Imaging the Pituitary and Parasellar Region

Christopher P. Hess, MD, PhD*, William P. Dillon, MD

KEYWORDS

• Pituitary gland • Infundibulum • Sella • Suprasellar cistern • Magnetic resonance imaging

KEY POINTS

- Key distinguishing features for lesions arising in and around the sella on magnetic resonance imaging (MRI) include the site of origin, intrinsic signal and enhancement pattern, and the presence or absence of distinguishing features including cysts, calcification, and fluid-fluid levels.
- Although adenoma is by far the most common abnormality of the pituitary gland, there are several mimics of adenoma that should be considered when reviewing MRI of the sella.
- Pituitary infundibular masses invoke a specific differential diagnosis, depending on the imaging abnormalities present, the presence or absence of the posterior pituitary bright spot, clinical history and demographics, and the presence or absence of other lesions.

Imaging remains the cornerstone of diagnosis for lesions arising in and around the sella. Exquisite soft-tissue contrast and the ability to interrogate the pituitary gland and parasellar anatomy with high spatial resolution and without artifacts from surrounding bony structures have made magnetic resonance imaging (MRI) the primary modality for evaluation of sellar, parasellar, and suprasellar lesions, with computed tomography (CT) reserved for patients with contraindications to MRI and for those undergoing emergent evaluation. This article focuses on the use of MRI to distinguish among common masses and pseudomasses that arise within the sella and parasellar regions. Primary disorders of other surrounding structures that may present with similar clinical symptoms are not discussed.

DIAGNOSTIC APPROACH TO THE SELLA AND INFUNDIBULAR REGION

Imaging Technique

MRI evaluation of the pituitary and parasellar region is best undertaken on modern 1.5-T or 3-T scanners using a protocol that includes both noncontrast and gadolinium-enhanced sequences. Sagittal and coronal planes are most useful, using 3-mm or thinner slices without any interslice gap to adequately evaluate small structures that may be involved in the diseases that occur in this region.

The intrinsic composition of lesions, as characterized based on their T1-weighted and T2-weighted relaxation properties without contrast, usually differs significantly from the pituitary gland, cerebrospinal fluid (CSF), and brain because of the presence of intralesional fluid, protein, hemorrhage, or tumor. Imaging performed after the administration of gadolinium chelate may increase contrast between abnormalities and normal tissues, show otherwise occult disease, and allow one to more confidently differentiate between solid and cystic lesions. Fat suppression is recommended for both T2-weighted and gadolinium-enhanced images, as normal high T2 and T1 signal within the bones of the central skull base may obscure a pathologically high T2 signal or enhancement.

In addition to T1-, T2-, and gadolinium-enhanced T1-weighted images, dynamic contrast-enhanced imaging, gradient-echo T2*-weighted imaging,

Disclosures: None.
Neuroradiology Division, Department of Radiology & Biomedical Imaging, University of California, 505 Parnassus Avenue, San Francisco, CA 94143-0628, USA
* Corresponding author.
E-mail address: christopher.hess@ucsf.edu

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and diffusion-weighted imaging play an important role in the diagnosis of certain disorders and should be added when these disorders are suspected. These abnormalities are discussed individually in subsequent sections.

Normal MRI Appearance of the Pituitary and Infundibulum

The identification of abnormalities in the sella and parasellar region requires familiarity with normal anatomy and biological variability. The normal size of the gland varies with age, measuring up to 12 mm in height in lactating women, 10 mm in menstruating women, 8 mm in males and postmenopausal women, and 6 mm in infants (**Table 1**).

The anterior aspect of the gland, or adenohypophysis, comprises roughly 70% of its volume, and should appear uniform in signal on both unenhanced and enhanced images. Posteriorly within the gland, the neurohypophysis exhibits intrinsic T1 hyperintensity on unenhanced images referred to as the posterior pituitary bright spot (PPBS). The pituitary stalk comprises pars tuberalis cells from the adenohypophysis that surround neurohypophyseal axons descending from the hypothalamus. The normal pituitary infundibulum is wider at its origin from the hypothalamus and tapers inferiorly, reaching its minimum thickness at the level of the pituitary gland. The upper limit for stalk thickness has been reported as 3.5 mm near the median eminence, 2.8 mm at its midpoint, and 2.0 mm at its most inferior aspect. In children, the maximum thickness of the infundibulum is somewhat less, around 2.5 mm.[1]

Interpretative Strategy

A systematic approach to image interpretation is required to develop an accurate differential diagnosis for lesions within or intimately associated with the pituitary gland and/or infundibulum. Key considerations include the following:

- Verification of the normal imaging appearance of the gland and infundibulum, noting its size, enhancement pattern, and presence or absence of the PPBS
- Localization of abnormalities as entirely intrasellar, both sellar and intrasellar, or entirely suprasellar, and as within or separate from the pituitary gland
- Characterization of lesions as entirely solid, entirely cystic, or mixed solid and cystic
- Evaluation of lesion margins (circumscribed or invasive), morphology, and relationship to the normal pituitary
- Distinguishing imaging features that are unique or highly suggestive of certain lesions, such as cysts, low T2 signal, calcification, and fluid-fluid levels
- Presence or absence of mass effect on the optic apparatus, invasion of the cavernous sinuses, and abnormalities located elsewhere in the brain

LESIONS PRIMARY TO THE PITUITARY GLAND

Pituitary Adenoma

Adenoma is the most common abnormality of the pituitary gland and represents 15% of all intracranial neoplasms. It is a slowly growing, benign tumor that almost exclusively arises within the sella and occasionally from the pituitary stalk. Adenomas are rarely found in ectopic sites such as the sphenoid sinus, nasopharynx, cavernous sinuses, and sphenoid bone. Whereas small tumors become clinically manifest owing to excess hormone secretion, larger tumors are more frequently nonsecreting, and tend to present

Table 1
University of California San Francisco magnetic resonance imaging protocol for imaging of the sella

Pulse Sequence	Slice/Gap	Parameters
1. Coronal and sagittal T1	2.7 mm no skip	TR/TE = 600 ms/min, NEX = 3
2. Fat-suppressed coronal T2	2.0 mm no skip	TR/TE = 3000/100 ms, ETL = 16, NEX = 3
3. Dynamic gadolinium-enhanced T1[a]	2.0 mm no skip	TR/TE = 600 ms, ETL = 8, NEX = 2
4. Postgadolinium coronal and sagittal T1	2.7 mm no skip	TR/TE = 800 ms/min, NEX = 3
5. Coronal T2* gradient echo[b]	3.0 mm no skip	TR/TE = 800 ms/25 ms, NEX = 2
6. Axial and coronal diffusion (b = 1000)[c]	2.0 mm no skip	TR/TE = 8000 ms/min, NEX = 1

Abbreviations: ETL, echo train length; NEX, number of excitations; TE, echo time; TR, repetition time.

[a] Dynamic gadolinium-enhanced imaging performed in cases of suspected adenoma and postoperatively after macroadenoma resection.

[b] T2*-weighted (susceptibility sensitive) imaging used for suspected or known hemorrhage or calcification (ie, pituitary apoplexy and craniopharyngioma).

[c] Diffusion-weighted imaging used in cases with suspected or known infection.

with symptoms related to compression of adjacent structures or elevated intracranial pressure.

Prolactin-secreting and growth hormone–secreting adenohypophyseal cells are located more laterally within the normal pituitary gland and corticotropin-secreting, thyroid-stimulating hormone–secreting, and gonadotropin-secreting cells are located more medially. This inherent spatial organization of adenotrophs within the gland imparts a similar spatial distribution to the origin of hormone-secreting adenomas. Pathologically, adenomas are circumscribed and contained within a pseudocapsule of compressed surrounding pituitary tissue, or are locally invasive, equipped on a molecular basis with microscopic machinery that facilitates contiguous spread through the dura into adjacent bone or cavernous sinus.

Microadenomas, tumors that measure less than 1 cm in diameter, exhibit T1 signal on MRI that is the same as or lower than the gland signal unless intratumoral hemorrhage is present (**Fig. 1**). T2 signal is more variable. Most tumors exhibit high T2 signal, and tend to be softer and more readily resected at surgery. Low-T2–signal tumors are less common, but as a group tend to be firmer and more adherent to surrounding tissue on surgical manipulation. Approximately 80% of prolactinomas have high T2 signal, and between 40% and 60% of growth hormone–secreting adenomas have low T2 signal.[2,3] Most tumors are round or discoid in morphology. Subtle contour deformity of the pituitary gland may be present, as may displacement of the infundibulum. The direction of infundibular displacement is usually opposite the side of the tumor, but this finding is only variably seen and is considered unreliable.

Following administration of intravenous gadolinium chelate, microadenomas are relatively hypoenhancing or isoenhancing relative to the normal pituitary gland during the wash-in phase of contrast. Dynamic imaging, whereby high-resolution pituitary images are obtained immediately following bolus injection of contrast, is useful for illustrating the differential uptake of contrast between a microadenoma and normal pituitary gland, and is used to enhance sensitivity to small tumors by up to 10%.[4] Some tumors retain contrast on delayed imaging more avidly than does the gland, such that MRI obtained during the washout phase of contrast may also increase sensitivity, revealing tumors as hyperenhancing relative to the gland.

Tumors larger than 1 cm are referred to as macroadenomas or, if larger than 4 cm, giant adenomas. Slow tumor growth results in progressive enlargement of the sella. The direction of growth is variable. Approximately 80% extend superiorly into the suprasellar cistern, but the remaining 20% grow in any of the remaining 5 directions to invade the cavernous sinuses, sphenoid sinus, or dorsum sella. MRI often reveals more heterogeneous intrinsic signal than microadenoma on both T1-weighted and T2-weighted images, especially when internal tumor cysts, necrosis, and/or hemorrhage develop within the tumor (**Fig. 2**). Enhancement is moderate to avid; rare hypoenhancement has been described as a feature of thyrotropin-secreting tumors.[5] The normal pituitary gland, often compressed around large

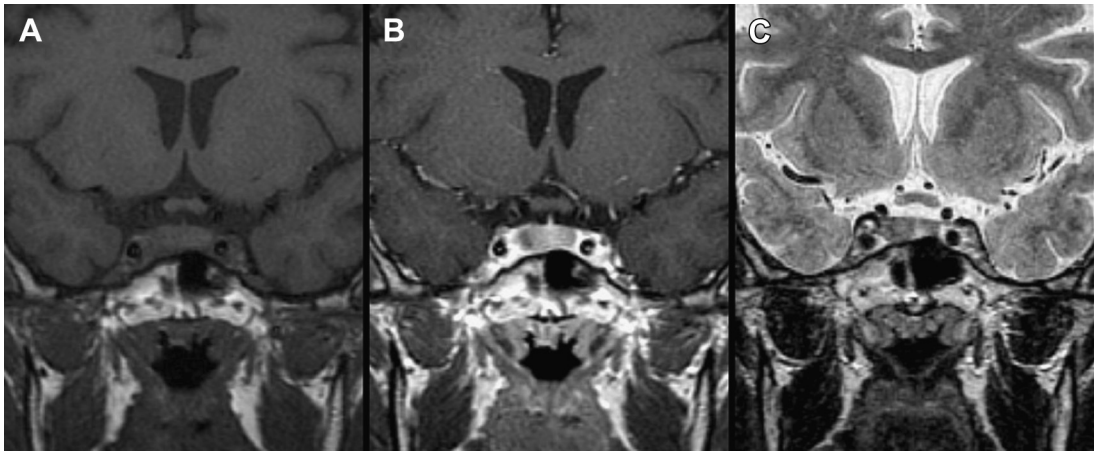

Fig. 1. Microadenoma. Subtle intrinsic low T2 signal in the right lobe of the pituitary (*A*), seen to better advantage on gadolinium-enhanced T1-weighted image as hypoenhancing relative to the surrounding gland (*B*). This growth hormone–secreting microadenoma appears relatively T2 hypointense compared with normal adenohypophyseal tissue (*C*).

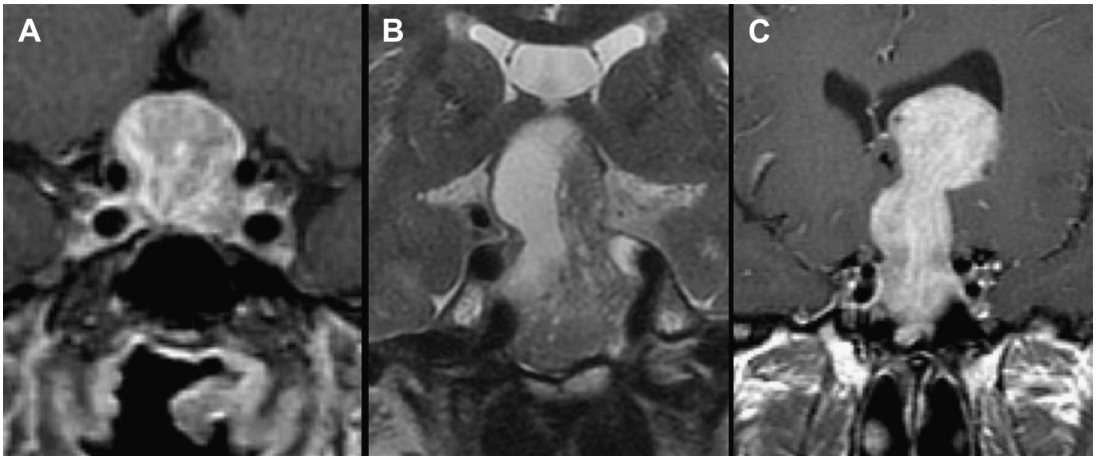

Fig. 2. Macroadenoma. "Dumbbell" or "snowman" appearance of a typical macroadenoma, which shows a narrower waist as it passes through the sellar diaphragm (*A*). Larger macroadenomas are frequently more heterogeneous and contain areas of cystic degeneration (*B*). Tumor growth in adenomas occurs in any direction and may be dramatic, as illustrated in this case in which the superior tumor extends into the third and left lateral ventricle (*C*).

adenomas, is important to identify preoperatively, as preservation of this tissue is a surgical goal in preventing pituitary insufficiency. The PPBS may be difficult to see or even absent, although it is rare for patients with macroadenoma to have central diabetes insipidus (DI).

Pituitary apoplexy is due to acute intratumoral hemorrhage or bland tumor infarction. Although uncommon, it is a surgical emergency with specific features on MRI. The term apoplexy refers to the clinical syndrome that results when hemorrhage causes compression of parasellar structures, especially the optic nerve or chiasm, and/or meningismus.[6] Acute presentation distinguishes this entity from subclinical tumoral hemorrhage, a more common phenomenon referred to as silent apoplexy by some investigators. It is also considered a separate entity from postischemic pituitary hemorrhage in patients with prolonged hypotension, referred to as Sheehan syndrome and classically occurring in women with severe postpartum bleeding. Both are more common in patients with known adenomas.

As rapid loss of vision or acute cranial neuropathy may occur, any mass effect on the optic chiasm should be sought on imaging and discussed as an indication for emergent neurosurgical decompression. Subarachnoid and retroclival hemorrhage may also be present. MRI in the acute setting may be subtle, particularly on the routine T1-weighted images. If blood is present, this appears as intratumoral heterogeneous signal and occasionally fluid-fluid levels, which may be T1 hyperintense owing to the presence of methemoglobin. T2-weighted images typically show hypointensity within hemorrhagic areas, which evolves with time into hyperintensity. T2*-weighted gradient-echo images are more sensitive to the presence of blood products and may demonstrate areas of "blooming," signal loss around areas of hemorrhage. CT is useful to confirm the presence of blood products in acute or equivocal cases.

Nonadenomatous Tumors of the Pituitary Gland

Pituicytomas are histologically benign, World Health Organization Grade 1 tumors derived from pituicytes, populations of astroglial cells in the posterior pituitary and stalk that assist in the regulation of oxytocin and vasopressin secretion. The controversial pathology of these rare tumors is evident from the range of names they have been assigned, including infundibuloma, choristoma, and pilocytic astrocytoma of the neurohypophysis. Clinical presentation varies with location, with sellar tumors most commonly found incidentally or as a result of hypopituitarism, and suprasellar tumors usually present with visual symptoms related to mass effect.

Although most pituicytomas are located in the suprasellar cistern or have both sellar and suprasellar components, it is the only nonadenomatous primary pituitary tumor that has been reported with a purely intrasellar presentation.[7] The tumor is solid and frequently infiltrative, and inseparable from the pituitary gland. Intrinsic signal on MRI is isointense to cortex on unenhanced T1-weighted images and hyperintense to cortex on T2-

weighted images. Pituicytoma is more vascular than adenoma, and enhancement is more frequently uniformly homogeneous than heterogeneous. Primarily because of their posterior location and vascularity, gross total resection of pituicytomas may be difficult or impossible.

Spindle-cell oncocytoma and granular cell tumor of the neurohypophysis are pathologically distinct nonadenomatous tumors of the pituitary gland that are less common even than pituicytoma. The former arises from the adenohypophysis, is commonly both sellar and suprasellar, and is radiologically indistinguishable from the far more common adenoma or lymphocytic hypophysitis. Granular cell tumors, in contradistinction, arise from the neurohypophysis and are entirely suprasellar in most cases, with a smaller number reported with simultaneous sellar and suprasellar location. Hyperdensity on CT may also be a useful distinguishing feature.[7]

Pituitary Carcinoma

Unlike locally invasive adenomas, pituitary carcinomas are rare, with a reported incidence of only 0.2%.[8] These tumors arise from the adenohypophysis and are frequently hormonally active, most commonly secreting corticotropin, prolactin, or growth hormone. Pituitary carcinomas are indistinguishable from adenomas using histologic criteria, and are currently diagnosed only when systemic or craniospinal metastatic disease is identified.

Most pituitary carcinomas present initially as invasive macroadenomas greater than 1 cm in size, demonstrate an aggressive course with rapid growth and multiple recurrences, and are typically diagnosed as carcinomas some 4 to 7 years later when metastases are identified.[9] Central nervous system (CNS) metastases, which are less common than systemic metastases, usually involve the cortex, the cerebellum, the cerebellopontine angle, or the CSF. Outside of the CNS, the liver, lymph nodes, bones, and lung are the most frequent sites of disease. Although most pituitary carcinomas are locally invasive, there are no distinguishing features by imaging save for the presence of metastatic disease.

Pituitary Hyperplasia

Pituitary hyperplasia is a nonneoplastic, polyclonal proliferation of one or more functionally distinct adenohypophyseal cells that results in enlargement of the gland. Hyperplasia can be physiologically normal, for example during pregnancy or lactation, or may be pathologic, either primary or secondary to endocrine gland failure. Most cases are found in hypothyroid patients, in whom the lack of thyroxine from the nonfunctioning thyroid gland results in overproduction of hypothalamic thyrotropin-releasing hormone. Excess of this hormone, in turn, stimulates the pituitary to produce thyroid-stimulating hormone but also results in excess prolactin secretion. Clinically the symptoms of hypothyroidism may be minimal, and masked by symptoms of hyperprolactinemia. MRI in pituitary hyperplasia shows symmetric enlargement of an otherwise normal-appearing, homogeneously enhancing gland (**Fig. 3**). The gland may be mildly or markedly enlarged, and can occasionally enlarge to a point at which adjacent structures including the optic chiasm are compressed.[10] However, in contrast to macroadenoma, there is no remodeling of the sella, and the gland homogeneously enhances.

Lymphocytic Hypophysitis

Lymphocytic hypophysitis is an autoimmune disorder of the pituitary gland that occurs 5 to 8 times more frequently in women than in men, often occurring in the time period 6 months before to 6 months after pregnancy. Clinically, patients present with hypopituitarism, pituitary insufficiency, DI, and/or symptoms related to mass effect on surrounding structures. Many patients have a personal or family history of autoimmune disease, such as Hashimoto or Graves thyroiditis, systemic lupus erythematosus, or primary biliary cirrhosis. The disease is associated with HLA DR4 and DR5.

MRI findings mirror microscopic pathology, which shows edema and infiltration of the pituitary gland by lymphocytes and plasma cells with areas of glandular fibrosis. Although neurohypophysisitis has been described, the disease is more often confined to the adenohypophysis. The normal PPBS may be absent. The pituitary gland and/or infundibulum may be enlarged within a normal volume sella (see **Fig. 3**). Uncommonly, inflammation may be cystic or necrotic, resulting in areas with higher T2 signal and hypoenhancement within the pituitary. Enhancement may be homogeneous or heterogeneous, and an adjacent enhancing dural tail (thought to represent enhancement of adjacent inflamed diaphragma sellae) is a useful secondary finding. Inflammation infrequently extends to secondarily involve the clivus and/or cavernous sinuses, where narrowing of the lumen of the internal carotid arteries can occur.

Because of its relative infrequency, lymphocytic hypophysitis is often mistaken on MRI for adenoma or other disorders. Symmetric suprasellar extension and midline pituitary stalk position

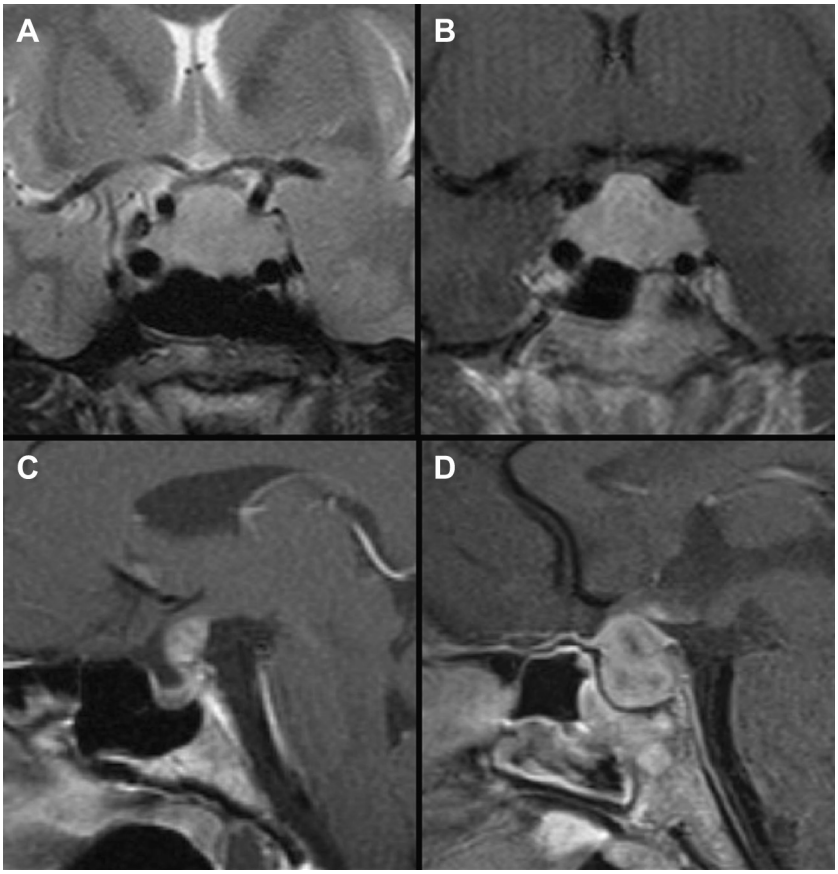

Fig. 3. Pituitary hyperplasia (*A*, *B*) and lymphocytic hypophysitis (*C*, *D*). Both T2-weighted (*A*) and gadolinium-enhanced T1-weighted (*B*) images show enlargement the pituitary gland with uniform T2 signal intensity and enhancement, without sellar enlargement, in a 28-year-old woman presenting with hyperprolactinemia and hypothyroidism. (*C*, *D*) Two cases of lymphocytic hypophysitis, one with infundibular thickening (*C*) and the other showing heterogeneous enhancement within an enlarged pituitary gland (*D*). In *D*, note subtle thickening of the sellar diaphragm with adjacent "tails" of inflammatory dural enhancement anterior and posterior to the gland along the planum sphenoidale and dorsum sellae.

help to differentiate this disorder from adenoma. Nakata and colleagues[11] have also recently described low signal on T2-weighted images around the pituitary gland and in the cavernous sinus as uncommon but highly specific to lymphocytic hypophysitis. Although the disease usually responds to immunotherapy, the natural history is usually one of multiple remissions and relapses.

NONPITUITARY SELLAR LESIONS

Intrasellar Meningioma

Intrasellar meningiomas arising from the inferior layer of the diaphragma sellae or along the anterior wall of the sella from the periosteal meningeal layer of the tuberculum sella, limbus sphenoidale, or the chiasmatic sulcus can masquerade as macroadenomas.[12] Similar to large adenomas, these tumors present more frequently with changes in vision or signs of elevated intracranial pressure than with pituitary dysfunction. However, mechanical compression of the pituitary infundibulum may be associated with a "stalk effect" whereby the loss of normal dopaminergic inhibition from the hypothalamus results in mild pituitary hypersecretion of prolactin.

Intrasellar meningiomas may reside entirely within the sella or extend superiorly into the suprasellar cistern. Tumors that arise from the inferior surface of the diaphragma sellae displace the normal pituitary inferiorly, and the more common tumors arising from the anterior wall of the sella displace the gland posteriorly. Meningiomas calcify more frequently than adenomas, and may show a "tail" of contiguous thickened dura that extends peripherally from the edges of the mass, along the

dural reflections of the cavernous sinuses or planum sphenoidale (**Fig. 4**). Bony hyperostosis and pneumosinus dilatans (focal enlargement of adjacent air-filled paranasal sinus), if present, are useful distinguishing features. Enhancement on MRI is variable, but meningiomas typically enhance slightly less than the pituitary gland. A cleavage plane between the tumor and the pituitary assists in its differentiation from macroadenoma. Meningiomas that extend into the cavernous sinus narrow the lumen of the cavernous internal carotid artery more frequently than invasive adenomas.

Lymphoma

Sellar presentation of lymphoma is exceedingly rare. Primary CNS lymphoma, which most frequently has a B-cell non-Hodgkin histology, most commonly arises in the periventricular white matter and corpus callosum. Low T2 signal and reduced diffusion are typical features on MRI. Leptomeningeal and intraventricular spread of lymphoma may involve the chiasmatic, infundibular, and suprasellar cisterns. Multifocal disease can help to distinguish this disorder from the far more common adenoma. Although CNS lymphoma usually enhances homogeneously elsewhere in the brain, more heterogeneous enhancement has been described in primary sellar lymphoma.[13]

Metastasis

Although metastases to the pituitary gland or stalk are frequent in autopsy studies of patients with widely disseminated cancer, antemortem diagnosis of pituitary metastases is uncommon. Breast and bronchogenic carcinoma are the most common primary cancers, with pituitary metastases more common in patients with concomitant osseous metastases or with multifocal metastatic disease in 5 or more locations.[14] Asymptomatic lesions are now commonly identified with 3-T MRI techniques; symptomatic lesions are

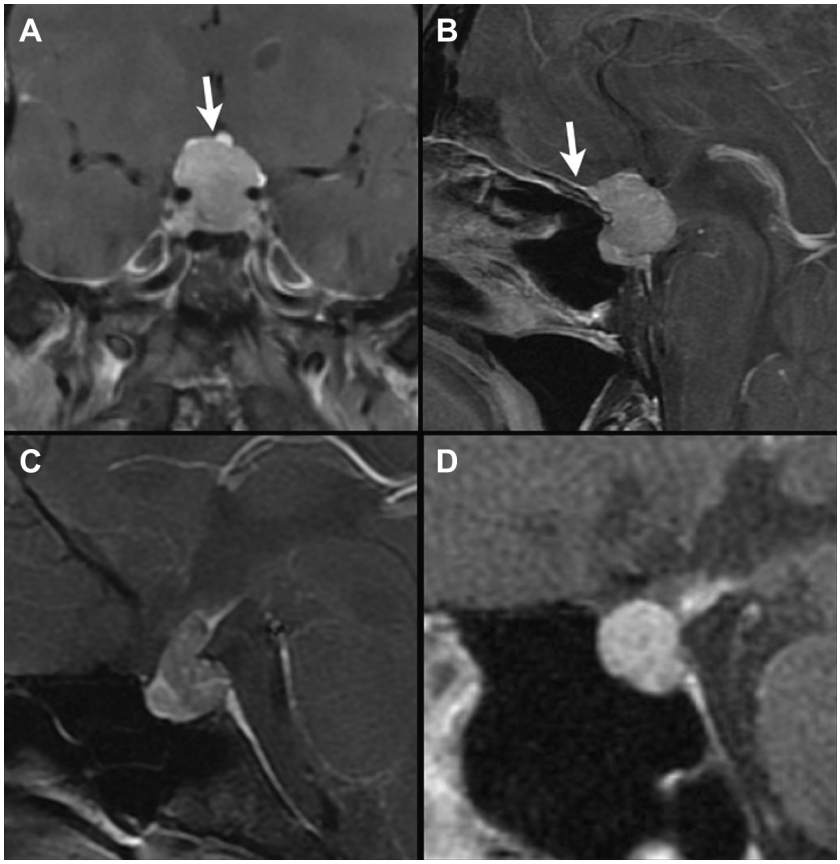

Fig. 4. Macroadenoma mimics. Coronal (*A*) and sagittal (*B*) gadolinium-enhanced T1-weighted images showing sellar and suprasellar mass with portions of the residual pituitary displaced superiorly by the mass (*A*, *arrow*) and anterior dural tail along the planum sphenoidale (*B*, *arrow*). Breast (*C*) and bronchogenic (*D*) carcinoma metastatic disease may also mimic adenoma.

associated with DI, anterior pituitary insufficiency, or retro-orbital pain. Because of its direct blood supply, the posterior lobe of the gland is involved more frequently than the anterior lobe. Imaging shows locally invasive and rapidly growing lesions within or separable from the pituitary (see **Fig. 4**). Erosion of the dorsum sella or the inferior sellar wall may help to distinguish metastases from other adenomas or craniopharyngiomas, which are more typically invasive than destructive.

INFUNDIBULAR ABNORMALITY

Lymphocytic hypophysitis, metastatic disease, and rarely primary pituitary tumors may show isolated involvement of the pituitary infundibulum. The differential diagnosis of lesions is broad, however, and several other disorders also frequently affect this structure (**Box 1**).

Germinoma

Germinoma and Langerhans cell histiocytosis (LCH) are the most common causes of central DI in the pediatric age group. In both disorders, MRI reveals absence of the normal PPBS in more than 90% of children presenting with this symptom, and infundibular thickening in roughly one-third.[15] When the infundibulum is normal and DI persists, serial reimaging at 3- to 6-month intervals is indicated, as a time lag of up to 14 months has been reported between the initial onset of symptoms and development of lesions on MRI.[16]

Pineal and hypothalamic tumor locations are more common than infundibular disease in germinoma. Isolated sellar disease is rare, although infundibular tumors may extend inferiorly into the posterior sella.[17] The PPBS is characteristically absent on MRI in patients presenting with central DI. High cellularity results in hyperdensity relative to the normal brain on CT (**Fig. 5**) as well as low signal on T2-weighted MRI, although both intrinsic T1 and T2 signals are variable. Tumor cysts may be present in some cases. Because synchronous tumors in the pineal gland are not uncommon, this region should be critically scrutinized. Leptomeningeal dissemination may also occur, resulting in tumoral studding of the ventricular surface or CSF spaces. Measurement of serum and CSF β–human chorionic gonadotropin and α-fetoprotein may assist in diagnosis of germinoma and sometimes obviate biopsy.

Box 1
Infundibular mass differential

- Germinoma
- Lymphocytic hypophysitis
- Langerhans cell histiocytosis
- Adenoma or nonadenomatous pituitary tumors
- Granulomatous disease (sarcoid, Wegener granulomatosis, tuberculosis)
- Lymphoma
- Metastatic disease
- Other infiltrative disease: Erdheim-Chester, Rosai-Dorfman

Langerhans Cell Histiocytosis and Other Histiocytoses

LCH is a rare disorder of unknown etiology, characterized by localized or systemic clonal proliferation of antigen-presenting cells derived from the monocyte-macrophage system. The hypothalamic-pituitary axis is the most common site of intracranial disease. Although most frequently observed in the pediatric age group, the disorder can present at any age from neonate to geriatric. Central DI occurs as the initial presentation in up to 25% of patients, followed by a deficit in at least one other anterior pituitary hormone in many patients at some point during the disease course.

The most common MRI finding in LCH is absence of the normal PPBS. Nearly an equal proportion of patients show diffuse or focal thickening of the pituitary infundibulum (see **Fig. 5**). Rarely, infundibular thinning is observed. Lesions may extend to involve the hypothalamus superiorly and/or the sella and pituitary inferiorly. Except in cases of large masses, the stalk remains midline. T1 signal is usually low relative to cortex, although subtle T1 hyperintensity has been described and can be useful for differential diagnosis. Lesions are T2 hyperintense and enhance homogeneously. Rarely, LCH occurs as a separate lesion in the meninges, choroid plexus, or brain parenchyma.

Both absence of the PPBS and infundibular thickening are not specific to LCH, and can be found in germinoma and other infiltrative diseases. When one or both of these findings is present, however, other imaging abnormalities may suggest LCH. In a series of 163 patients with LCH,[18] craniofacial osseous lesions were seen in 56%, nonspecific paranasal sinus and/or mastoid opacification in 55%, enlarged Virchow-Robin spaces in 70%, and leukoencephalopathy in 36%. The skull base, especially the temporal bone around the mastoids, is the most frequent site of osseous craniofacial disease,[19] with lytic "punched-out" lesions showing characteristic beveled edges at their periphery. These locations

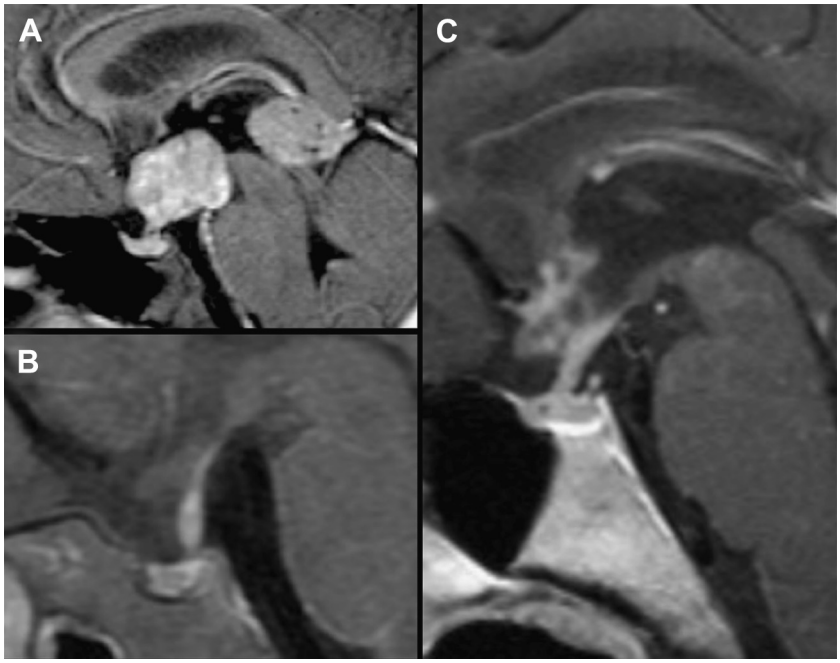

Fig. 5. Infundibular disease. (*A*) Infundibular and pineal masses in a patient with germinoma. (*B*) Subtle thickening of the infundibulum in a child with diabetes insipidus and Langerhans cell histiocytosis. (*C*) Thickening of the pituitary stalk accompanied by irregular enhancement along the anterior recesses of the third ventricle (and inferiorly in the tectal plate) in a patient with neurosarcoid.

may be better than CNS lesions for obtaining histologic confirmation.

Rarely, non–Langerhans cell histiocytoses may also involve the pituitary. Erdheim-Chester disease is a lipogranulomatous disorder in which abnormal lipid-laden macrophages accumulate in various body systems, most commonly the musculoskeletal system. Isolated pituitary infundibular disease has been reported, although hypothalamic disease and dural disease are more common in the CNS.[20,21] Similarly, Rosai-Dorfman disease is an unusual proliferative disease of histiocytes characterized by pale eosinophilic cytoplasm that usually presents with cervical lymphadenopathy or nasal obstruction and, rarely, extranodal disease, including the sella.[22,23]

Granulomatous Hypophysitis

Granulomatous hypophysitis is a less common but histologically distinct variant of adenohypophysitis that may be idiopathic or associated with granulomatous inflammatory disease (tuberculosis, sarcoid, or syphilis, for example), or systemic diseases such as Takayasu arteritis, Crohn disease, Wegener granulomatosis, and thyroiditis. Granulomatous inflammation can also result after rupture of Rathke cleft cyst. Unlike lymphocytic hypophysitis, granulomatous hypophysitis occurs with roughly equal incidence in men and women. The imaging appearance overlaps that of lymphocytic hypophysitis, although high T2 signal may be more common in Wegener granulomatosis.[24,25] Concomitant disease elsewhere in the CNS is common in cases of tuberculosis and sarcoidosis, with characteristic nodular leptomeningeal enhancement present in the basilar cisterns, perivascular spaces, or along cranial nerves in many cases (see **Fig. 5**).

CYSTIC LESIONS

Different lesions with cystic composition that arise in the sella are given in (**Box 2**).

Arachnoid Cyst

The pituitary gland and stalk are enveloped within a thin membranous capsule that is derived from the pia, but the sella does not normally contain arachnoid cells.[26] True arachnoid cysts in this location that are isolated from the subarachnoid space are thus distinctly uncommon, hypothesized to arise either as obstructed herniations through the sellar diaphragm or de novo from subarachnoid rests within the sella. Pathologically, the cyst wall comprises a single layer of mesothelial cells surrounded by a collagenous layer. The

Box 2
Cystic mass differential

- Arachnoid cyst
- Rathke cleft cyst
- Craniopharyngioma
- Cystic or hemorrhagic adenoma
- Abscess
- Dermoid cyst
- Epidermoid cyst

clinical presentation mimics that of a nonsecreting adenoma, usually in older patients. On imaging, arachnoid cysts approximate CSF signal intensity on all sequences. A discrete cyst wall is not identified, although the normal gland is compressed posteriorly and inferiorly.

Similar but distinct from true arachnoid cysts of the sella, the so-called empty sella results when the subarachnoid herniates through the diaphragmatic hiatus and enlarges over time. More common in middle-aged and elderly women, it has been speculated that empty sella "syndrome" results from enlargement of the diaphragmatic hiatus by physiologic enlargement of the pituitary gland during pregnancy and later herniation of the arachnoid through the secondarily incompetent hiatus.

Rathke Cleft Cyst

Nonneoplastic cysts arising from embryonic Rathke cleft, which normally regresses following development of the adenohypophysis, are most often discovered incidentally during cranial imaging for other causes. Clinical symptoms arise from mass effect; headache and visual symptoms are more common than hypopituitarism. Histologically, a single layer of columnar or cuboidal epithelial cells envelops the fluid within the cyst. The natural history is one of slow growth over time. A roughly 20% recurrence rate is documented following surgical resection and is increased by fat graft, which is consequently avoided by most surgeons. Squamous metaplasia within the epithelial layer of the cyst on pathologic examination also makes recurrence more likely.

MRI of Rathke cleft cyst demonstrates a sharply circumscribed, unilocular cyst, which (unlike cystic adenoma) is usually located in the midline. The cysts are more commonly intrasellar but sometimes sellar and suprasellar. Purely suprasellar cysts are unusual. Within the sella, cysts arise between the anterior and posterior lobes of the adenohypophysis, within the pars intermedia region of the gland. In cases of suprasellar extension, cysts are located along the anterior aspect of the infundibulum. Intrinsic signal varies based on cyst contents, with roughly two-thirds containing "machine oil" fluid with high T1 and variable T2 signal, and the other third containing simple serous fluid that more closely approximates the composition and signal intensity of normal CSF (**Fig. 6**). Of the roughly 70% cysts with high T2 signal, an intracystic, T2 hypointense and nonenhancing mural nodule is diagnostic. Hemorrhage within Rathke cysts is extremely rare, but when it occurs patients may present with symptoms of apoplexy, and fluid-fluid levels may be identified within cysts with hemorrhage. Thin or absent cyst-wall enhancement is characteristic of these lesions. Infection of Rathke cleft cyst is also a rare complication. Features suggestive of infection include rapid enlargement of the cyst, enhancement, and surrounding edema.

Craniopharyngioma

Unlike most other cystic sellar and suprasellar lesions, craniopharyngioma is a true neoplasm of epithelial cells.[27] Presenting clinical symptoms are related to elevated intracranial pressure, visual changes, hypopituitarism, and, interestingly, neuropsychiatric deficits related to compression or invasion of frontal or temporal lobe structures. Pathologically these tumors are divided into 2 subtypes, adamantinomatous and squamous-papillary; it is speculated that the former originate from squamous cell rests along the involuted embryologic craniopharyngeal duct and the latter arise in squamous metaplasia of cells deriving from the pars tuberalis of the adenohypophysis. The adamantinomatous variant occurs in adults but is far more common in children, and with rare exception the squamous-papillary type is seen only in adults. Tumors with adamantinomatous histology (or mixed or transitional histology) are histologically benign but biologically aggressive, and their tendency to invade surrounding structures often prevents gross total surgical resection. Gross total resection of squamous-papillary craniopharyngioma is curative.

Adamantinomatous craniopharyngiomas arise from anywhere along the primitive craniopharyngeal duct, but in contrast to Rathke cleft cyst, 90% to 95% have a suprasellar component; pure intrasellar tumors are rare, seen in 5% or fewer of cases. Unlike Rathke cleft cysts, which are smaller and most commonly intrasellar, craniopharyngiomas are larger (>2 cm) and typically centered in the suprasellar cistern with inferior extension into

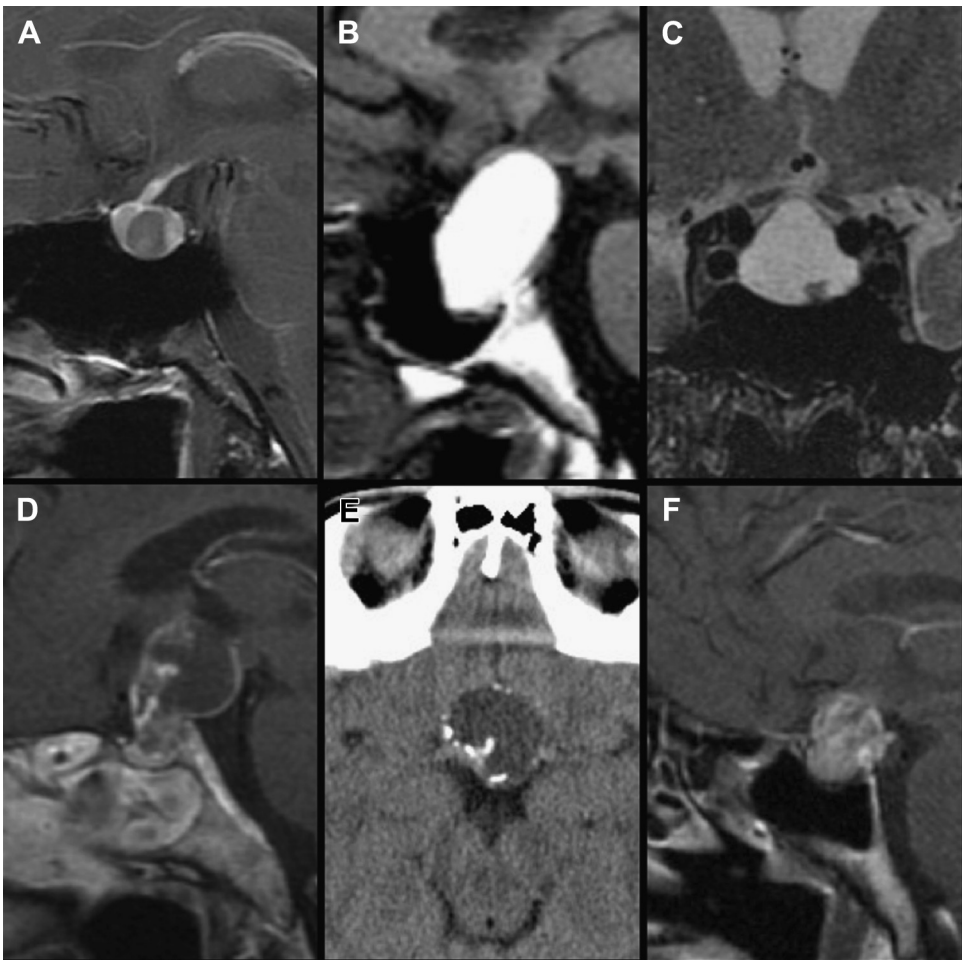

Fig. 6. Rathke cleft cysts (*A–C*) and craniopharyngioma (*D–F*). (*A*) Classic Rathke cleft cyst seen as a rounded, nonenhancing sellar mass within the pars intermedia. (*B*) "Machine oil" cyst with uniform high T1 signal on unenhanced T1-weighted image. (*C*) Fluid-type Rathke cyst with high T2 signal and eccentric mural nodule. (*D*) Adamantinomatous craniopharyngioma gadolinium-enhanced MRI and (*E*) unenhanced CT in the same pediatric patient, showing solid and cystic mass with eccentric mural calcification. (*F*) Note the more solid appearance of squamous-papillary craniopharyngioma in an adult.

the sella (see **Fig. 6**). A single unilocular cyst is less common than multiple conglomerate cysts, the former characterized by a smooth contour and the latter by a lobulated contour. High T1 signal is evident within one or more cysts in 80% of cases. Unlike Rathke cleft cysts, enhancement of cyst walls can be prominent, and a solid enhancing component, although typically small, is usually present.

Calcification, present in 90% of cases and seen at the periphery of individual cystic components, can be challenging to identify on MRI. Low T1 and T2 signal that blooms on gradient-echo images is typical, although calcification may also be seen with high T1 or T2 signal or may be occult if present in low concentrations. CT obtained in equivocal cases can assist in distinguishing these tumors from Rathke cleft cysts and macroadenomas, in which calcification is far less common. Hydrocephalus may be present when there is significant invasion of surrounding structures or extension into the third ventricle. Although uncommon, malignant transformation may occur after irradiation, and dissemination through the CSF or along the surgical tract are known complications.

Tumors with squamous-papillary and mixed histology have a less prominent cystic component and a spherical morphology, and may be entirely solid. Calcification is atypical, and tumor infiltration of surrounding structures is less frequent than with the adamantinomatous subtype. Papillary tumors

may occasionally arise in ectopic locations such as the floor of the third ventricle, the posterior fossa, and the nasopharynx.

Cystic and Hemorrhagic Adenoma

Microadenoma may occasionally present with intrapituitary hemorrhage or tumor cyst formation, without a discrete solid enhancing component on MRI. Although the former may contain fluid levels or heterogeneous signal intensity to suggest the presence of intralesional hemorrhage, a unilocular cyst without enhancement may also be observed. Unlike Rathke cleft cysts, adenomas are almost always off midline (**Fig. 7**). However, follow-up MRI in 1 to 3 months to characterize the temporal evolution of lesions may be the only method to distinguish hemorrhagic and cystic adenomas from other pituitary cysts. Specifically, hemorrhage typically evolves in signal over time, becomes smaller, and may result in spontaneous obliteration of the adenoma. Adenomas with tumor cysts, by contrast, remain similar in signal and either increase in size or develop a solid enhancing component that can be more readily visualized on follow-up.

Pituitary Abscess

The diagnosis of abscess within the pituitary gland is seldom made prospectively; pus is more commonly identified during transsphenoidal resection of preoperatively presumed cystic neoplasms. An underlying lesion such as adenoma, Rathke cyst, or craniopharyngioma can serve as the initial nidus for infection, but abscess is more commonly the result of either contiguous or hematogenous spread from a separate nidus of infection. Prior surgery and radiation are the major risk factors. Only one-third of patients have fever and/or leukocytosis; one-fourth present with frank meningitis. Hypopituitarism is frequent, leading to clinical suspicion for other pituitary abnormalities.

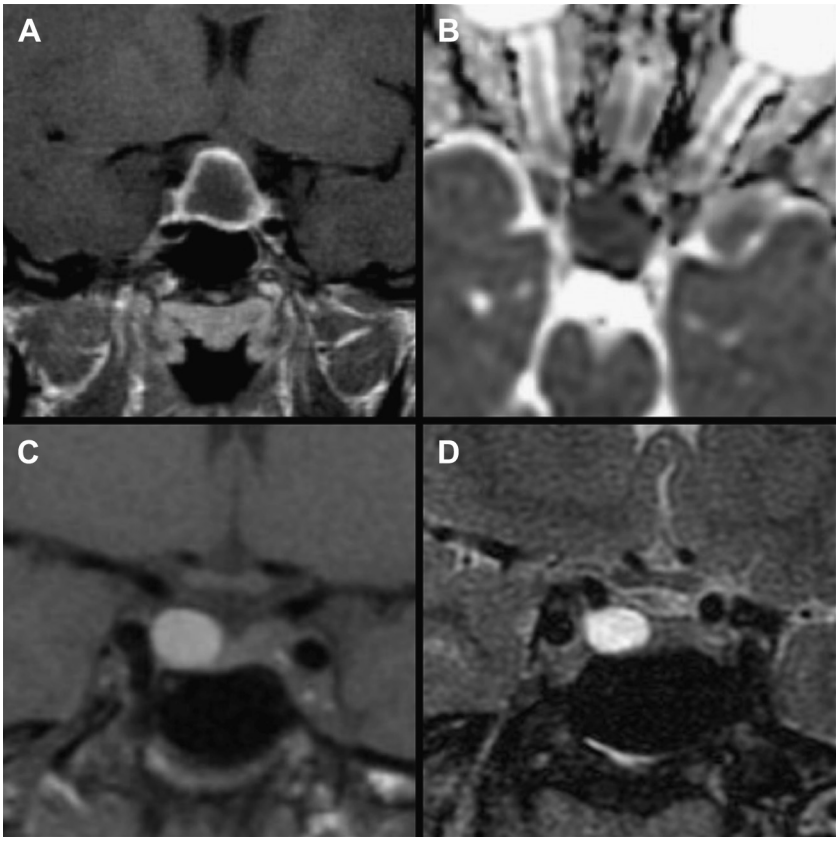

Fig. 7. Cystic sellar masses. Gadolinium-enhanced T1 (*A*) and axial apparent diffusivity map (*B*) in a patient with intrapituitary abscess. Irregular enhancement of the abscess wall and reduced diffusion distinguish this lesion from other cystic lesions in the pituitary gland. (*C*) High T1 signal within a hemorrhagic adenoma on unenhanced T1-weighted image, which resolved on follow-up. (*D*) Cystic adenoma showing high T2 signal laterally within the pituitary. Only 10% of Rathke cleft cysts are located off the midline.

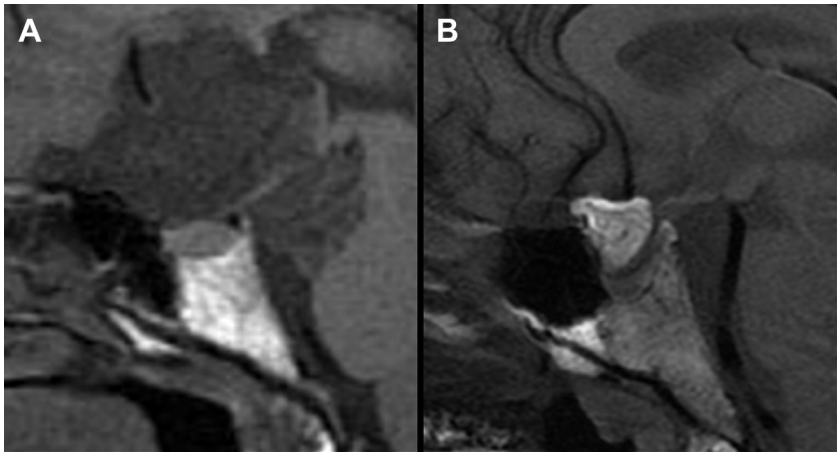

Fig. 8. Epithelial cysts. Unenhanced T1-weighted image shows multilobulated epidermoid cyst (*A*) with subtle T1 hyperintensity relative to normal prepontine CSF surrounding the sella and displacing surrounding structures. The same sequence in a patient with a sellar dermoid cyst (*B*) illustrates intrinsic T1 hyperintensity caused by fat within the tumor.

MRI appearance of pituitary infection overlaps with the appearance of other pituitary cystic disease. Subtle T1 hyperintensity and slightly heterogeneous T2 hyperintensity may herald the presence of infectious debris and trace blood products often seen with infections (see **Fig. 7**). Reduced diffusion on diffusion-weighted imaging, when performed, is very suggestive of infection, and may be useful in monitoring treatment. Furthermore, the peripherally enhancing rim of pyogenic abscess is less commonly smooth and thin than with cystic neoplasm, and abscesses may instead show subtle indistinctness and nonuniform thickness of the enhancing wall.

Epidermoid and Dermoid Cysts

Epidermoid tumors usually present in adults because of local mass effect. Unlike dermoid cysts, these tumors are often either off midline or asymmetric to one side of the midline. These cysts frequently insinuate around local anatomic structures, including the skull base and cranial nerves. MRI shows relatively circumscribed lesions with signal intensity that differs slightly from CSF, often slightly higher than CSF on T1-weighted and T2-weighted images (**Fig. 8**). Similar to the case of infection, high signal on diffusion-weighted images can be an important finding for differentiating epidermoid from other cystic lesions.

Dermoid cysts are up to 10 times less common than epidermoid cysts. Almost always found in the midline, these tumors represent congenital inclusion cysts that result when ectodermal and mesodermal epithelial elements remain trapped intracranially during embryonic closure of the neural tube. Dermoid cysts often contain fat, calcification, and fluid in various proportions, and may present with cyst rupture and chemical meningitis. High T1 signal caused by lipids within the tumor (see **Fig. 8**), or within the CSF spaces in cases of rupture, are characteristic.

REFERENCES

1. Atkins D, Sanford R. Infundibuloneurohypophysitis in children. Padiatr Neurosurg 1999;30:267–71.
2. Lundin P, Nyman R, Burman P, et al. MRI of pituitary macroadenomas with reference to hormonal activity. Neuroradiology 1992;34:43–51.
3. Hagiwara A, Inoue Y, Wakasa K, et al. Comparison of growth hormone-producing and non-growth hormone-producing pituitary adenomas: imaging characteristics and pathologic correlation. Radiology 2003;228:533–8.
4. Bartynski WS, Lin L. Dynamic and conventional spin-echo MR of pituitary microlesions. AJNR Am J Neuroradiol 1997;18:965–72.
5. Sarlis NJ, Gourgiotis L, Koch CA, et al. MR imaging features of thyrotropic-secreting pituitary adenomas at initial presentation. AJR AM J Roentgenol 2003; 181:577–82.
6. Nawar RN, Abdel Mannan D, Selman WR, et al. Pituitary tumor apoplexy: a review. J Intensive Care Med 2008;23:75–89.
7. Covington MF, Chin SS, Osborn AG. Pituicytoma, spindle cell oncocytoma, and granular cell tumor: clarification and meta-analysis of the world literature since 1893. AJNR Am J Neuroradiol 2011;32:2067–72.
8. Kaltsas GA, Nomikos P, Kontogeorgos G, et al. Clinical review: diagnosis and management of pituitary carcinomas. J Clin Endocrinol Metab 2005;90: 3089–99.

9. Pernicone PJ, Scheithauer BW, Sebo TJ, et al. Pituitary carcinoma: a clinicopathologic study of 15 cases. Cancer 1997;79:804–12.
10. Wolansky LJ, Leavitt GD, Elias BJ, et al. MRI of pituitary hyperplasia in primary hypothyroidism. Neuroradiology 1996;38:50–2.
11. Nakata Y, Sato N, Masumoto T, et al. Parasellar T2 dark sign on MR imaging in patients with lymphocytic hypophysitis. AJNR Am J Neuroradiol 2010; 31:1944–50.
12. Chi JH, McDermott M. Tuberculum sellae meningiomas. Neurosurg Focus 2003;14:1–6.
13. Kaufmann TJ, Lopes MB, Laws ER, et al. Primary sellar lymphoma: radiologic and pathologic findings in two patients. AJNR Am J Neuroradiol 2002;23: 364–7.
14. Morita A, Meyer F, Laws E. Symptomatic pituitary metastases. J Neurosurg 1998;89:69–73.
15. Alter CA, Bilaniuk LT. Utility of magnetic resonance imaging in the evaluation of the child with central diabetes insipidus. J Pediatr Endocrinol Metab 2002;15(Suppl 2):681–7.
16. Mootha SL, Barkovich AJ, Grumbach MM, et al. Idiopathic hypothalamic diabetes insipidus, pituitary stalk thickening, and the occult intracranial germinoma in children and adolescents. J Clin Endocrinol Metab 1997;82:1362–7.
17. Kanagakia M, Mikia Y, Takahashib JA, et al. MRI and CT findings of neurohypophyseal germinoma. Eur J Radiol 2004;49:204–11.
18. Prayer D, Grois N, Prosch H, et al. MR imaging presentation of intracranial disease associated with Langerhans cell histiocytosis. AJNR Am J Neuroradiol 2004;25:880–91.
19. D'Ambrosio N, Soohoo S, Warshall C, et al. Craniofacial and intracranial manifestations of Langerhans cell histiocytosis: report of findings in 100 patients. Am J Roentgenol 2008;191:589–97.
20. Wright RA, Hermann RC, Parisi JE. Neurological manifestations of Erdheim-Chester disease. J Neurol Neurosurg Psychiatr 1999;66(1):72–5.
21. Adem C, Hélie O, Lévêque C, et al. Case 78: Erdheim-Chester disease with central nervous system involvement. Radiology 2005;234:111–5.
22. Kelly WF, Bradey N, Scoones D. Rosai-Dorfman disease presenting as a pituitary tumour. Clin Endocrinol 1999;50:133–7.
23. Woodcock RJ, Mandell JW, Lipper MH. Sinus histiocytosis (Rosai-Dorfman disease) of the suprasellar region: MR imaging findings—a case report. Radiology 1999;213:808–10.
24. Katzman GL, Langford CA, Sneller MC, et al. Pituitary involvement by Wegener's granulomatosis: a report of two cases. AJNR Am J Neuroradiol 1999;20:519–23.
25. Goyal M, Kucharczyk W, Keystone E. Granulomatous hypophysitis due to Wegener's granulomatosis. AJNR Am J Neuroradiol 2000;21:1466–9.
26. Dubuisson AS, Stevenaert A, Martin D, et al. Intrasellar arachnoid cysts. Neurosurgery 2007;61:505–13.
27. Zada G, Lin N, Ojerholm E, et al. Craniopharyngioma and other cystic epithelial lesions of the sellar region: a review of clinical, imaging and histopathological relationships. Neurosurg Focus 2010;28:E4.