking followed by curative adjuvant radiation therapy).
- secreting tumors - aggressive normalization of hypersecretion while preserving normal pituitary function (usually by total surgical excision*, but some MICROADENOMAS are better controlled medically).

*response to radiation therapy is slow and less predictable.

**Natural history with no treatment of asymptomatic NFPAs**


- 28 patients, mean follow-up was 118 months:
  - 50% - radiologic evidence of tumor growth.
  - 21% - required operation due to onset of visual field deficits.
  - 29% - spontaneous reduction in tumor volume.

Arora V et al. Natural course of incidentally found non-functioning pituitary adenomas, with special reference to pituitary apoplexy during follow-up examination. J. Neurosurg. 2006;104(6):884-891

- 42 patients, FU 4 years:
  - 40% - tumor growth.
  - 24% - became symptomatic (9.5% developed pituitary apoplexy).
  - 28.6% - underwent surgical intervention due to new symptoms or increasing tumor size.

**Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016)**

- no evidence supporting routine genetic testing was available.

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A. Inhibition of hypersecretion:

- Proactin hypersecretion → dopamine agonists (e.g. BROMOCRIPTINE, CARBROPLINE).

- N.B. Increase cabergoline dosing incrementally to avoid too precipitous shrinkage of mass → dura mater tear → CSF leak.

- ACTH hypersecretion → KETOCONAZOLE, PROPOFOL, CARBROPLINE.

- GH hypersecretion → OCTREOTIDE, dopamine agonists, PREVOMIST (GH receptor antagonist)

- refinements in medical treatment may allow nonsurgical treatment for some MICROADENOMAS

- some antisecretory medications can lead tumors to be denser and more fibrotic - technically more challenging to remove during microsurgery.

- BROMOCRIPTINE, OCTREOTIDE may confer relative radiotolerance to tumors undergoing SRS.

B. Hormonal replacement most commonly includes thyroid and adrenal hormones.

**SURGERY**

- best way to definitive diagnosis and is usually curative. See p. Op305

See also craniopharyngioma aspects.

**POSTOPERATIVE**

- surgery often improves vision (over hours < years), relieves headache, etc; see below

- CSF leak prevention: 10-30 ± 45 all the time, no straws, no nose blowing, no straining, no sneezing with closed mouth for 1-2 weeks.

- nasal packs for 3 days, concomitantly abs to prevent toxic shock syndrome – analogy with vaginal tampons - Ancef / Keflex / Clindamycin, saline nasal spray every 2-3 hours while awake, phenylephrine nasal spray q4h PRN epistaxis

- monitor for DI; strict Is and Os, BMP and urine spec gravity QID and PRN; patient must have easy access to drinking water (if urinary output < 300 for 2 consecutive hours or Na persistently > 145 H: DDADV 1 mcg q12h PRN as it may be transient; Dr. Sahni gives DDADV liberally; if DDADV required for > 5 days, transition to scheduled 0.5 mcg q12hr subQ and then intranasal if ENT clears for that)

- HYDROCORTISONE taper per endocrinology recs if BP is OK: 100 mg q8h → 50 mg q8h → 25 mg q12h → 15-20 mg + 5-10 mg (discharge on this dose)

- if has hibum drain - keep it clamped until nasal packs are out (if CSF leak - drain 10 ccs/hr)

**ENDOCRINOLOGICAL FOLLOWUP**

- close monitoring of hormonal status (at least thyroid and adrenal function) at frequent intervals (at 3 and 6 mo, and yearly thereafter) - replacement hormonal therapy is usually required and adjustments continue even years later.

- MICROADENOMAS often can be removed without damage to normal pituitary tissue!

- Dr. Broaddus prefers endocrinology consult postop; Dr. Holloway – only if patient was not seen by endocrinologist preoperatively.

Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016)

Level III Recommendations

- postoperative serum sodium levels on the first 2 days and on days 7-8 is recommended to prevent symptomatic postoperative hyponatremia (insufficient evidence to make a recommendation on the detection and treatment of postoperative diabetes insipidus).

- evaluation of adrenal function on postop day 2, 6 weeks, and 12 months after surgery is recommended.

- perioperative corticosteroid supplementation is recommended for NPFA patients with preoperative or immediate postoperative (day 2) hypocortisolism.

**MEDICAL THERAPY**

Further see p. 2738
Pituitary considerations

Optic considerations

Benign tumor as a target for SRS

- radiotherapy is normally adjunctive to surgery)
- undefered endocrinologic follow-up is recommended in all patients after radiotherapy or with abnormal pituitary function after surgery.

Level III / inconclusive recommendations

- There is insufficient evidence to make a recommendation on the detection and treatment of postoperative diabetes insipidus (DI).
- There is insufficient evidence to make a recommendation regarding the frequency of endocrinologic follow-up evaluation after surgery or radiation therapy.

OPHTHALMOLOGICAL FOLLOW-UP

Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016)

Level III Recommendations

- ophtalmologic follow-up after surgical / radiation therapy for NFPAs is recommended (insufficient evidence to make a recommendation on the length of time for this surveillance and the frequency).

IMAGING FOLLOW-UP

- MRI same night and at 3 months: then annually for 10 years — so recurrence can be detected early and, while small, can be treated with radiation, thus, avoiding redo surgery (Dr. Holloway).
- *some surgeons (Dr. JRC, Holloway) skip immediate postop MRI (as it does not change anything, plus, blood and grafts in sella mask picture) but Dr. Broaddus does always want it.

Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016)

Level III Recommendations

- MRI with fat suppression* is recommended for follow-up after surgical or radiation treatment.
- first radiologic study to evaluate the resection extent must be 3-4 months after surgery (insufficient evidence to make a recommendation regarding the timing of initial radiologic follow-up after radiation therapy), immediate postoperative radiographic studies may be misleading in determining the amount of tumor residual.
- radiologic surveillance has to be long-term (insufficient evidence to make a recommendation on the length of time of surveillance and its frequency).
- gross total resection of the NPPA requires radiologic surveillance less frequently than subtotal resection.

- to distinguish hemorrhage, fat graft, and the posterior lobe of the pituitary gland

POSTOPERATIVE COMPLICATIONS

CSF leak (4.7%), meningitis (2.0%), visual deterioration (2.0%)

- Tran-sphenoidal approach

- mortality < 1%
- major complications (stroke, visual loss, meningitis, CSF leak, cranial palsy) < 3.5%
- permanent diabetes insipidus appears in 0.1% (microadenomas) or 1-5% (macroadenomas).
- olfactory dysfunction – depends on approach. see p. Rx11 >>

RADIOThERAPY

Types

A. Radiotherapy – historically, only if distance from optic chiasm is > 10 mm; modern approach –
- SRS from day 1

B. Stereotactic fractionated – can radiate even if tumor contacts chiasm (max fraction dose is 1.9 Gy); delivers radiographic and functional outcomes similar to those seen with SRS but latency is longer with more frequent side effects (e.g. risk of hypopituitarism) is significantly higher as compared to SRS.

C. Conventional fractionated (45 Gy in 25 fractions of 1.8 Gy, calculated at 95% isodose line - provides long-term control in 75-90% cases).

Studies of radiation therapy as a primary treatment modality have not shown superiority or equivalence to surgical resection of NFPAs.

General rule: radiotherapy is indicated when surgery is not an option.

INDICATIONS

(radiotherapy is normally adjunctive to surgery) – to control hypersecretion* and/or tumor mass:
- a) residual tumor after subtotal resection (esp. widely invasive MACROADENOMAS) - single session SRS provides growth control and long-term endocrine control that is superior to that of repeat resective surgery.
- b) cavernous sinus invasion*!
- c) recurrence (if previously received adjuvant radiotherapy) → remember; if previously did not receive radiotherapy → administer it now - single session SRS provides growth control and long-term endocrine control that is superior to that of repeat resective surgery.
- d) not surgical candidates (but histologic confirmation is generally desired?)
- e) not benefited from / intolerant to postsurgical medical intervention.

*Gamma knife is less effective than conventional radiotherapy (higher remission rates, no recurrences described) but Gamma knife carries lesser chances of panhypopituitarism

Benign tumor as a target for SRS

1. Well-circumscribed targets without infiltration
2. Easily visualized with sharp delineation
3. Slow growth rate makes high dose single fraction treatment desirable over fractionation (but late complications have time for expression)
4. Goal of SRS: accurately deliver adequate radiation to the “target” with a minimal dose outside of the prescribed area (i.e. provide the highest potential for growth control and normalization of hormone production + minimize the risk of cranial neuropathies)

METHOdology [SRS]

Highly conformal dose plan is needed to spare the optic apparatus as well as any remaining normal pituitary gland.

Optic considerations – see p. Rx11 >>

Pituitary considerations – see p. Rx11 >>
Tumor control

- Minimum tumor margin dose of 15.16 Gy for nonfunctioning, 16.35 Gy for functioning.
- Doses of at least 15 Gy to ensure reliable and early tumor growth control may be prescribed when distance from the tumor margin to the optic apparatus allows.
- NB: higher doses are needed for biochemical control (some investigators suggest up to 30–40 Gy to center, > 20 Gy to 50% margin isolate whenever possible for treating small volume secretory pituitary adenomas). SRS has better chances of biochemical control than fractionated XRT.

Cavernous sinus involvement
- Microsurgery and SRS are often utilized in a planned staged manner: initial first stage extracavernous microsurgery to reduce the tumor volume and create space between the tumor and the optic apparatus, thus allowing safe delivery of the highest dose of SRS possible.

Radiotherapy

- BIOGRAPHICITIS, OCULARIS?<br>May confer relative radioresistance to tumors undergoing SRS - many clinicians suggest stopping these agents 4-6 weeks prior to SRS and restart 1 week after SRS.
- Long acting drugs (e.g. slow release OCTREOTIDE) should be discontinued 3-4 months prior to SRS.

OUTCOMES

Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016): assessment of the efficacy of radiation therapy in the primary treatment of NFPAs is sparse (the risk of tumor progression and radiation-induced hypopituitarism are major disincentives).

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease in tumor size</td>
<td>19-85% (at 10 years)</td>
</tr>
<tr>
<td>Stable tumor size</td>
<td>26-7-62%</td>
</tr>
<tr>
<td>Increase in tumor size</td>
<td>3-3%</td>
</tr>
</tbody>
</table>

Unlike surgical resection, which eliminates the tumor on subsequent neuroimaging, the neoplastic goal of SRS is PERMANENT TUMOR CONTROL - a tumor, which has been enlarging, is made incapable of further tumor growth, and this control is confirmed through long-term neuroimaging follow-up.

- While permanent stabilization of tumor size is the desired goal, the majority of tumors will demonstrate varying degrees of tumor shrinkage over time.
- Tumor growth control success: 94-95% cases at 5 yrs, 76-85% at 10 yrs.

Radiation therapy is less effective in controlling endocrine hypersecretion (although reported success in 90-95% of cases with SRS vs. 31-80% with surgery):

- Normalization of hormone secretion requires time (median time to normal 1.09 yrs; cumulative normal 86% after 3-4 yrs).
- Normal vision can be achieved by irradiation alone in 2/3 patients (i.e. emergency radiotherapy is an option even with visual changes if surgery is not feasible).
- Control rates: ACTH > GH > prolactin.
- GH levels decrease only at rate of 10-30% per year (several years may be required for levels to normalize!).

Time to endocrinologic remission is 12-144 months

- Ideal situation - small target volume sufficiently far from optic chiasm (to avoid radiation-induced optic neuropathy).

Complications

- See also p. 831 for details.

1) hypopituitarism (risk 12-100% for fractionated XRT; 0-39% for SRS) may develop after years (largely correctable by hormone replacement therapy - patients treated for pituitary adenomas should be observed by endocrinologist for remainder of their lives); safe dose to gland is > 15 Gy, to stalk < 17 Gy.
- Optic chiasm radiation injury (risk 1-2% for fractionated XRT; especially sensitive in acromegaly) → optic nerve neuropa thy and ophthalmoplegia, optic structures should be decompressed before radiation therapy?
- Temporal lobe injuries (infarctions, temporal epilepsy, cognitive dysfunctions) – due to radiation shifted away from optic apparatus.
- Radiation-induced brain tumor - risk is small (1.3% at 10 years and 1.9% at 20 years).
- Cerebrovascular injury.

2-4) complications do not occur with Gamma knife:
- With Gamma knife, only 38-60% tumors demonstrate shrinkage postop – SRS is not good for decompression.
- No dose limits to carotid artery (but avoid hotspots > 25 Gy on it).

Chemotherapy

- Invasive pituitary adenomas may respond to TEMOZOLOMIDE.

Algorithms according to hormone

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Algorithm</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH</td>
<td></td>
</tr>
</tbody>
</table>
**PROGNOSIS**

- very favorable prognosis (success of surgical intervention).
- recurrence is possible only if resection is incomplete.
- after surgery for NFPA: visual function improved in 75-91%, hypopituitarism improved in 35-50%, new hypopituitarism developed in 12% of patients.
  - Dekkers et al (2007) showed that visual acuity improved significantly within 3 months of transsphenoidal surgery; further improvement was seen 1 year postoperatively (the beneficial effects of tumor decompression can be seen in a delayed progressive fashion).

**NATURAL HISTORY WITHOUT TREATMENT**

See above >>

**TREATMENT OF RECURRENCE/RESIDUAL TUMOR**

- recurrence after initial resection is 44-75% within 10 years.
- OK to watch; if starts growing – linear growth – can calculate when will reach optic chiasm.

1. Surgery – 1st choice
2. Radiotherapy – fractionated (esp. if tumor touches optic chiasm) or SRS.
   - invasive or imaging-negative functioning adenoma following failed resection → whole-sellar SRS can offer endocrine remission.

Guidelines on the Management of Patients with Nonfunctioning Pituitary Adenomas (CNS 2016) - adult patients with recurrent or residual NFPA (recurrence after initial resection has been noted to be as high as 44%-75% within a 10-year period of time).
**Level II Recommendations**

- SRS (12-20 Gy) and radiotherapy (fractionated 45-54 Gy) are recommended to lower the risk of subsequent tumor progression (local tumor control ≥ 90% at 5 years).
- no or only small residual intrasellar tumor postoperatively - serial neuroradiography is recommended.

**Level III Recommendations**

- repeat resection is recommended for symptomatic recurrent / residual NFPA; if repeat resection is too risky → SRS or radiation therapy
- assessment of NFPA proliferative index and ACTH staining (to identify silent corticotrophic adenomas) are recommended - risk of adenoma progression and the benefit of earlier adjuvant radiation.

**PITUITARY CARCINOMAS**

- extremely rare!
- despite highly invasive characteristics, rapid growth, and anaplastic features, histology is almost indistinguishable from adenoma - diagnosis confirmation needs distant metastases.

**EMPTY SELLA SYNDROME**

- anechoic herniation through incomplete diaphragm sellae → globular sella enlargement with no discernible hypophysis (gland is flattened on sellar floor)

**ETIOLOGY**

1. Primary (congenitally incompetent sellar diaphragm)
2. Secondary – after:
   1) trans-sphenoidal surgery
   2) radiotherapy
   3) pituitary apoplexy
   4) involution of silent pituitary tumor
   5) benign intracranial hypertension

**CLINICAL FEATURES**

- no endocrine / visual / neurologic disturbances (but hypopituitarism may be present).
- Chiasm herniation inside sella does not cause visual field defects!
- typical patient - female (> 80%), obese (75%), hypertensive (30%) with benign intracranial hypertension (10%) and CSF rhinorrhea (10%).
- occasionally, patients have small coexisting secreting pituitary tumors.

**DIAGNOSIS**

- MRI - enlarged pituitary fossa filled with CSF; infundibulum is seen extending down posteriorly to lower part of fossa (thereby excluding cystic tumor).
- on plain radiography, cannot be distinguished from sellar enlargement by tumor.

**TREATMENT**

- no specific therapy is needed for empty sella alone.

**PITUITARY APOPLEXY**

- hemorrhage into / acute ischemia of pituitary gland (esp. MACROADENOMAS - about 5% of their presentations; rarely into normal hypophysis) → hypothalamic, chiasmal, cavernous sinus, brainstem compression.

**CLINICAL FEATURES**

- reduced blood flow to gland (e.g. upper respiratory tract infection with frequent coughing and sneezing);
- sudden increment of blood flow
- stimulation of gland by endocrine mechanisms
- anticoagulation
- trauma.

**DIAGNOSIS**

- CSF – hemorrhagic.
- CT / MRI will differentiate from SAH.

**TREATMENT**

- 1V fluids + 1V high-dose steroid replacement!
- Conservative treatment for stable cases.

Indications for emergency surgical trans-sphenoidal decompression:

- a) rapidly deteriorating vision
- b) progression to coma!!!

**HYPOPHYSITIS**

- (s. autoimmune hypophysitis)

Two main forms:
1. Lymphocytic (adenohypophysitis, s. lymphoid adenohypophysitis) - the more commonly encountered form.
   - autoimmune inflammation of the pituitary stalk with lymphocytic infiltrate; the antigens have not been identified.
   - primarily in late pregnancy or early postpartum period.

2. Granulomatous hypophysitis - more aggressive, no gender bias, no association with pregnancy. May be autoimmune, but pathogenesis not definitely known.

### Table 59.2 Imaging characteristics of hypophysitis vs. adenomas33

<table>
<thead>
<tr>
<th>Feature</th>
<th>Hypophysitis</th>
<th>Adenoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enlargement</td>
<td>symmetric</td>
<td>asymmetric</td>
</tr>
<tr>
<td>Primary stalk</td>
<td>thickened, nonrupturing</td>
<td>not thickened, rupturing, deviated</td>
</tr>
<tr>
<td>Seller®</td>
<td>spared</td>
<td>may be eroded</td>
</tr>
<tr>
<td>Enhancement</td>
<td>intense, may be heterogeneous</td>
<td>less intense, usually homogeneous</td>
</tr>
<tr>
<td>Mean site at time of presentation</td>
<td>3 cm³</td>
<td>10 cm³</td>
</tr>
<tr>
<td>Posterior pituitary height spot</td>
<td>lost</td>
<td>preserved in 97%</td>
</tr>
</tbody>
</table>

N.B. CT scan:
- normal hypertensity of the posterior pituitary on T1W image (p. 737) ?

- often mimics a nonscrotal pituitary macroadenoma (enhancing sellar mass, with negative endocrine tests) - often undergo surgical resection instead of what may be more appropriate medical therapy (e.g. steroids, or discontinuing possible offending agents such as iplimamab).

### CRANIOPHARYNGIOMA

- slow-growing, extra-axial tumor.

#### EPIDEMIOLOGY

- 1.5% of all primary intracranial neoplasms
- 5-13% of all primary CNS tumors in children - 3rd most common tumor in childhood.
- **INCIDENCE**: 0.13-2.0 per 100,000 per year.
  - **bimodal age distribution** - first peak is in children 5-15 yrs; second peak at 50-74 yrs.
  - **median age at diagnosis is 5 years**.
  - **unusual before age 2 yrs**.
  - **male-to-female ratio is 1:1**.
  - **no known risk factors**.
  - **rare** - 2.5% of primary intracranial neoplasms (6-13% in children)

#### PATHOLOGY

**Hypotheses of origin**

1. **Embryogenetic theory** - embryonic rests of squamous epithelium along involuted HYPOPHYSIOPHARYNGEAL DUCT (i.e. congenital rests of Rathke's pouch stomodeal epithelium).
2. **Metaplastic theory** – metaplasia of residual mature squamous epithelium (derived from stomodeum and normally part of adenohypophysis).

**GROSSLY**

- smooth, lobulated masses with solid and cystic components (90% are at least partially cystic).
- suprasellar location (arises in pituitary stalk and projects into 3rd ventricle and hypothalamus).
- spheroidal (70%); oval or irregular (20%); purely gelatinous (10%).

- 80-90% are calcified (esp. in children).

- epithelial “fingers” can extend into adjacent tissues through gliotic scar (‘William Sweet finding’)

- stromal meningitis:
  - several epithelium are elevated in cyst fluid when compared with CSF:
    - IL-6 and TNF-alpha are elevated but lower than 10-fold.
    - IL-6 is > 50,000 times more concentrated in cystic fluid than CSF.
  - extend horizontally - along path of least resistance in various directions - anteriorly into prechiasmatic cistern and subfrontal spaces; posteriorly into preopticine and interpapillary cisterns, cerebellopontine angle, 3rd ventricle, posterior fossa, foramen magnum; **laterally toward subtemporal and temporal poles**.
  - N.B. **do not expand cells** (unless they become very large) - differentiating feature from suprasellar pituitary macroadenomas!
  - vascular supply from anterior circulation.

**HISTORY**

- well-differentiated tissue - two main histological types:
  1. **ADAMANTINO MATOUS form** (in majority of children, embryogenetic origin) - resembles enamel matrix; developing teeth, composed of interdigitated fibrous and necrotic tissue + multiloculated cysts
    - distinctive feature is **peripheral palisading** of basal epithelium layer, which encloses inner epithelium
    - inner epithelium may undergo hydropic vacuolization (**“stellate reticulum”**)
    - areas of compactly arranged squamous cells contain keratin nodules (**“wet” keratin**)
    - “wet” because of plump appearance of keratinocytes (*vs.* flat, flaky keratin.
    - inclusions: mucous, collagen; **“wet”** because of plump appearance of keratinocytes, **“wet” keratin nodules**
    - may form pseudocysts
    - “wet” keratin nodules frequently calcify.
    - encase vessels and cranial nerves, **invasion bone and recur after surgery**!
  2. **SQUAMOUS PAPILLARY form** (only in adults, metastatic origin) - no complex heterogeneous architecture; less cystic stratified squamous epithelium and fibrovascular islands of connective tissue; does not form keratin nodules; does not calcify!

- craniopharyngiomas stimulate significant glycol response (with profound numbers of eosinophilic Rosenthal fibers) - densely packed bundles of glial filaments in astrocytic cell processes) in contact areas with nervous tissue - thick glial layer may cause tumor (pseudocapsule)**34**, but small epithelial “fingers” can extend into adjacent tissues through glotic scar (**“William Sweet finding”**) - tight adherence to surrounding tissue can make complete resection difficult and hazardous; however, glial reaction is area to separate neoplasm from neuronal elements.

*Rosenthal fibers are characteristic feature of ADAMANTINOMATOUS CRANIOPHARYNGIOMA - biopsy that samples only surrounding neuropl of craniopharyngioma may yield erroneous diagnosis!"
**PITUITARY TUMORS**

Onc26 (19)

N.B. although histologically benign (do not undergo malignant degeneration), craniopharyngiomas may have malignant clinical course (location + adherence to critical structures with difficult removal + ability to recur).

- rarely undergo malignant degeneration

**Adamantinomatous craniopharyngioma:**

- Peripheral palisading of epithelium
- Inner epithelium with hydropic vacuolization (stellate reticulum)
- "Wet" keratin nodule
- Calcified "wet" keratin nodule

**Papillary craniopharyngioma:**

- Only simple squamous epithelium
- Rosenthal fibers in neuropils surrounding craniopharyngioma

---

**Figure 26-8.** A. Embryonic both buds illustrate similarity of epithelium to cells of adamantinoma. B. Craniopharyngioma (adamantinoma). A nest of cells containing central squamous elements embedded in a loose cellular structure.
**PITUITARY TUMORS**

Onc 26 (20)

**Typical epithelium showing basal squamous character with incarcerated keratin; note honeycombed character of epithelium in areas.**


**CLINICAL PRESENTATION**

- resembles pituitary adenomas, but most become symptomatic only after tumor has attained diameter of about 3 cm; symptom duration before diagnosis ≈ 1-2 yrs (i.e. chronic presentation).

1. **Increased ICP** (related to hydrocephalus) – headaches (55-86%), vomiting, etc. – most commonly bring patient to clinical attention;
   - superior tumor extension (obstruction of 3rd ventricle and foramen of Monro) → hydrocephalus in 50%.
   - because of slow growth, papilledema is less common than optic pallor.
2. **Visual field defects** (e.g. homonymous or bitemporal hemianopsia) of various degrees in 37-90%.
3. **Neuroendocrine deficits** (66-90%) esp. GH, TSH and ADH deficits
   - short stature and obesity are most common signs for pediatric endocrinological referral.
   - in contrast to pituitary adenomas, prolactin abnormalities are seen in only 20% cases.
   - 88-90% men complain of impotence, while 82% women complain of amenorrhea.

**DIAGNOSIS**

**Calcifications** are present in the majority of pediatric tumors (up to 90%) and over half of adult lesions?

1. **Plain skull X-ray** (valuable screening tool) – enlarged, distorted sella with suprasellar calcification
2. **CT** – partially cystic, low-density, contrast-enhancing (suprasellar lesion with calcification.
   - adult craniopharyngiomas often do not have calcifications – without biopsy difficult to differentiate from pituitary adenomas.
   - adult craniopharyngiomas often do not have calcifications – without biopsy difficult to differentiate from pituitary adenomas.
   - N.B. pituitary adenomas never have calcifications!
3. **MRI** (best visualization!)
   - cyst gives homogeneous high T2 signal and low T1 signal (cholesterol or blood products within cyst may give rise to high signal).
   - solid portions and capsule show contrast enhancement.
   - CT is enough for diagnosis (calcifications), but tumor extension (e.g. hypothalamic invasion) is evaluated by MRI.
4. **Evaluation of hypothalamic-pituitary axis** (esp. diabetes insipidus and hypoadrenalism – minimum evaluation in emergency cases)
   - before surgery, repeated postoperatively and periodically thereafter for at least 1 year (hormonal deficits often increase after surgery and may take several months to become fully apparent).
CT with contrast - partly calcified, partly cystic suprasellar lesion (note inhomogeneous enhancement of solid tumor components):

MRI - cystic contrast-enhancing suprasellar mass extending upward, compressing hypothalamus:

Gadolinium-enhanced MRI:
A) very large suprasellar mass extending to hypothalamus & thalamus (enhancement is confined to superior portion).
B) tumor extends bilaterally.
**PITUITARY TUMORS**

**TREATMENT**

Patient with suspected craniopharyngioma → surgery for cyst decompression and removal of accessible tumor:
- **total resection** may be attempted (using modern microsurgical techniques, 90% success rate); if successful → no further treatment is required, just serial neuroradiological follow-up
- N.B. radical attempts are not warranted for densely adherent tumors!
- alternative → radiosurgery, intracavitary radiocolloids
  - if tumor is subtotally resected:
    - a) adjuvant radiotherapy
    - b) serial neuroradiological follow-up

**SURGERY**

See also pituitary adenoma aspects >>

Problems with craniopharyngioms:
1) proximity to vital neurovascular structures (highest morbidity – hypothalamic damage).
2) difficult to cure - high recurrence rates - necessitate multimodality treatments (surgery, radiotherapy, radiosurgery, intracystic irradiation, local-intracystic/systemic chemotherapy*).

According to major literature studies, rate of recurrence ranges 0-53% in cases of total removal and 30-100% in cases of subtotal or partial removal.
*for craniopharyngioms that have undergone malignant transformation

- current treatments focus on the relief of symptoms, avoidance of treatment-related morbidity, preservation of quality of life, and prevention of recurrence.
- main goal - complete excision (followed by irradiation in cases of residual tumor).
- recent studies have shown survival rates 83-93% at 10 years of follow-up

**Preoperative corticosteroids** are strongly recommended in all patients regardless of their preoperative status (if not already receiving due to ICP↑)
- **HYDROCORTISONE 100 mg/m² i/v followed by 25 mg/m² q6h until maintenance steroids can be resumed postoperatively.**
- **fluid and electrolyte balance** should be monitored closely (diabetes insipidus, syndrome of inappropriate ADH secretion, cerebral salt wasting are common in postoperative period!).
vassopressin is not needed unless symptomatic deficit!

**Modalities of surgical approaches:**
- **open – still ’the standard’**
- **microscopic/endoptic transsphenoidal**
- **endoscopic endonasal (EES)**
- **stereotactic cyst aspiration** – for purely cystic tumors

**Approach**
- **tumors located primarily in sella can be removed transsphenoidally** (if sella is not enlarged, transsphenoidal approach is contraindicated); large cysts that enter sella can be drained and resected transsphenoidally;
- **subtotal resection** - for lesions that lie anterior to optic chiasm.
- **petroclival approach** - for lesions extending onto dorsum sella or into temporal fossa.
- **lateral and middle fossa** craniotomy
- **posterior fossa** transpetrosal approach
- **ipsilateral transtemporal** approach
- **endoscopic transsphenoidal** approach
- **transcranial** approach

**Extent of surgical removal**
- 

**Radiation therapy**
- decreases recurrence rates and enhances survival in incomplete tumor resections and even in minimum resections (biopsies, cyst drainages).
- should start within 3 weeks of surgery.
- **recommended regimens:**
  - **54-55 Gy** in daily 1.8-Gy increments to local fields only (using relatively small margins around tumor).
  - **preoperative volume plus 1.5-cm margin**
  - **31.5-Gy marginal dose (90% isodose) SRS** - the only benign tumor that can completely disappear after SRS!!!
  - **for children < 3 yrs delay radiotherapy.**

**Chemotherapy**
- *no established role*
- **intrathecal BLEOMYCIN** reduces cyst size and toughens and thickens cyst wall (= safer surgery) – studies do not show the improved outcomes.
- **anechoic response to VINCristine, BCNU, and PROCARbazine** combination has been described in one patient.

**PROGNOSIS**

*Most important prognostic factor – extent of tumor resection (recurrences usually occur at primary site within first year).*
- **tumor size** is probably not independent variable, but rather is related to extent of resection.
- **purely cystic lesions** survive longer than solid or mixed lesions.
- **excellent survival for patients < 20 yrs (99% at 5 yrs); vs. 38% at 5 years for those > 65 yrs.**
- **10-year survival-free survival: > 70% if no visible calcification / tumor in postsurgical CT / MRI,**
- **< 50% if incomplete resection without radiotherapy (50-75% recur within 2-5 years).**
neuroendocrine deficit increase is common after aggressive surgery; permanent diabetes insipidus occurs in 68-75% adults and 80-93% children; replacement of ≥ 2 anterior pituitary hormones is necessary in 80-90% patients; obesity occurs in 50% patients. Some craniopharyngiomas express IGF-1 and/or sex hormone receptors → ↑ recurrence in patients receiving growth hormone and/or sex hormone replacement.

postsurgical declines in neuropsychologic status are seen in many patients. Neuropsychological deficits represent major limiting factor of independent social functioning because patients often can overcome minor neurological deficits and hormone-replacing therapies are widely available. Psychosocial impairment correlates directly with degree of hypothalamic injury sustained at time of surgery!

Female sex is independent predictor of increased cardiovascular, neurological, and psychosocial morbidity!

**BIBLIOGRAPHY** for ch. “Neuro-Oncology” → follow this [LINK >>](http://www.NeurosurgeryResident.net)