Pituitary Imaging for the Endocrinologist

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Learning Objectives

- Review the anatomic relationships of the sella an para-sellar structures
- Develop an understanding of the evolution of pituitary imaging
- Illustrate pituitary imaging phenotypes:
  - Anatomic variants
  - Tumor
  - Infiltrative disorders
  - Vascular disorders
Development of the Pituitary Gland

Adenohypophysis (anterior lobe) - oral ectoderm; neurohypophysis (posterior lobe) - neural ectoderm

Rathke pouch gives rise to the anterior pituitary gland. Behind Rathke pouch, a hollow neural outgrowth extends toward the mouth from the floor of the third ventricle. As Rathke pouch extends toward the third ventricle, it fuses on each side of the infundibular process and subsequently obliterates its lumen, which sometimes persists as Rathke cleft. Remnants of Rathke pouch may persist at the boundary of the neurohypophysis, resulting in small colloid cysts.

Blood Supply of the Pituitary Gland

Arterial blood: 2 paired systems of vessels: from above and from below. The sinusoids of the anterior lobe receive their blood supply from the hypophysial portal vessels, which arise from the capillary beds within the median eminence and the upper and lower portions of the infundibular stem & are intimately related to the great mass of nerve fibers of the hypothalamo-hypophysial tract—on excitation, these nerve fibers liberate into the portal vessels, releasing hormones (eg, corticotropin-releasing hormone) and inhibitory factors (eg, somatostatin)

Anatomy of the Pituitary Gland

The pituitary gland is reddish-gray and ovoid, measuring 12 mm transversely, 8 mm A-P & 6 mm in its vertically. It weighs 500 mg in men and **600 mg in women**. Contiguous with the end of the infundibulum it is situated in the hypophysial fossa of the sphenoid bone. A circular fold of dura mater, the diaphragma sellae, forms the roof of this fossa & is pierced by a small central aperture through which the pituitary stalk passes. The hypophysis is bound on each side by the cavernous sinuses & the structures that they contain. The subarachnoid space often extends a variable distance into the anterior sella & may be referred to as a "partially empty sella". The optic chiasm, superior to the pituitary gland—it rests on the diaphragma sellae just behind the optic groove of the sphenoid bone.
Pituitary Gland Relationship to the Cavernous Sinus

On the medial wall of each cavernous sinus, the internal carotid artery is in close contact with CNs VI; III, IV, and the ophthalmic & maxillary divisions of CN V are on the lateral wall.

The 2 cavernous sinuses communicate with each other by means of 2 intercavernous sinuses. The anterior sinus passes in front of the pituitary gland and the posterior behind it. Together they form a circular sinus around the hypophysis. These channels are found between the two layers of dura mater that comprise the diaphragma sellae and are responsible for copious bleeding when this structure is incised. Sometimes profuse bleeding from an inferior circular sinus is encountered in the transsphenoidal approach to the pituitary gland.

The sella turcica is a deep depression in the body of the sphenoid bone—the normal mean AP length is <14 mm & the height is <12 mm. The anterior boundary of the sella is formed by the tuberculum sellae; posterior boundary of is formed by an elongated plate of bone, the dorsum sellae.

Evolution of Pituitary imaging: Pre-1965 – plain skull X-ray

Lateral skull XR – expanded sella, double floor, enlarged frontal sinus = acromegaly
Evolution of Pituitary Imaging: Pre-1965 – plain skull X-ray

Lateral skull XR – expanded sella, double floor, normal frontal sinus, eroded posterior clinoids, = “chromophobe adenoma” – S/P craniotomy
Evolution of Pituitary Imaging: early 1970s – sellar polytomography

Sellar polytomograms are normal in this patient with pituitary-dependent Cushing syndrome.
Evolution of Pituitary Imaging: early 1970s – sellar polytomography

Sellar tomogram shows sellar and suprasellar calcification in a patient with a craniopharyngioma.
Evolution of Pituitary Imaging: early 1970s – sellar polytomography

Skull XR and sellar tomogram (inset) shows suprasellar calcification in a patient with a craniopharyngioma
Evolution of Pituitary Imaging: early 1970s – pneumoencephalogram

Pneumoencephalogram used to distinguish between a pituitary tumor and an empty sella
The first clinical CT scan on a patient took place on 1st October 1, 1971, at Atkinson Morley's Hospital, in London, England. The patient had a cystic RT frontal lobe brain tumor.

Godfrey Hounsfield Awarded Nobel Prize in 1979
Evolution of Pituitary Imaging: late 1970s – metrizamide cisternography with coronal CT

The Primary Empty Sella Syndrome Diagnosis With Metrizamide Cisternography

William F. Young, Jr, MD; Luis F. Ospina, MD; David Wesolowski, MD; Alfred Touma, MD

Metrizamide-enhanced coronal computed tomographic section demonstrates contrast medium (arrow) within empty sella.

JAMA, Dec 4, 1981—Vol 246, No. 22
Evolution of Pituitary Imaging: early 1975-1986 – head CT scan with axial and coronal views

Head CT (coronal view) 1984 - showing pituitary macroadenoma
Evolution of Pituitary Imaging: 1986 – present: head MRI

Gadolinium T-1  
Pre-contrast T-1
The normal anterior pituitary gland enhances slightly inhomogeneously with gadolinium administration. The optic chiasm is several mm above the sellar diaphragm.
The stored vasopressin in neurosecretory granules in the posterior pituitary produces a bright signal on T1-weighted MRI—the "posterior pituitary bright spot." The bright spot is present in most healthy individuals and is absent in individuals with central diabetes insipidus.
Serial Coronal MRI images
Anatomic variants

- Empty sella
- Young women
- "Brain sag"

Tumor

- Pituitary microadenoma
- Pituitary macroadenoma (& giant)
- Cyst
- Craniopharyngioma
- Meningioma
- Germinoma
- Malignant pituitary tumor
- Metastatic disease to the pituitary

Infiltrative

- Lymphocytic hypophysitis
- Langerhans cell histiocytosis (LCH)

Vascular

- Pituitary apoplexy
- Aneurysm
Primary Empty Sella
The term empty sella (ES) refers to an enlarged sella turcica that is not entirely filled with pituitary tissue. A secondary ES occurs when a pituitary adenoma enlarges the sella but is then surgically removed or damaged by radiation or infarction. In primary ES, a defect in the sellar diaphragm allows CSF to enter and enlarge the sella (<50% of patients with a primary ES have benign increased intracranial pressure). With primary ES, pituitary function is usually intact. On MRI, pituitary tissue is usually compressed against the sellar floor.
The pituitary may look full in premenopausal women to the point that the sellar diaphragm is convex upward or a mild “tenting” of the diaphragm.

Spontaneous CSF leak (usually lower spine) is not rare & presents with headaches. The loss of CSF volume & is compensated by subdural fluid collections & by increase in intracranial venous blood which, in turn, causes pachymeningeal thickening, enlarged pituitary (which is exaggerated by the brain sagging), and engorgement of cerebral venous sinuses.

Pituitary microadenoma (≤10 mm)
Pituitary macroadenoma (>10 mm)

Look at associations with: optic chiasm, cavernous sinuses, anterior extension.
Pituitary macroadenoma (>10 mm)

Anterior extension decreases the probability of complete resection by the transsphenoidal route.
Suprasellar extension (SSE) usually results in visual field defects (VFDs) – most typically bitemporal hemianopsia.
VFD: Lt Temporal Hemianopsia
Marked suprasellar extension (SSE) and parasellar extension (LT>RT) makes the probability of surgical cure extremely low.
Pituitary giant macroadenoma (>4 cm)

Marked RT parasellar extension through the cavernous sinus and into the temporal lobe means that the chance of a surgical cure is zero.
18-yr-old man with MEN-1 – PRL = 6,100 ng/dL

Rx with cabergoline & 6 months later – PRL = 10 ng/dL
Most pituitary cysts are present at birth, although they may enlarge or shrink over time. Most pituitary cysts should be observed, unless they are large and causing VFD.
Pituitary cyst
Pituitary cyst – can spontaneously shrink over time.
Pituitary cyst – can spontaneously shrink over time (same patient, sagittal view)
Pituitary cyst – can grow very slowly—if this patient was operated back in 1997, she would have had anterior pituitary failure—something that a wise endocrinologist can avoid!
Pituitary cyst – can get large and cause VFD

When VFD are present, the surgical approach to the pituitary cyst is justified!
Craniopharyngioma is the most common pituitary region tumor in children & adolescents. Craniopharyngiomas—histologically benign epithelioid tumors arising from embryonic squamous remnants of Rathke pouch—may be large (e.g., >6 cm in diameter) and invade the third ventricle and associated brain structures. This tumorous process is usually located above the sella turcica, depressing the optic chiasm and extending up into the third ventricle.
Craniopharyngioma

The findings on radiologic imaging are quite characteristic. Plain skull radiographs and CT show irregular calcification in the suprasellar region. MRI typically shows a multilobulated cystic structure that is usually suprasellar in location, but it may also appear to arise from the sella.
Craniopharyngioma

The cystic regions are usually filled with a turbid, cholesterol-rich, viscous fluid. The walls of the cystic and solid components are composed of whorls and cords of epithelial cells separated by a loose network of stellate cells.
Meningioma should be suspected when there is major invasion of temporal or frontal lobes of the brain—rather than the “pusher” imaging phenotype of a pituitary tumor, meningiomas have a “invading” imaging phenotype.
Meningioma

Invader—note major impact on arterial structures
Tuberculum Sellae Meningioma

Meningiomas are frequently labeled based on primary location
Meningiomas are frequently labeled based on primary location.
Germinomas typically affect young adults. They usually enhance with gadolinium administration. They are usually located in the pituitary stalk or just above the stalk. On the coronal image they can look like a round mass and on the sagittal image they can look like a “tornado.”
Malignant Pituitary Tumor

1991: Cushing syndrome → -- transsphenoidal surgery
1992: Persistent CS -- Bilateral adrenalectomy gamma knife RoTx
1997: Acute abdominal pain → Abd CT: multiple liver lesions & ACTH = 33,000 pg/mL → Resection of liver lesions – pathology + for corticotroph for pituitary carcinoma; postop -- ACTH = 1,800 pg/mL
1998: Diplopia → progression of tumor on MRI, ACTH = 3,000 pg/mL → Rx with 8 cycles of Cyclophosphamide, Vincristine, and Dacarbazine (CVD); post-chemo: pituitary tumor shrinkage, neg liver CT, ACTH = 450 pg/mL
2003: ACTH = 35 pg/mL; MRI unchanged; 2005: died from fatal MI
1978: 29-yr-old woman – galactorrhea/amen – PRL 103 ng/dL – pit macro → TSS
1983: recurrent macroadenoma → TSS #2
1989: recurrent macroadenoma with LT CS extension → RoTx
2000: VFD due to 10-cm recurrence → TSS #3 + craniotomy
2001: back pain – imaging shows widespread polyostotic metastatic disease; bone bx = metastatic gonadotrope pituitary tumor; progressive VFD → TSS #4
2002: 7 cycles of CVD → dramatic response
2005: new 6\textsuperscript{th} CN palsy, bone lesions stable $\rightarrow$ CVD $\times$ 4 cycles $\rightarrow$ improved CN palsy and ↓ tumor size

2014: VFD and complete LT 6\textsuperscript{th} nerve CN paralysis $\rightarrow$ temozolomide
Metastatic Disease to the Pituitary

63-yr-old man with Hx of renal cell CA - LT nephrectomy 3 yr previously 3-yrs later presents with symptoms of hypopituitarism → serum cortisol = 1 mcg/dL and ACTH <5 pg/mL; free T4 = .64 and TSH = 0.7 mIU/L. With corticosteroid replacement symptomatic diabetes insipidus became evident. Also noted blurred vision
Head MRI shows sellar and suprasellar mass and RT temporal lobe met TSS debulking confirmed metastatic RCC; died 9 months later
Metastatic Disease to the Pituitary

Metastasis is a rare cause of an intrasellar mass discovered during life. When the pituitary gland of patients with cancer is examined at autopsy, pituitary metastases are found in about 3.5% of patients. When detected during life, the most common clinical presentations are DI, VFD, CN deficits, and varying degrees of hypopituitarism. The most common locations for the primary malignancy are shown on the right. In 80% of cases, the pituitary metastasis is discovered after or concurrent with the primary malignancy—avg. interval is 3 yrs. Most of these patients have metastatic disease to >5 or more sites in addition to the sellar region. A pituitary metastasis may closely mimic pituitary adenoma—the clinical presentation, neuroimaging, and endocrinologic data may suggest a nonfunctioning pituitary adenoma. Because DI is a very unusual (<1%) component of the presentation of benign pituitary adenomas, sellar metastasis should be highly suspected when patients present with DI and a rapidly growing pituitary mass. Metastatic disease to the pituitary is a poor prognostic sign; the 1-yr mortality rate is 70%. Because of the poor prognosis associated with sellar metastases, the most reasonable therapeutic approaches are palliative radiotherapy, pituitary target hormone replacement therapy when indicated, and primary tumor-directed chemotherapy.
Lymphocytic Hypophysitis

An autoimmune disorder characterized by lymphocytic infiltration and enlargement of the pituitary gland followed by selective destruction of pituitary cells. The most common clinical setting is in late pregnancy or in the postpartum period. Patients typically present with headaches and signs and symptoms of deficiency of one or more pituitary hormones. Frequently, there is a curious preferential destruction of corticotrophs. However, these patients may have panhypopituitarism (including DI).
Lymphocytic Hypophysitis

MRI usually shows a homogeneous, contrast enhancing sellar mass with pituitary stalk involvement—the finding of a thickened pituitary stalk is key. TSS should only be considered if there are VFDs. The inflammation typically resolves without any intervention. The pituitary hormone deficits are usually permanent, but recovery of both anterior and posterior pituitary function may occur.

In the absence of VFD, avoid BIOSPY & CORTICOSTEROIDS!!
Langerhans cell histiocytosis (LCH)—previously known as histiocytosis-X, eosinophilic granuloma, Hand-Schuller-Christian disease, or Letterer-Siwe disease—is a disorder of the Langerhans cell, a bone marrow-derived dendritic cell that has a key role in antigen processing. Normal Langerhans cells—process antigens and then migrate to lymphoid tissues where they function as effector cells stimulating T-cell responses. In LCH, the Langerhans cell loses its ability to present antigens. With pituitary/hypothalamic involvement the MRI findings can be indistinguishable from germinoma or sarcoidosis.
Langerhans cell histiocytosis (LCH)

LCH in adults is rare, affecting one to two persons/million/yr. The mean age at the time of dx is 32 yrs. Because of the diverse presentation and the rarity of this disorder, LCH may not be accurately diagnosed for many years. In some cases, apparent isolated DI is diagnosed in childhood, and the other sites of involvement and associated symptoms do not develop until later in life. DI, caused by Langerhans cell infiltration of the hypothalamus and pituitary stalk, occurs in approximately 25% of patients with LCH and is irreversible.
The most common presentation is dermatologic symptomatology (rash) followed by pulmonary symptoms (e.g., cough, dyspnea, tachypnea), pain (e.g., bone pain), DI, systemic symptoms (e.g., fever, weight loss), lymphadenopathy, ataxia, and gingival hypertrophy. The skin rash of LCH is papular and pigmented (red, brown). Papule size ranges from 1 mm to 1 cm. Some of the skin lesions may become ulcerated, especially in intertriginous areas. Treatment based on prognosis stratification may include cladribine (2-chlorodeoxyadenosine) or a combination of chemotherapeutic agents.
Pituitary apoplexy (acute hemorrhage of the pituitary gland) is an endocrine emergency and prompt Dx and Rx are critical. The typical presentation is acute onset of severe headache (frequently described as "the worst headache of my life"); vision loss (the hemorrhagic expansion takes the path of least resistance and extends superiorly and compresses the optic chiasm); facial pain; nausea and vomiting; or ocular nerve palsies (e.g., ptosis, diplopia) caused by impingement of the 3rd, 4th, and 6th cranial nerves in the cavernous sinuses. Look for the ‘fluid-fluid level’!!!
Pituitary apoplexy occurs most often in the setting of a preexisting pituitary macro-adenoma or cyst, and the hemorrhage may be spontaneous or triggered by head trauma, coagulation disorders or anticoagulant administration. MRI is diagnostic and typically shows signs of intrapituitary or intra-adenoma hemorrhage, fluid-fluid level, and compression of normal pituitary tissue. Hormonal evaluation typically shows complete anterior pituitary failure. Because of the anatomy of the pituitary circulation and the sparing of the infundibular circulation (inferior hypophysial arteries), the posterior pituitary is infrequently affected by pituitary apoplexy. Thus, DI is rare in this setting.
Intrasellar Carotid Artery Aneurysm
Parasellar Carotid Artery Aneurysm