Non-Neoplastic Disorders of Pituitary Gland

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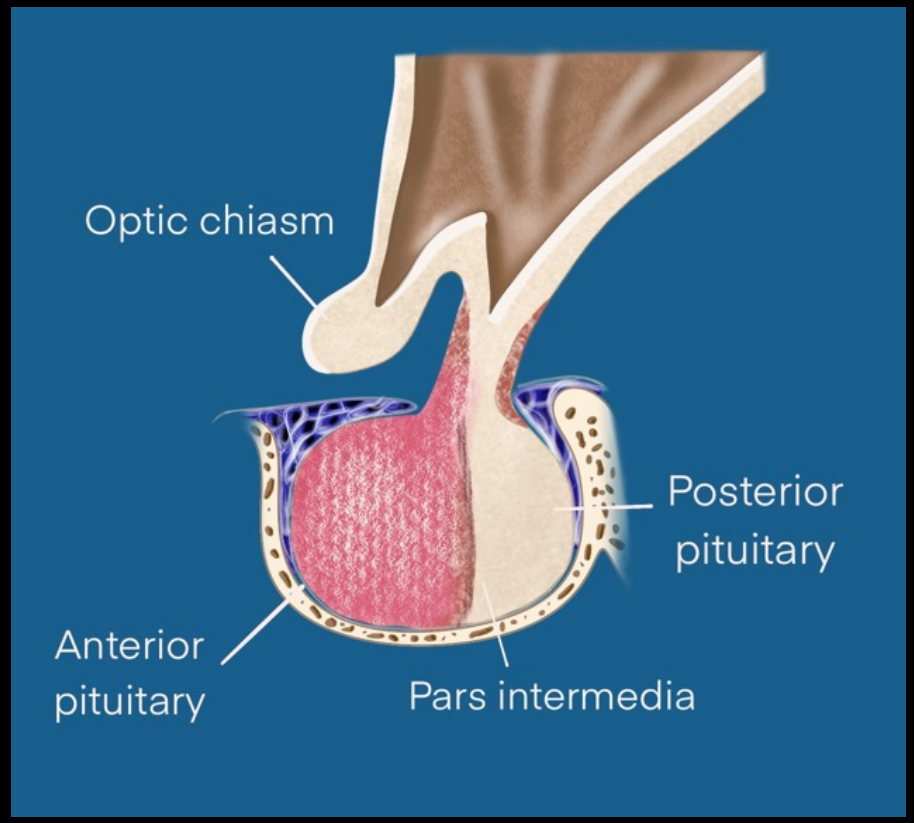
Teaching Points

- Review sellar, parasellar and suprasellar anatomy.
- Understand key imaging features of non-neoplastic pituitary gland disorders.
- Emphasize the importance of distinguishing non- neoplastic pituitary disorders from neoplastic entities to avoid unnecessary surgeries.
- Walk the reader through didactic cases using a combination of MR images and medical illustrations.

Outline

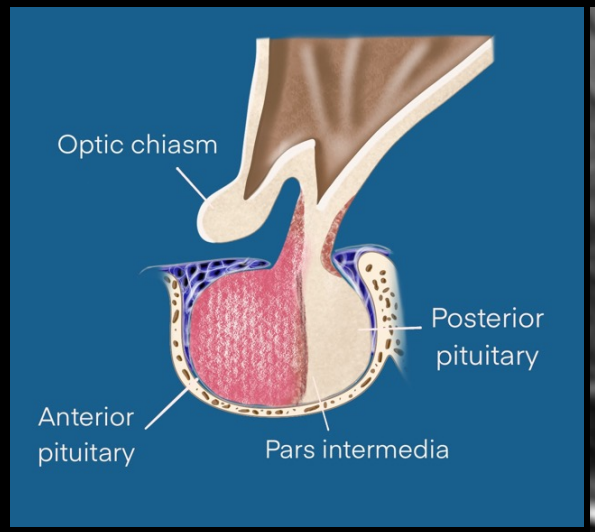
- Anatomy of sellar, parasellar and suprasellar regions.
- Classification, epidemiology, etiology, and clinical features of non-neoplastic pituitary disorders.
  - Hypophysitis
  - Pituitary abscess
  - Rathke’s cleft cyst
  - Neurosarcoidosis
  - LCH
  - Pituitary apoplexy

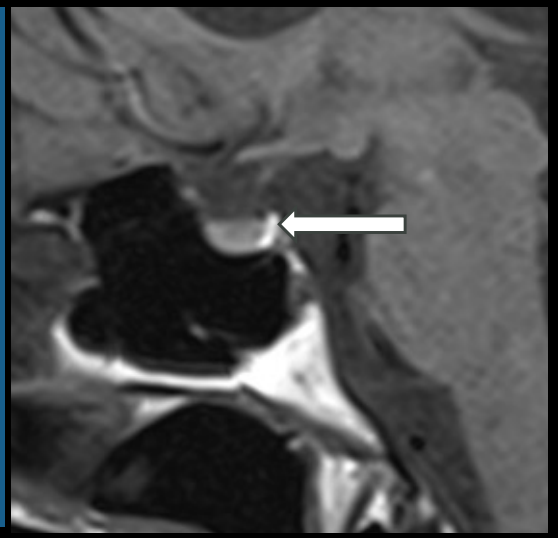
Anatomy of sellar region



- The pituitary gland is located in the sella turcica. It has an anterior lobe (adenohypophysis) and posterior lobe (neurohypophysis).
- The adenohypophysis is where most pituitary hormones (GH, PL, TSH, ACTH, FSH, and LH) are synthesized.
- The pars intermedia is the zone between the adenohypophysis and neurohypophysis and can contain microscopic Rathke cleft remnants.

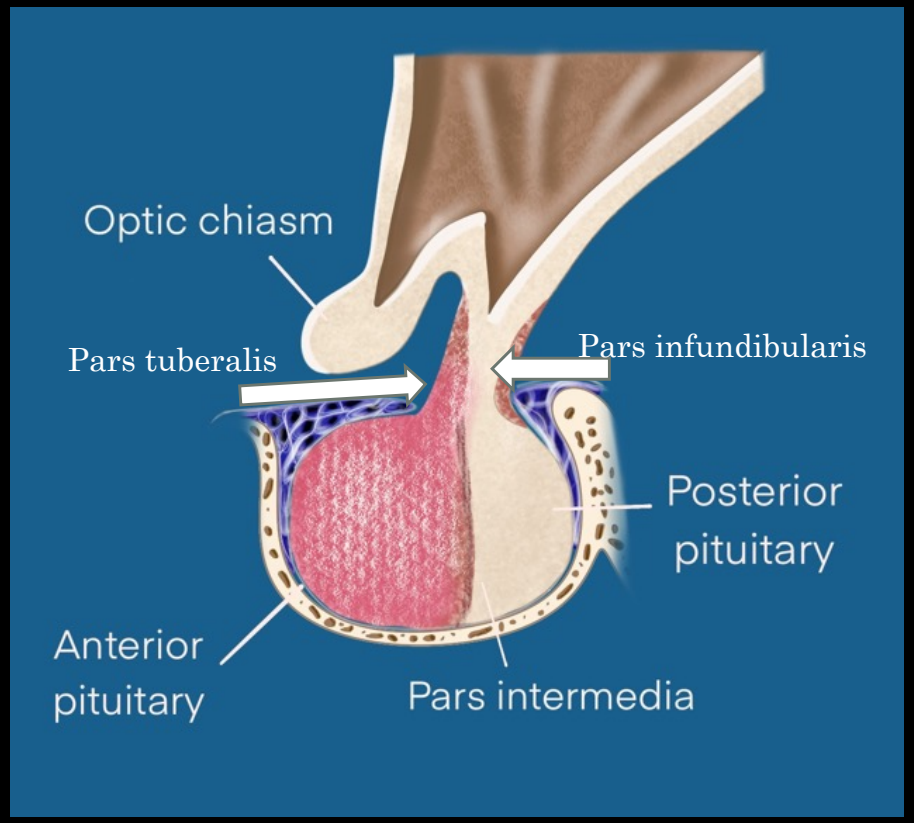
Anatomy of sellar region





- Posterior pituitary gland (Neurohypophysis) is derived from the neural ectoderm and extends from the hypothalamus to the sella. It is composed of axons arising from hypothalamic neurons of the supraoptic and paraventricular nuclei and forming the hypothalamohypophyseal tract.
- Its distal axonal terminals include neurosecretory granules that contain oxytocin or vasopressin.
- Deposition of vasopressin in the posterior pituitary gland is presumed to be responsible for the hyperintense signal identified on T1-weighted, the so-called pituitary bright spot (arrow).

Anatomy of sellar, parasellar and suprasellar regions

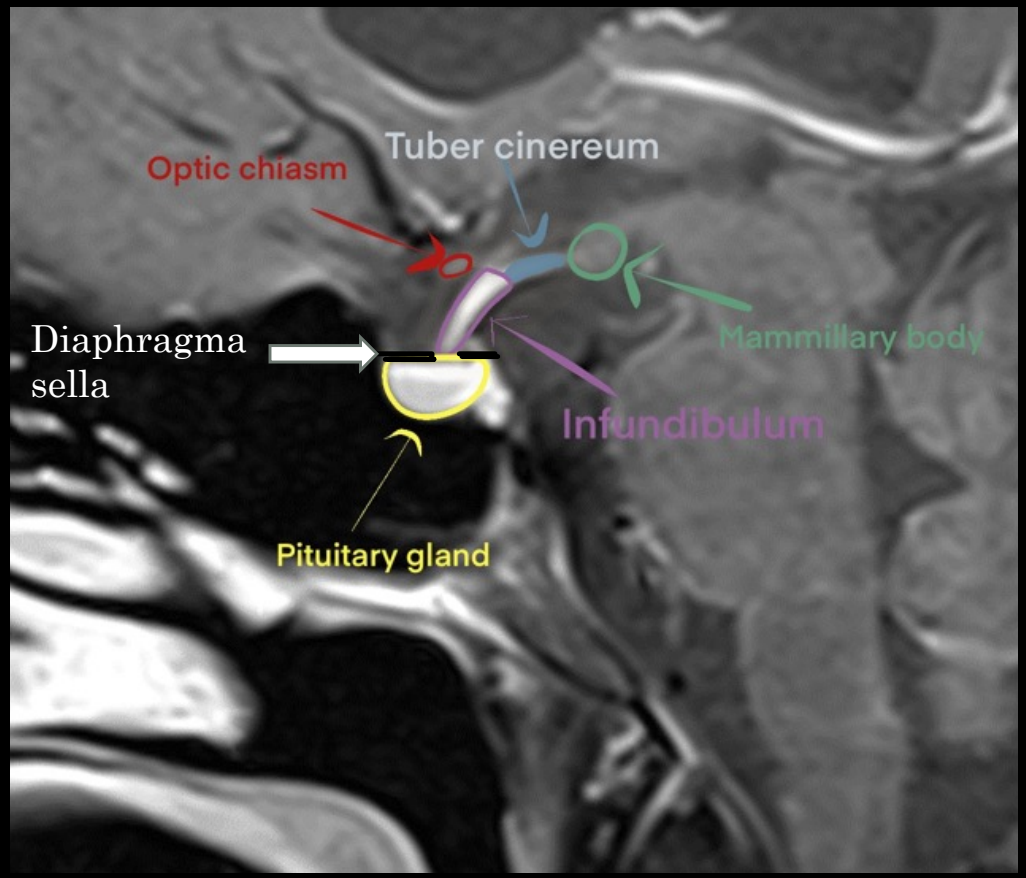


Infundibulum (pituitary stalk) is a linear structure extending from the hypothalamus to the pituitary gland. It is comprised of the anterior pars tuberalis and pars infundibularis .

Pars tuberalis is considered to be part of the adenohypophysis. It partially surrounds the pars infundibularis, which contains unmyelinated axons of the hypothalamic neurons that extend to the posterior lobe.

Pituitary stalk measures 4.4 mm or less at the level of the optic chiasm, and 2.7 mm or less just above the pituitary gland in 95% of patients.

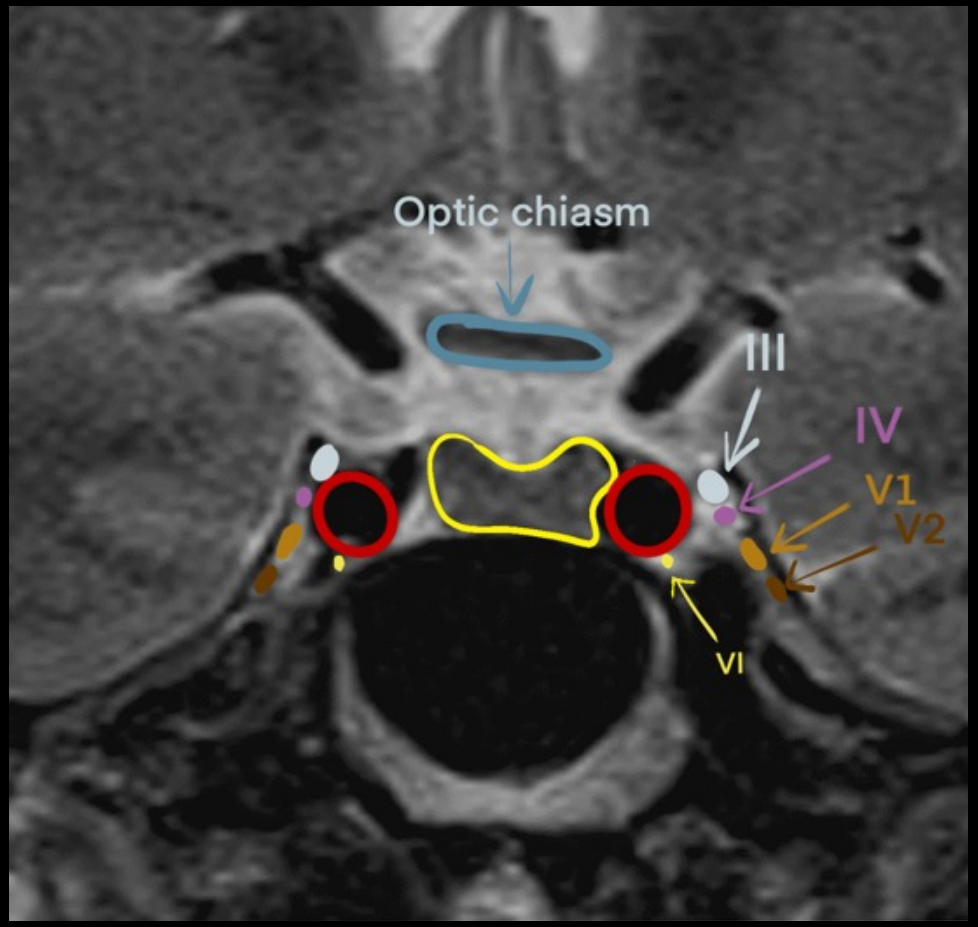
Anatomy of sellar, parasellar and suprasellar regions



- Diaphragma sella is a dural reflection which separates the sella from suprasellar space. It is attached to the clinoid processes and contiguous with the dural covering of the cavernous sinus roofs bilaterally.

- The optic chiasm lies within the suprasellar cistern. The optic chiasm can be compressed by enlarged pituitary masses resulting in compromise of peripheral vision.

Anatomy of sellar, parasellar and suprasellar regions



The parasellar region encompasses the cavernous sinuses on both sides of the sella turcica. The cavernous sinus contains the internal carotid artery and several cranial nerves. Abducens nerve (CN VI) traverses within the cavernous sinus next to the ICA. The remainder of the cranial nerves pass through the lateral wall of the carotid sinus, and from superior to inferior they are:

Oculomotor nerve (CN III)
Trochlear nerve (CN IV)
Ophthalmic division of the trigeminal nerve (CN V1)
Maxillary division of trigeminal nerve (CN V2)

Hypophysitis

Hypophysitis can be classified based on primary or secondary mechanisms, histology (lymphocytic, granulomatous, xanthomatous, plasmacytic/IgG4 related, necrotizing, or mixed), and anatomy (adenohypophysitis, infundibuloneurohypophysitis, or panhypophysitis).

Secondary causes of hypophysitis include systemic granulomatous diseases, infection, sellar tumors or cysts (such as a ruptured Rathke cleft cyst, craniopharyngioma, adenoma, or germinoma), and drugs.

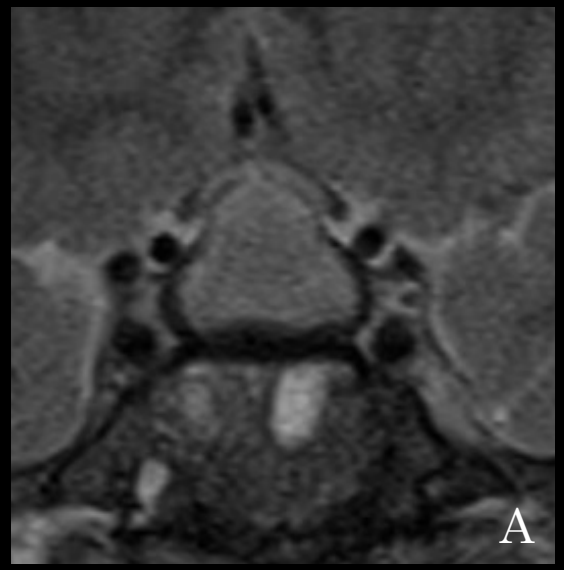
Lymphocytic hypophysitis

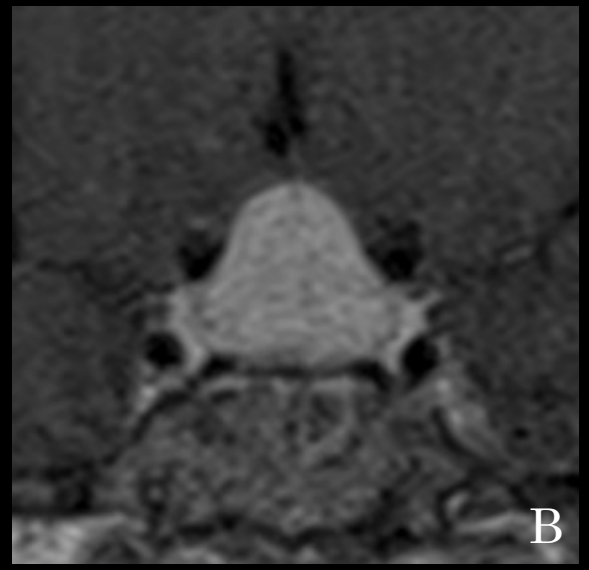
Lymphocytic hypophysitis is the most common type of primary hypophysitis. It is thought to be due to autoimmune mechanisms and associated with other autoimmune diseases such as Graves disease, Hashimoto's disease, and Addison's disease. Lymphocytic hypophysitis is most commonly seen during pregnancy and in the early postpartum period.

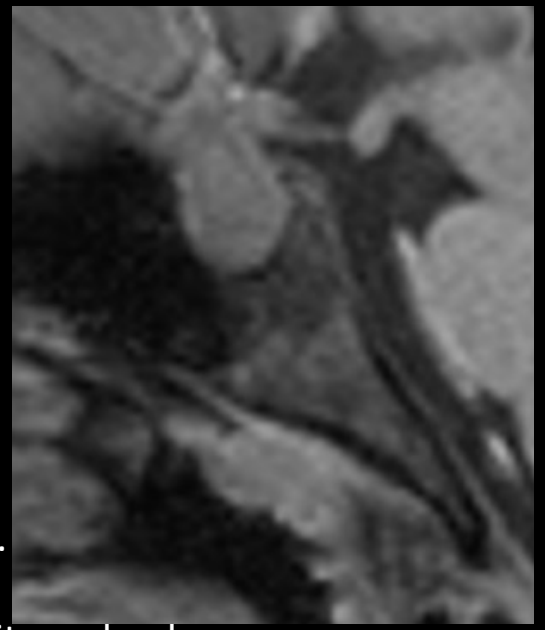
High-dose corticosteroids are the mainstay of treatment, but spontaneous regression is also frequent. Surgical decompression is occasionally indicated in refractory cases.

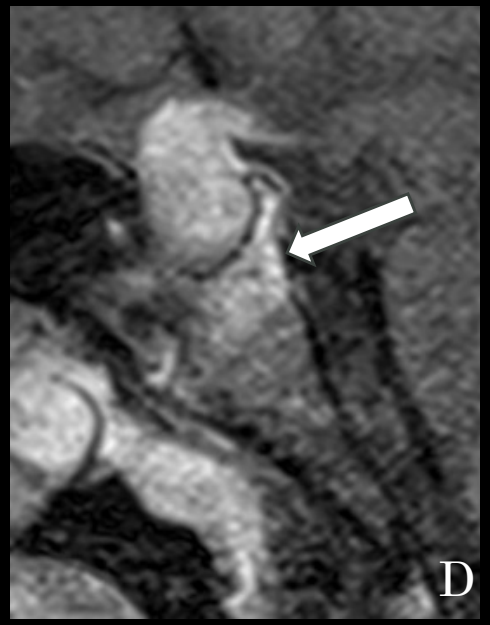
MRI features include pituitary gland enlargement, loss of posterior pituitary T1-weighted bright spot, enlarged pituitary stalk, and homogeneous contrast enhancement. The parasellar T2 dark sign is present in 35% of cases, which can be helpful in differentiating lymphocytic hypophysitis and pituitary neuroendocrine tumor (PitNET). However, the parasellar T2 dark sign can also be observed in other chronic inflammatory diseases such as LCH and IgG4 disease.

Lymphocytic hypophysitis





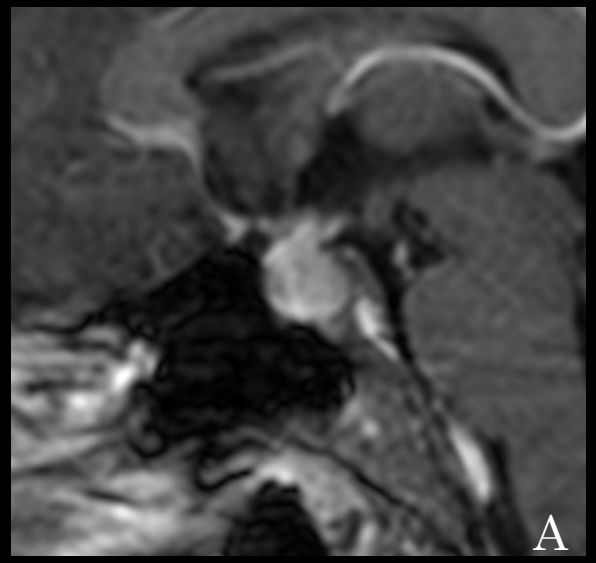


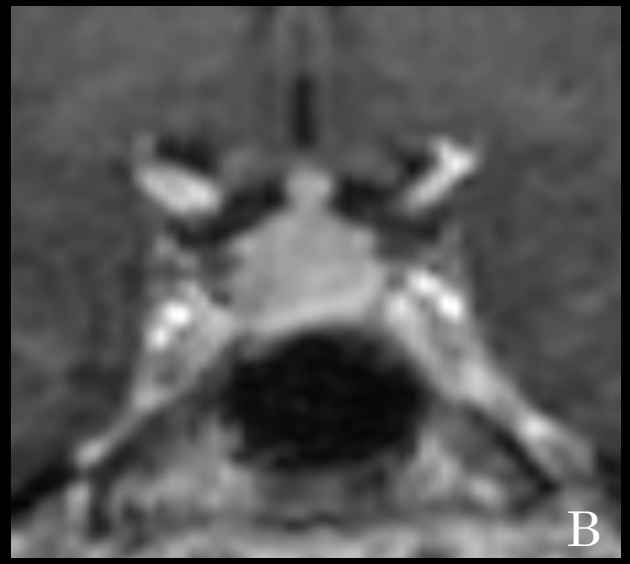


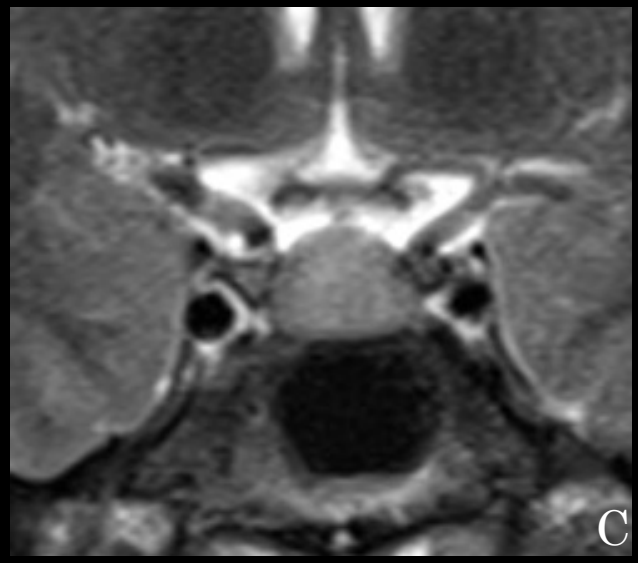
18 yo male presented with vomiting, loss appetite, and weight loss.

A. Coronal T2WI shows diffuse, symmetric enlargement of the pituitary gland causing mass effect on optic chiasm with increased signal. T2 hypointense rim surrounding pituitary gland.
B. Coronal post contrast T1WI shows diffuse enhancement of the pituitary gland.
C. Posterior pituitary bright spot is not seen.
D. Sagittal post contrast T1WI shows enlarged pituitary gland and stalk. Enhancement in basisphenoid (arrow).

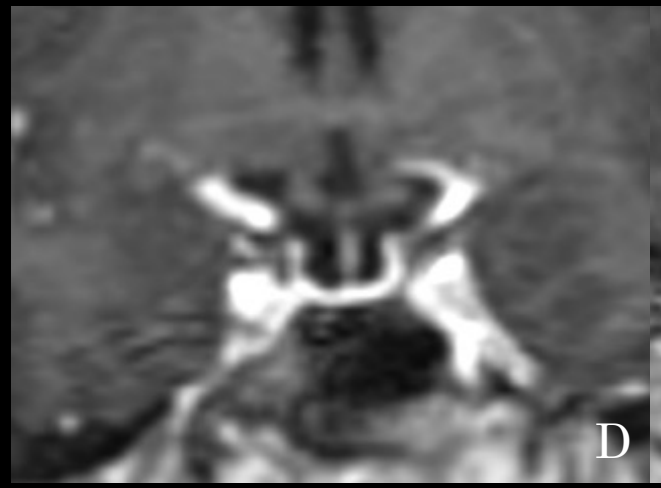
Ipilimumab induced hypophysitis

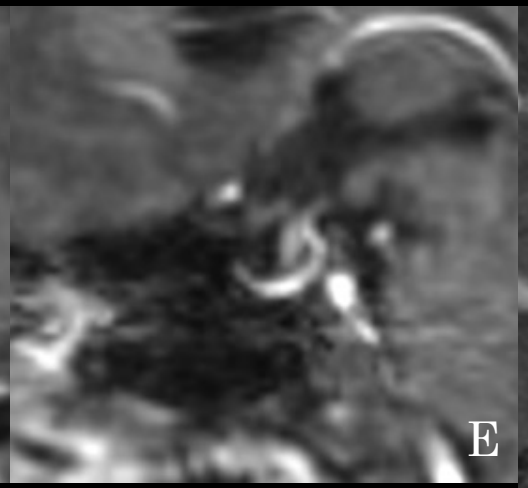


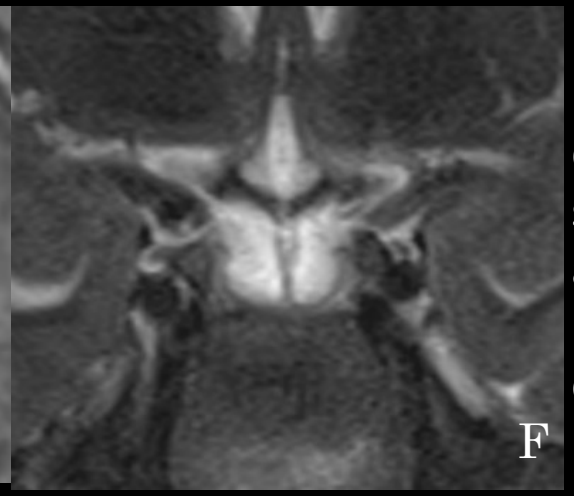




A. B. and C. Patient with melanoma. He had a headache after two cycles of Ipilimumab/Nivolumab. MRI revealed diffuse enlargement of pituitary gland and stalk.

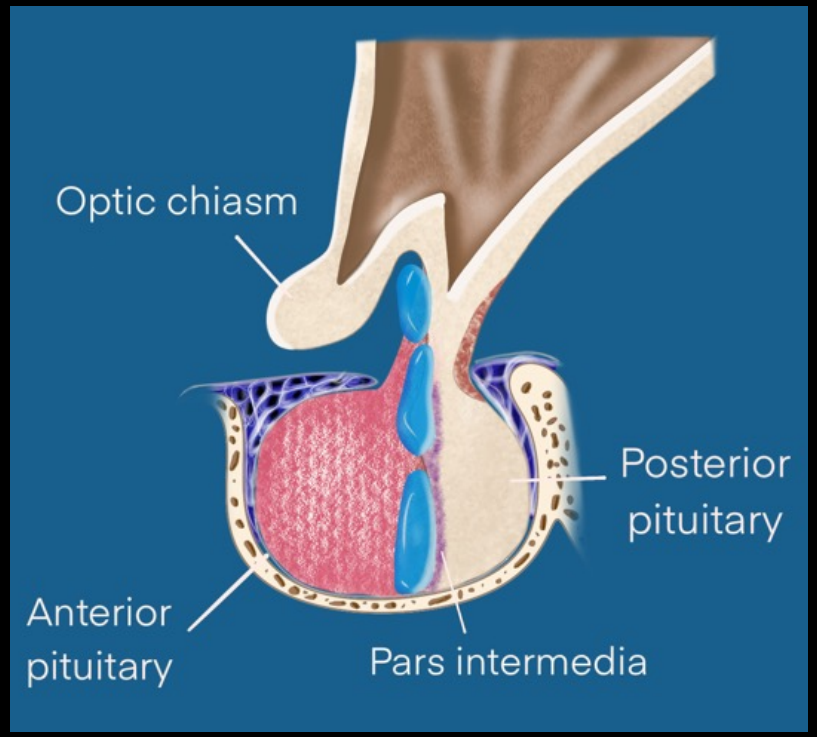






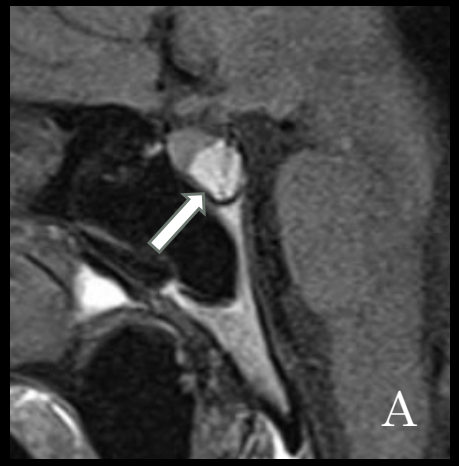
D. E. and F. Interval decrease in size of pituitary gland and stalk 10 months after cessation of Ipilimumab/Nivolumab.

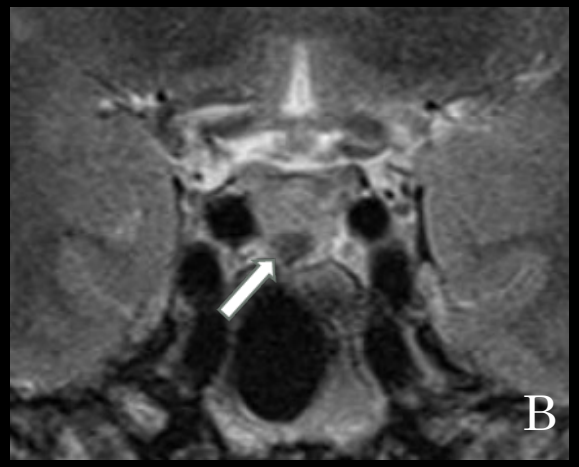
Rathke cleft cyst

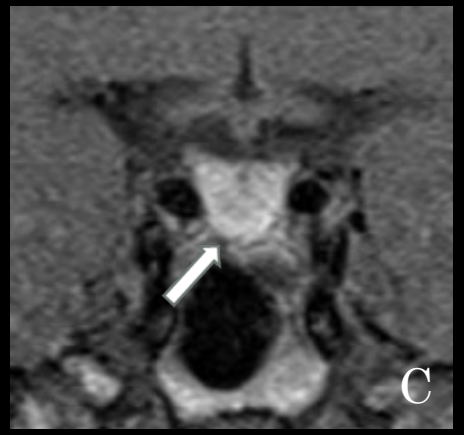


- Rathke cleft cysts (RCCs) are benign, epithelial lined non-neoplastic lesions hypothesized to be derived from remnants of the Rathke's pouch. These cystic lesions are usually discovered incidentally within the sellar and/or suprasellar region. Prevalence among autopsy series is up to 33%. Histologically RCCs demonstrate a columnar or cuboidal epithelium with internal thick or mucoid material, consisting of cholesterol and protein.

- Symptomatic RCC usually occurs during the 4th or 5th decade of life with a higher prevalence in females. Symptoms which are related to mass effect can include headache, visual impairment, and endocrine dysfunction.







A. Sagittal precontrast T1WI shows hyperintense lesion in mid sella.

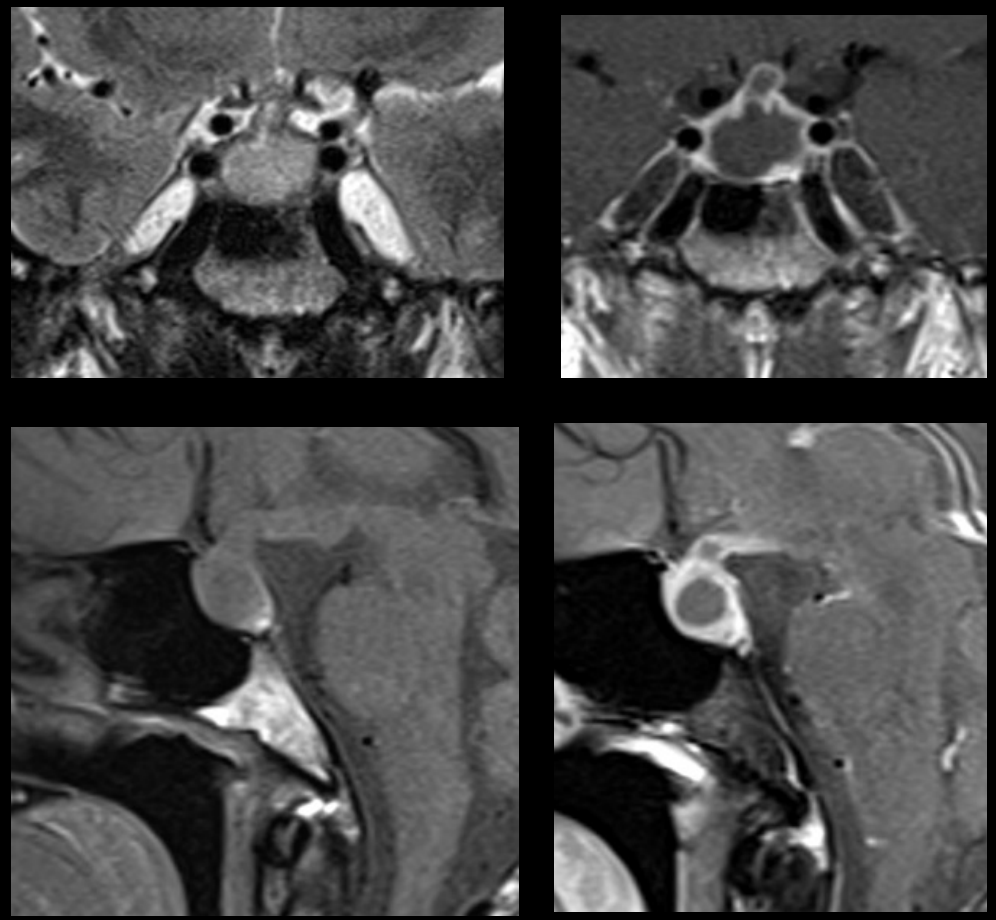
B. Coronal T2WI shows T2 hypointense signal in the cyst.

C. Coronal T1WI shows T1 hyperintense nodule inseparable from cyst.

Rathke cleft cyst

- Typical imaging findings are those of a nonenhancing, noncalcified, intrasellar/suprasellar cyst.
- Depending on its cystic content, an RCC may show various signal intensities on both T1- and T2-weighted images.
- T1 hyperintensity (50%) and T2 hypointensity (30%) of an RCC associated with a high intracystic protein content can mimic cystic pituitary adenoma with hemorrhage, which makes imaging diagnosis of a cystic pituitary adenoma versus RCC a challenge.
- A nonehancing intracystic nodule may be present in some cases, typically hyperintense on T1 and hypointense on T2 relative to the remainder of the cyst contents. Squamous metaplasia cell debris is the main component of the nodule.

Rathke cleft cyst with squamous metaplasia and significant inflammatory reaction.



Most Rathke cleft cysts show no enhancement. When present, the enhancement can be attributed to the inflammation and/or squamous metaplasia in the cyst wall.

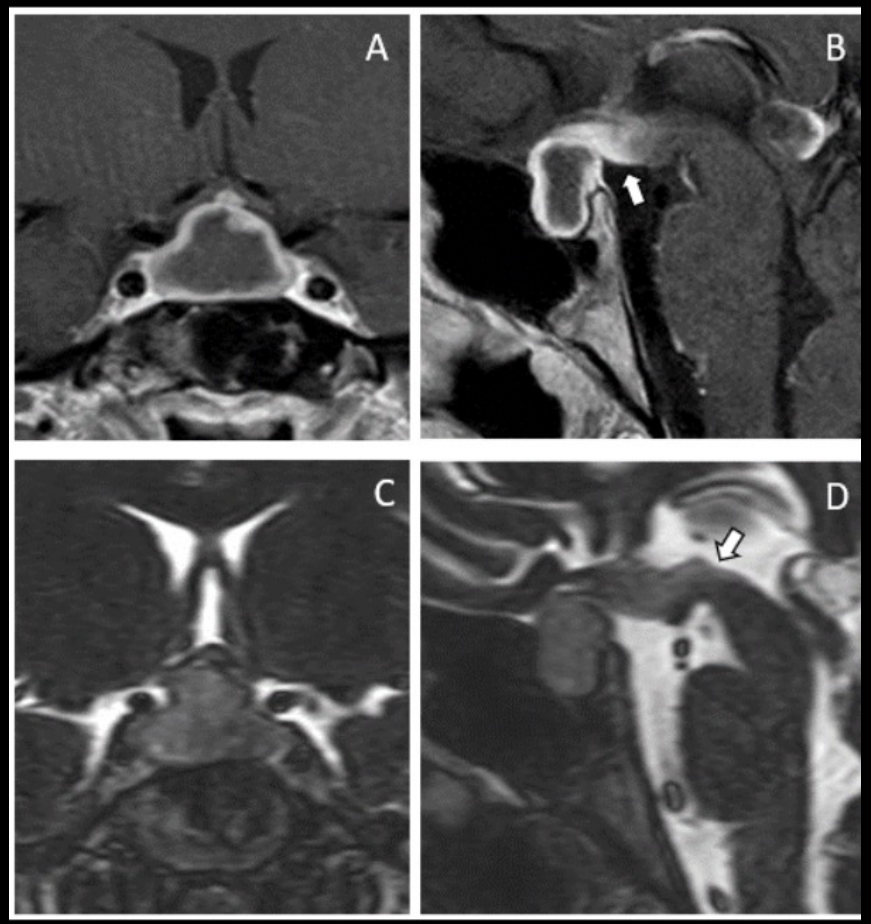
40 y.o. male who was found to have a pituitary mass on evaluation for central diabetes insipidus. Cystic sellar/suprasellar mass with peripheral enhancement involving the pituitary stalk. Pathology revealed Rathke cleft cyst with squamous metaplasia and significant inflammatory reaction.

Rathke cleft cyst versus Pituitary neuroendocrine tumors

The presence of a fluid-fluid level, a hypointense rim on T2-weighted images, septation, and an off-midline location are more common with Pituitary NET, whereas the presence of an intracystic nodule is more common with Rathke cleft cysts.

Rathke's cleft cyst	PitNET (Pituitary adenoma)
Midline	Off-midline location
T2 hypointense nodule (70%)	Tilting of the pituitary stalk
T2 hypointense hemosiderin rim (less common)	Fluid-fluid level, Septations
	T2 hypointense hemosiderin rim (more common)

Rathke cleft cyst with squamous metaplasia associated with secondary hypophysitis.



A 16-year-old female with a history of migraines presented with a 1-month history of morning headaches, photophobia, nausea, and vomiting.

MRI of the brain revealed a peripherally enhancing sellar and suprasellar mass extending posteriorly to involve the pituitary stalk, tuber cinereum of the hypothalamus, and floor of the third ventricle. Mass extension to the floor of the third ventricle is best demonstrated on sagittal 3D T2WI (D). There was mass effect on the optic chiasm. Endocrine evaluation revealed diabetes insipidus and hyperprolactinemia.

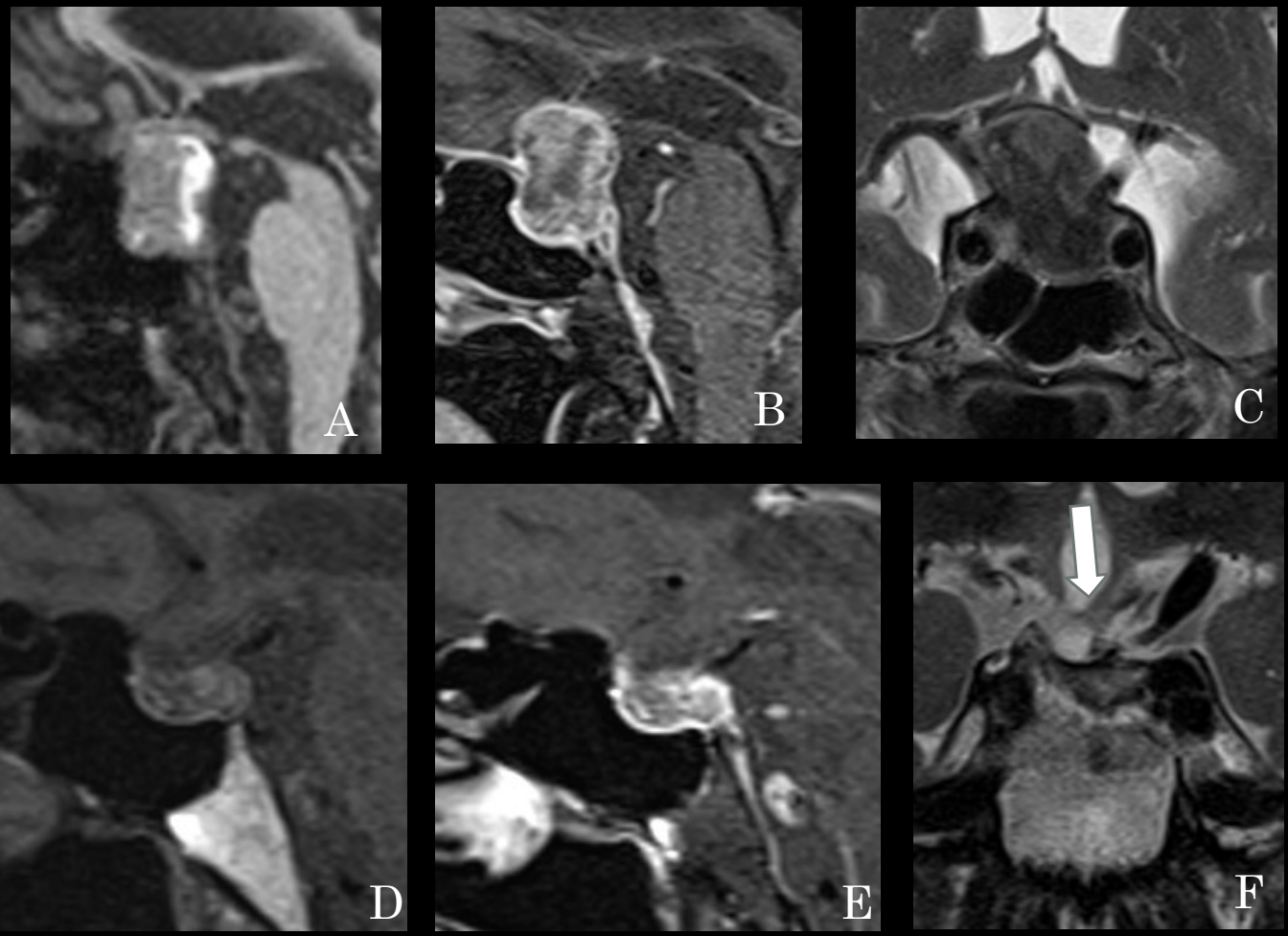
Endoscopic endonasal transsphenoidal resection of pituitary mass was performed.

Histologic examination revealed Rathke cleft cyst with squamous metaplasia associated with secondary hypophysitis. The anterior pituitary showed intense inflammatory infiltrate composed mostly of mature lymphocytes and plasma cells.

Pituitary apoplexy

- Pituitary apoplexy is a clinical syndrome that occurs when an existing pituitary adenoma undergoes an acute hemorrhage (more common) or infarction. Apoplexy is most common in non-functioning macroadenomas and prolactinomas, but can also occur in normal pituitary or microadenoma.
- Clinical presentation includes abrupt onset of severe headache, visual disturbance, ophthalmoplegia, and acute hypopituitarism.
- Often the first imaging test performed in an acute setting is an unenhanced CT scan, which can reveal a sellar mass with variable hyperdensity.
- Imaging features on MRI include variable intensity content on T1 and T2 depending on presence of hemorrhage and its age. Fluid level and underlying adenoma may be seen. Peripheral enhancement and diffusion restriction is usually present in the acute phase.
- T2* weighted images can potentially differentiate between hemorrhagic apoplexy and other conditions. Hemorrhagic apoplexy shows blooming due to paramagnetic effects of blood products. However, susceptibility artifact from adjacent bone often limits evaluation of the sellar region.
- Thickening of the sphenoid sinus mucosa is a finding on MR imaging that can suggest pituitary apoplexy in the acute phase of hemorrhage. This mucosal thickening is thought to be related to venous congestion in this region and typically resolves spontaneously later.

Pituitary apoplexy



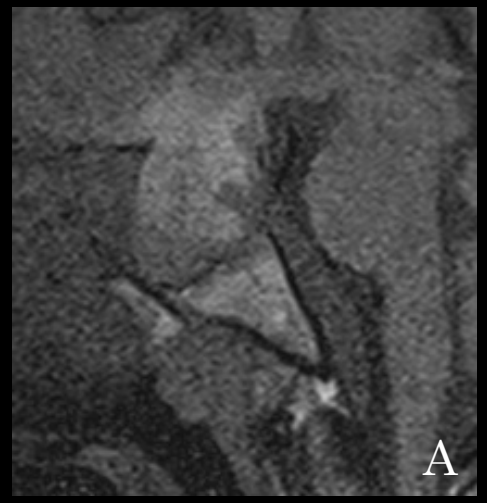
79 y.o. male with a four day history of headaches, and visual decline.

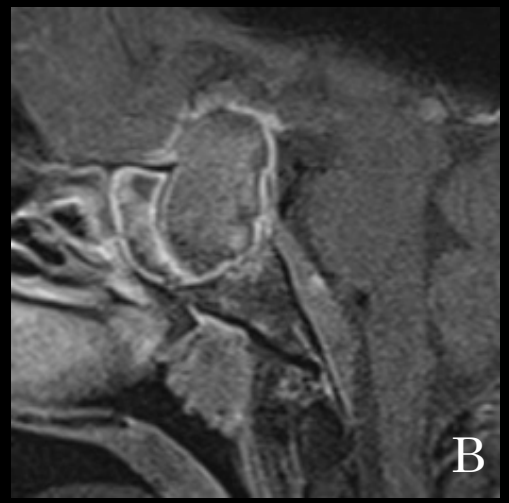
A. B. and C. Initial MRI showed areas of T1 and T2 shortening corresponding with hemorrhage. Post contrast images show heterogenous enhancement.

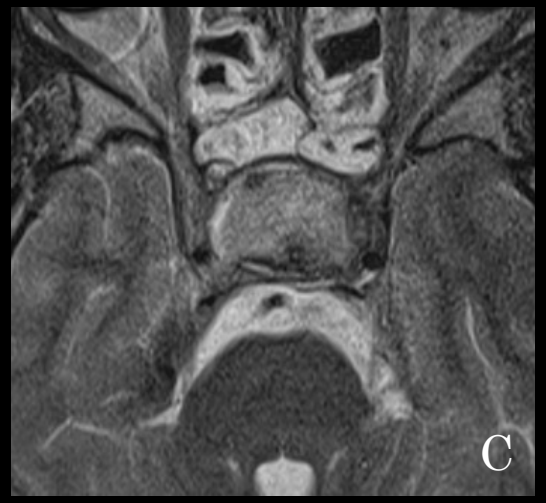
Given stable neurological examination with mild deficit, the patient was managed conservatively with high dose steroids and pituitary replacement as needed.

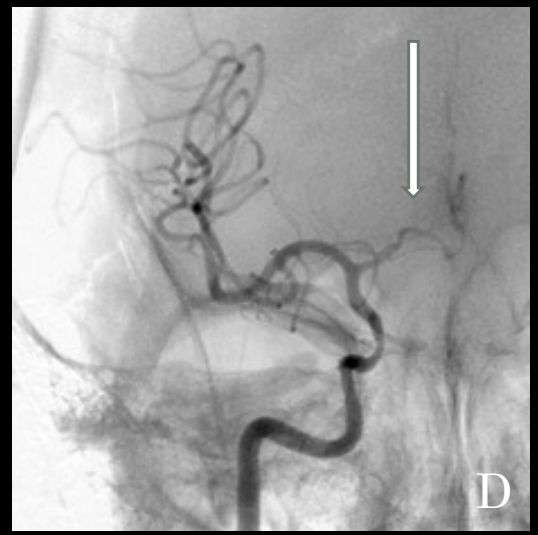
D. E. and F. Interval decrease in size of the pituitary gland on follow up exam. Optic chiasm is displaced inferiorly with increased T2 signal (arrow).

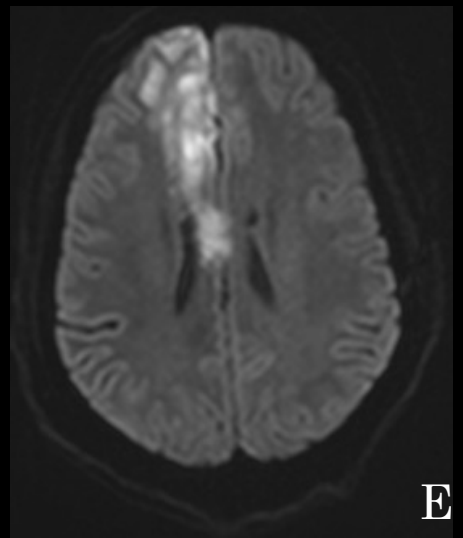
Pituitary apoplexy complicated by stroke

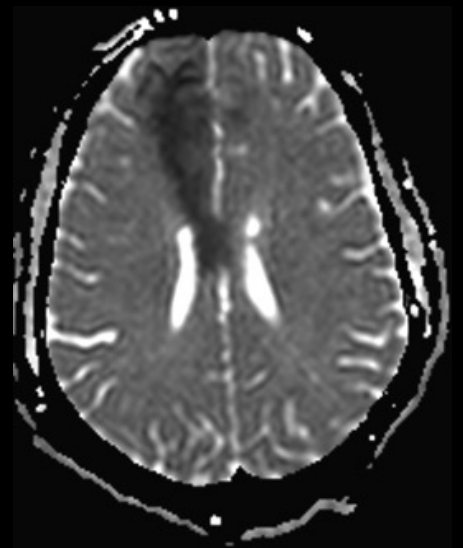












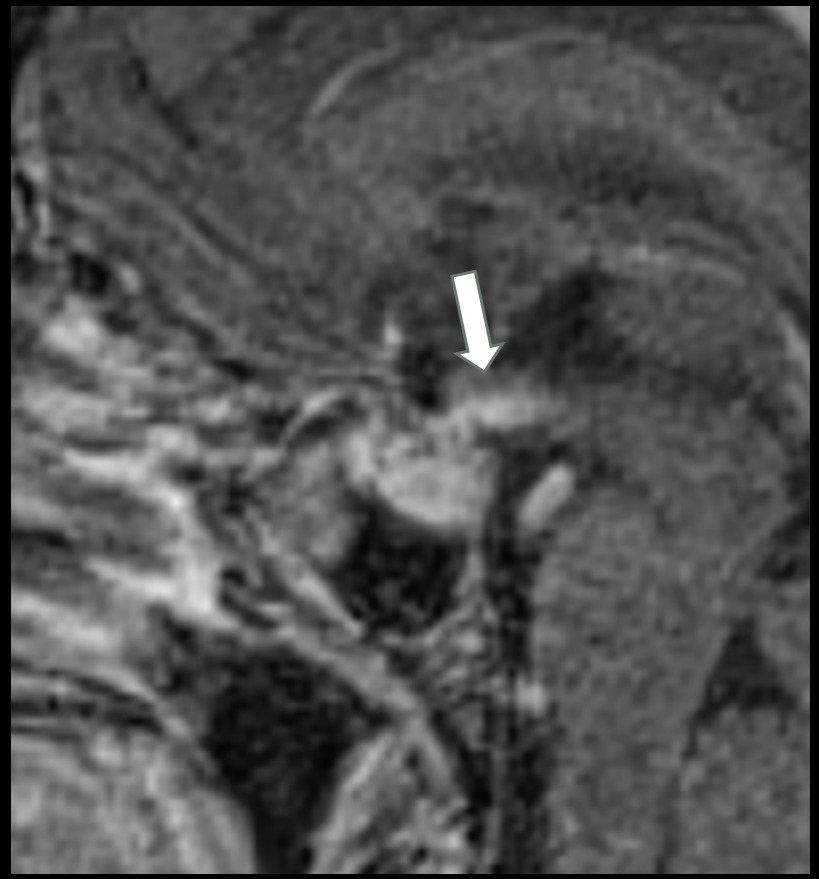
22 yo with altered mental status.

A. B. and C. Sellar/suprasellar mass with areas of T1 shortening and peripheral enhancement.

E. and F. DWI and corresponding ADC map showed acute infarct in bilateral ACA territories, right greater than left.
Cerebral angiogram showed diffuse vasospasm of ACA arteries, right greater than left.

D. Pathology revealed ‘apoplectic pituitary adenoma with gonadotroph differentiation’.

Neurosarcoidosis

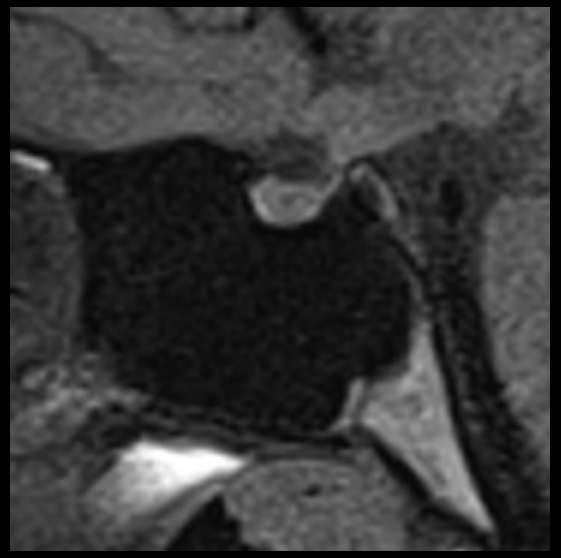


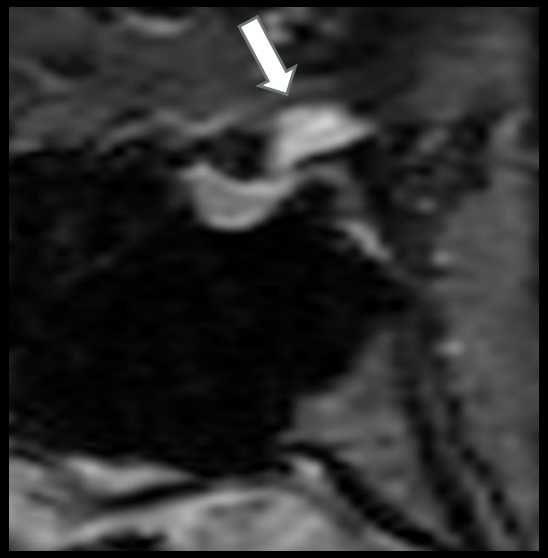
Central nervous system involvement by sarcoidosis occurs in a minority of patients with systemic sarcoidosis.

While pituitary involvement is frequently seen in conjunction with leptomeningeal disease, it may also be isolated, and sometimes confined to the infundibulum.

Sagittal postcontrast T1WI shows pituitary stalk thickening and enhancement extending into the floor of the third ventricle.

Langerhans cell histiocytosis





18 year-old woman who developed symptoms of diabetes insipidus as well as secondary amenorrhea. Abnormal soft tissue thickening of the pituitary infundibulum.

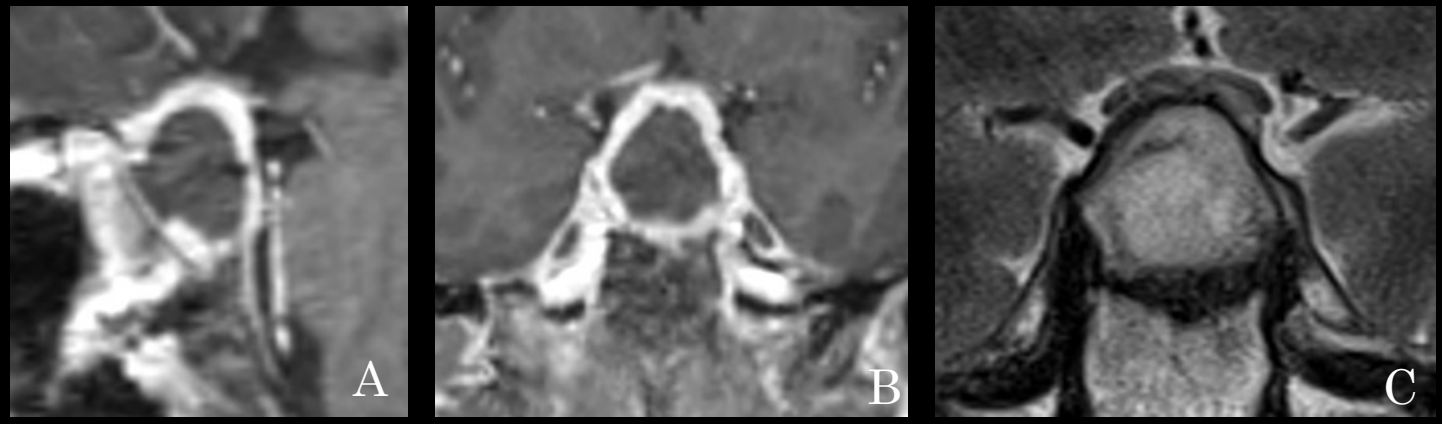
Langerhans cell histiocytosis (LCH) is an idiopathic condition characterized by proliferation of abnormal Langerhans cells which is more commonly seen in children.

Diabetes insipidus is the most common CNS manifestation of LCH. Patients with diabetes insipidus in LCH demonstrate a lack of T1-weighted high intensity of the posterior pituitary with associated enhancement and thickening of the infundibulum. This loss of the normal posterior pituitary bright spot is thought to be a result of the loss of vasopressin stores and is characteristic of CNS involvement in LCH, but is also non-specific.

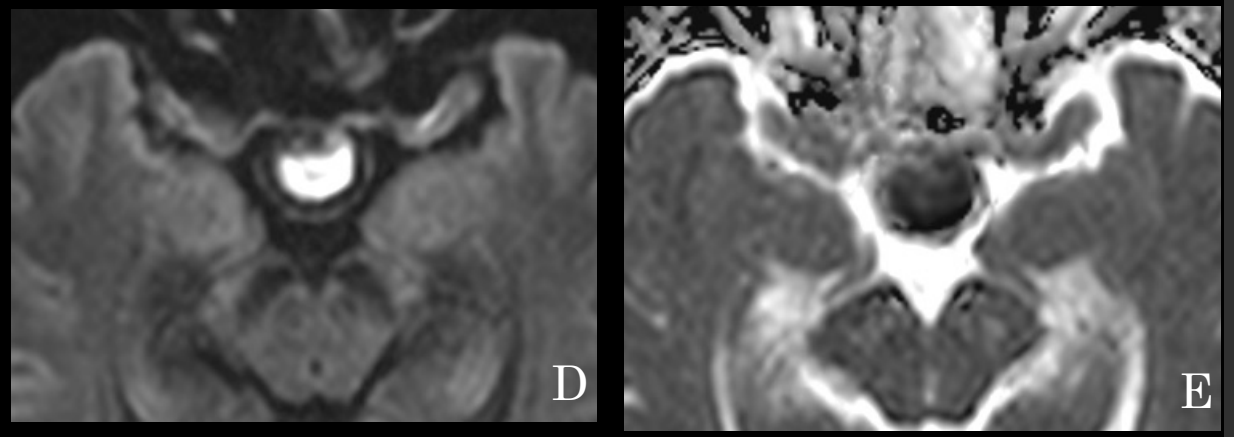
Pituitary abscess

Pituitary abscesses typically develop in patients who have other sources of infection or disruption of the normal suprasellar anatomy by either surgery, radiation or other pre-existing pathology; however, they can develop in the absence of known risk factors.

- 52 year old with history of pituitary macroadenoma status post transphenoidal resection and septoplasty; postop course complicated by CSF leak and sellar abscess. Endoscopic endonasal transsphenoidal fenestration and drainage of pituitary abscess was performed and cultures were notable for MSSA and *Finegoldia magna*. IV ceftriaxone and PO metronidazole administered with good response.



A. and B. Sagittal and coronal postcontrast T1WI show peripherally enhancing sellar/parasellar cystic mass.
C. T2 hypointense rim.
D. and E. DWI and corresponding ADC map show restricted diffusion.



Conclusion

It is important to differentiate non- neoplastic pituitary disorders from neoplastic entities to avoid unnecessary surgeries, healthcare costs, and potential complications.

Neoplastic and non-neoplastic pituitary disorders require different treatment approaches. Misdiagnosis can lead to ineffective treatment and health complications.

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