Anatomic and Pathologic Spectrum of Pituitary Infundibulum Lesions

OBJECTIVE. The pathologic spectrum of pituitary infundibulum disease is diverse. We reviewed 65 infundibular lesions in 44 adult and 21 pediatric patients and summarized their imaging features and clinical presentation.

CONCLUSION. The spectrum of pathology involving the pituitary infundibulum is broad yet distinct from other pathology in the sella and parasellar region. Pituitary stalk lesions can be grouped into three categories: congenital and developmental, inflammatory and infectious, and neoplastic. Knowledge of the imaging appearance of diseases specific to adults and to children is important for accurate diagnosis and treatment.

The spectrum of pathology involving the pituitary infundibulum is broad yet distinct from other pathology in the sella and parasellar region. Infundibular pathology is usually considered with more general sellar and parasellar disease.

We reviewed 65 infundibular lesions and summarized their imaging features and clinical presentation. Lesions affecting the pituitary infundibulum were grouped into three broad categories: congenital and developmental, inflammatory and infectious, and neoplastic.

Materials and Methods
A retrospective review of our institutional case archive from 1995 to 2003 revealed 65 infundibular lesions. Imaging and clinical presenting features were evaluated to better characterize the pathologic spectrum of pituitary infundibulum disease. For the purposes of this study, patients older than 21 years were considered to be adults. Patients 21 years or younger were considered pediatric.

High-resolution MRI was performed in 45 patients using 3-mm sections through the pituitary gland with unenhanced T1-weighted and contrast-enhanced T1-weighted sagittal and coronal images, and coronal 3-mm T2-weighted images through the gland. Three patients underwent dynamic gadolinium-enhanced MRI through the gland. Routine enhanced brain MRI using 5-mm axial slices was performed in 15 patients. Contrast-enhanced CT of the brain was performed in five patients.

Imaging studies were reviewed for morphology, signal intensity, and enhancement characteristics of the pituitary gland and stalk. Abnormalities relevant to the primary disease process were noted when present. These included midline malformations in pituitary dwarfism (absent septum pellucidum, hypoplastic optic and olfactory nerves) and secondary mass lesions (periventricular, pineal masses) in neoplasms. Clinical presenting features were noted in all cases. Diagnosis was established by histopathology in 26 patients and by characteristic imaging findings or associated clinical features in 39 patients.

Results
Infundibular pathology included a broad range of neoplasms, inflammatory and infectious disorders, and congenital and developmental lesions (Fig. 1). Neoplasms slightly predominated over other disease categories, accounting for 24 (37%) of 65 cases overall.

Pediatric infundibular lesions accounted for 21 (32%) of 65 lesions. We found 13 congenital lesions (all pituitary hypoplasias) and eight tumors in children. Pediatric neoplasms included four cases of Langerhans cell histiocytosis (LCH), two germinomas, and one case each of metastatic glioblastoma multiforme and primitive neuroectodermal tumor. The pediatric pathologic spectrum is presented in Figure 2.

Adult infundibular pathology accounted for 44 (68%) of all lesions. These included 19 inflammatory lesions, 16 neoplasms, and nine congenital or developmental lesions (Fig. 3). Infundibuloneurohypophysitis (INH) was the most common inflammatory lesion in adults, accounting for 12 of 44 cases. Other inflammatory lesions included sarcoidosis (n = 6).
Hamilton et al.

and one intracranial Whipple’s disease confined to the pituitary stalk and the median eminence of the hypothalamus.

Neoplasms were found in 16 (36%) of 44 adults. Five cases of metastatic disease were identified. Primary cancers were lung cancer in three patients, breast cancer in one, and unknown in one. Three pituitary adenomas, one primary and two recurrent, involved the infundibulum. Only adenomas centered in the stalk and not the pituitary gland proper were included in this series. Two cases each of germinoma, lymphoma, and leukemia were found. Leukemias consisted of one acute myelogenous leukemia and one chronic myelogenous leukemia. Two primary pituicytomas were also found.

Congenital and developmental lesions accounted for nine (20%) of 44 adult cases. Five pituitary dwarfs, two cysts, one hypothalamic and one intracranial Whipple’s disease were also identified.

Discussion

The goal of this study is to review the diverse spectrum of pituitary infundibular disease. The retrospective nature of data collection and our own institutional referral bias were limitations of this study that did not permit an accurate assessment of specific disease prevalence. Despite this, some conclusions may still be drawn regarding specific pathologic entities and corresponding therapeutic implications. Inflammatory disease in adults, for example, is likely underappreciated as a cause of stalk thickening, given its surprisingly high frequency in this series.

Normal Anatomy

The pituitary infundibulum is an anatomically complex area (Fig. 4). We briefly review normal development and histology of the pituitary gland and stalk and discuss the normal imaging appearance of the stalk.

Normal Pituitary Development

The pituitary gland forms after primary neurulation and has two distinct embryologic origins. The anterior gland (adenohypophysis) arises from invaginating placoid ectoderm in the roof of the stomodeum at approximately 3 weeks of gestation. This invagination is also known as Rathke’s pouch, which normally loses its connection to the oral cavity in the second gestational month [1].

Both the posterior pituitary (neurohypophysis) and the median eminence of the hypothalamus arise from neuroectoderm in the floor of the forebrain. The infundibular stalk is a variably hollow tube that arises from the ventromedial hypothalamus and is contiguous with the infundibular recess of the third ventricle. The pars tuberalis encircles the infundibular stem as it enters the adenohypophysis. The pars intermedia separates the adenohypophysis from the posteriorly located neurohypophysis [1].

Normal Histology

The histopathologic composition of the neurohypophysis is complex. Two specialized modified glial cells, the tanyocyte and the pituicyte, appear to play a supportive role for the axons of vasopressin and oxytocin, producing neurons, the cell bodies of which arise in the hypothalamus [2]. Both of these cells appear to be responsible for specific tumors in the suprasellar hypophysial region: pituicytomas and the recently described tanyctyoma [3].

Normal Imaging

The normal pituitary stalk tapers from superior to inferior. It measures 3.25 ± 0.56 (SD) mm at the level of the optic chiasm and narrows to 1.91 ± 0.40 mm at its insertion into the pituitary gland [4]. The signal intensity of normal stalk on T1 weighting is usually less than that of the optic chiasm and is less than that of normal neurohypophysis in all cases. The stalk lacks a blood–brain barrier and thus enhances intensely. Deviation or tilt of the infundibulum is common and does not necessarily imply underlying disease.

The normal hyperintensity of the posterior pituitary gland on T1-weighted sequences is believed to be related to vasopressin neurosecretory granules or lipid bodies (lysosomes) in pituicytes that are normally located in the neurohypophysis [5].

Developmental and Congenital Lesions

Pituitary hypoplasia was the single most common infundibular abnormality we found in children (13/21). Five adults were also imaged with pituitary hypoplasia. Patients present clinically with dwarfism or growth hormone deficiency. All showed abnormal appearing stalks with posterior pituitary ectopia, seen as a bright spot at the median eminence on unenhanced T1-weighted images. Twelve of these patients had hypoplasia or absence of the stalk. In two cases, the stalk was so attenuated that it was identified only after contrast administration. Six patients had short, thickened stalks. One patient with an absent stalk presented clinically with anemia and was noted to have absence of the septum pellucidum, although vision and the optic nerves were normal (Fig. 5).

One hypophyseal duplication was discovered in an asymptomatic adult (Fig. 6). Hypophyseal duplication results in complete duplication of the entire gland, including the infundibulum. Most reported cases in the literature are associated with midline facial or oral anomalies, particularly the median cleft facial syndrome, and many die in infancy. Hypertelorism is invariably present, and hypothalamic thickening may be seen [6].

Two unenhancing cystic masses confined to the infundibular stalk were thought to represent Rathke cleft or pars intermedia cysts. One case of infundibular thickening in an asymptomatic adult appeared to be secondary to a vascular malformation resulting in venous congestion.

Inflammatory Lesions: INH

Inflammatory and infectious infundibular lesions were found exclusively in adults. INH was the most common inflammatory lesion accounting for 12 cases in this series (Fig. 7). Imaging features of INH include an enhancing masslike thickening of the pituitary infundibulum. The normal T1 hyperintensity of the neurohypophysis is almost invariably absent [7].

The earliest reported cases of hypophysitis (or adenohypophysitis) involved the anterior gland and were typically seen in women in late pregnancy or shortly postpartum (Fig. 8). Later, it became clear that a pathologically similar process involved the stalk (INH or neurohypophysitis); this process is also more common in women [8]. Although typically seen in young adults, INH and adenohypophysitis have occurred in children and elderly patients. Pathologic features of INH and hypophysitis include chronic inflammatory changes, hyaline fibrosis, and infiltration of the pituitary gland and stalk by plasma cells and lymphocytes.

INH is increasingly recognized radiographically and clinically. It may be the underlying pathology in many cases that have historically been categorized as idiopathic central diabetes insipidus; it is believed to be autoimmune-mediated. Central diabetes insipidus is characterized by deficient arginine–vasopressin (AVP) synthesis from the hypothalamus or deficient secretion from the neurohypophysis.

Autoimmune central diabetes insipidus is diagnosed by documenting the presence of serum autoantibodies to AVP-secreting cells or by the coexistence of autoimmune polyendocrine syndromes. Clinical information is helpful in determining the cause of stalk thickening.
in adults with central diabetes insipidus. Age of onset of less than 30 years suggests INH as the likely cause of diabetes in about 80% of cases. Patients who also have a history of antecedent autoimmune disease, such as Hashimoto’s thyroiditis, atrophic gastritis, or pernicious anemia, raise the likelihood of INH as the underlying cause to 99% [9].

Desmopressin or steroid treatment can result in clinical and imaging improvement or even disease regression in some cases of INH or hypophysitis. This is particularly true in patients with partial central diabetes insipidus, who have less stalk or glandular destruction [9]. Surgery may therefore be best reserved for patients with persisting local mass effect that is refractory to medical management.

This paradigm is not useful in very young children in whom LCH is a frequent cause of stalk thickening and central diabetes insipidus. Patients with LCH are generally younger than 30 years and have high serum AVP-secreting cells. Some authors think antibodies in patients with LCH may be a secondary autoimmune process [9]. Regardless, INH or hypophysitis is usually a disease of young adults.

Infectious Lesions: Granulomatous and Infectious Causes
Sarcoidosis involved the stalk in six cases in this series, all of whom were adults. Sarcoidosis rarely presents with isolated clinical hypothalamic–pituitary involvement, although stalk thickening on imaging is not rare in patients with CNS involvement (Fig. 9).

One adult case of stalk thickening in this series was diagnosed at pathology as Whipple’s disease (Fig. 10). Although rare, this finding has been previously reported [10]. Other granulomatous processes that may involve the pituitary stalk include tuberculosis and Wegener’s disease.

Neoplasms in Children
Neoplasms accounted for eight (38%) of 21 pediatric infundibular abnormalities (Fig. 2). The most common pediatric infundibular tumor is LCH. Controversy exists regarding the most appropriate categorization of LCH, which is variably classified as a neoplasm and as an inflammatory (granulomatous) process. Meningeal involvement and choroid plexus lesions, although not seen in this series, are secondary abnormalities that provide a clue to diagnosis when present [11]. Central diabetes insipidus is a common indication for imaging the pituitary hypothalamic axis. Prior reports suggest a mass is found in two thirds of patients with central diabetes insipidus, with LCH the most common diagnosis in children [5].

In nearly all cases of LCH, the normal T1 hyperintensity of the neurohypophysis is absent [11]. This nonspecific finding was present in all cases in this series. The most common specific finding is stalk thickening (Fig. 11). Erdheim-Chester disease is a rare condition that is also characterized by histiocytic infiltration of the pituitary stalk [5].

Four germinomas—in two pediatric patients and two young adults—all showed stalk thickening and an absent posterior hypophyseal bright spot. CSF seeding and secondary pineal region masses may be important clues to diagnosis (Fig. 12). Metastatic glioblastoma multiforme and primitive neuroectodermal tumor were isolated causes of stalk masses in two cases.

Neoplasms in Adults: Secondary Tumors
Neoplastic conditions of the stalk in the adult population are diverse (Fig. 3). Metastatic disease was the most common adult infundibular tumor in this series. Metastatic disease to the pituitary is frequent in autopsy series, with breast and lung the most common primary sites. Metastatic disease usually presents in older patients, with a tendency for local invasion and rapid growth [12].

Leukemia (one acute myelogenous leukemia, one chronic myelogenous leukemia) and lymphoma each occurred in two adults. These causes of stalk thickening are not usually a diagnostic dilemma because the diagnosis is typically known long before the development of this late complication. Leukemia patients with stalk involvement present clinically with diabetes insipidus, and the prognosis is poor. Lymphoma may present intracranially as isolated stalk thickening or in conjunction with periventricular enhancing masses (Fig. 13). Pituitary adenomas occasionally arise in the infundibulum, as in three patients in this series (Fig. 14).

Neoplasms in Adults: Primary Gland Tumors
Primary tumors of the neurohypophysis are rare. Two primary gliomas of the infundibulum were found in this series, both pituicytomas. One occurred in a 33-year-old woman presenting with delayed growth and panhypopituitarism (Fig. 15). The other was found in a 35-year-old man with normal hormone levels. No other primary gliomas occurred in our series. Hypothalamic–chiasmatic astrocytomas may occur primarily in the stalk or involve the stalk by secondary extension. Ependymoma and pleomorphic xanthoastrocytoma of the stalk have also been described. Although rare, primary gliomas should be included in the differential diagnosis of stalk masses.

Neurohypophyseal-Specific Gland Tumors: Pituicytoma, Tanyctoma, and Granular Cell Tumor
A number of gliomas have been described as arising in the pituitary stalk; however, two types in particular are highly location-specific to the stalk: pituicytomas (sometimes called infundibulomas) and tanyctomas. Occasionally, granular cell tumors (also called granular cell myoblastoma or choristoma) have been seen in this location, although they are somewhat less specific to the stalk. Confusion has arisen in the literature regarding these unusual tumors because of overlapping terminology and pathologic mischaracterization in the past [13].

Pituicytomas are highly specialized glial cells found nearly exclusively in the normal pituitary stalk and posterior gland. Pituicytomas have been confused with several benign and malignant tumors. They may superficially resemble pilocytic astrocytomas, meningiomas (particularly fibrous), schwannomas, and adenomas on histopathology. These tumors may be difficult to differentiate by imaging and histology. Improved morphologic characterization, immunohistochemical techniques, and electron microscopy now aid in differentiating these tumors pathologically [13].

Pituicytomas most commonly occur in middle-aged men in the third to fifth decade, although there is a documented case in an 83-year-old man [14]. None have been described in children. Common clinical presenting features of pituicytomas include panhypopituitarism and fatigue.

Imaging features of pituicytomas include isodensity or isointensity to normal brain and homogeneous contrast enhancement in most cases (Fig. 14). These tumors are localized to the pituitary stalk and posterior gland and frequently grow into the suprasellar cistern, potentially compressing the optic nerves and hypothalamus. The normal T1 hyperintensity of the neurohypophysis is typically absent. Sellar expansion is uncommon and is a feature that may help differentiate stalk tumors from adenomas.

Pituicytomas are benign tumors that have shown no recurrence after gross total resection on long-term follow-up; thus, the correct diagnosis has relevant implications for treatment and prognosis. Patients undergoing gross total resection may be cured, requiring no adjuvant chemotherapy or radiation. Recurrences in pa-
patients who have undergone incomplete resection have been followed up conservatively [13].

Tanycytomas are another recently described tumor in the hypothalamic–suprasellar region, so named because of specific staining and ultrastructural characteristics identical to normal tanycyte morphology. These tumors may overlap pathologically with pilomyxoid astrocytomas, a recently described tumor [3, 15] with histopathologic features matching those of tanycytoma. Electron microscopy has not been performed in these patients; thus, the most appropriate pathology terminology remains unclear. Tanycytomas are characterized by large suprasellar masses; their relationship to the pituitary stalk is difficult to determine. Tanycytomas are clinically aggressive, with increased recurrence rates, possibly accounting for the larger size at presentation than typically seen with pituicytoma [3].

Conclusion

The spectrum of pathology involving the pituitary infundibulum is broad yet distinct from other pathology in the sella and parasellar region. The pituitary infundibulum presents a differential diagnosis of adult infundibular disease is important because it may allow the option for noninvasive treatment and improved clinical course, particularly in patients with INH or adenohypophysitis.

Inflammatory disorders are likely underrecognized as a cause of masses of the pituitary stalk in adults. Their inclusion in the differential diagnosis of adult infundibular disease is important because it may allow the option for noninvasive treatment and improved clinical course, particularly in patients with INH or adenohypophysitis.

References


For Your Information

This article is available for CME credit. See www.arrs.org for more information.
Anatomy and Pathology of Pituitary Lesions

Fig. 1—General pathologic spectrum of pituitary infundibulum lesions.

Fig. 2—Pathologic spectrum of pediatric infundibular disease.

Fig. 3—Pathologic spectrum of adult infundibular disease. INH = infundibuloneurohypophysitis, RCC = Rathke cleft cyst, Whipple’s = Whipple’s disease.

Fig. 4—Sagittal graphic of pituitary stalk anatomy: infundibulum is composed of infundibular stem (curved arrow), median eminence of hypothalamus, from which it arises, and pars tuberalis (straight arrow). (Reprinted with permission from Harnsberger H. Head and neck digital teaching file. Salt Lake City, UT: Amirsys, 2002 [16])
Fig. 5—17-year-old boy with growth hormone deficiency and anosmia. (Reprinted with permission from Harnsberger H. Head and neck digital teaching file. Salt Lake City, UT: Amirsys, 2002 [16])

A and B, Sagittal (A) and coronal (B) unenhanced T1-weighted images through sella reveal pituitary hypoplasia. Pituitary gland and sella turcica are small. Note ectopic neurohypophyseal T1 hyperintensity (open arrow). Infundibular stem is always abnormal; in this case, it is markedly attenuated (solid arrow). Stalk may be well seen only after gadolinium administration. Associated abnormalities are frequent, as in this patient in whom septum pellucidum is absent.

Fig. 6—Sagittal T1-weighted contrast-enhanced image through sella is diagnostic of hypophysial duplication in this 69-year-old asymptomatic man. Complete pituitary gland and stalk (arrows) are duplicated. (Reprinted with permission from Harnsberger H. Head and neck digital teaching file. Salt Lake City, UT: Amirsys, 2002 [16])
Anatomy and Pathology of Pituitary Lesions

Fig. 7—Adult male with infundibuloneurohypophysitis (INH). (Reprinted with permission from Harnsberger H. Head and neck digital teaching file. Salt Lake City, UT: Amirsys, 2002 [16])

A and B, Coronal (A) and sagittal (B) contrast-enhanced T1-weighted images through sella reveal typical imaging findings of INH. Note masslike thickening of infundibulum (arrow).

Fig. 8—23-year-old postpartum woman with hypophysitis and atypical infundibuloneurohypophysitis involving pituitary gland and stalk. (Reprinted with permission from Harnsberger H. Head and neck digital teaching file. Salt Lake City, UT: Amirsys, 2002 [16])

A and B, Coronal (A) and sagittal (B) contrast-enhanced T1-weighted images through sella. Note masslike enlargement of entire pituitary gland and stalk. Neurohypophyseal involvement was supported by clinical presentation of diabetes insipidus. With this degree of involvement, imaging appearance is indistinguishable from macroadenoma; however, histopathologic evaluation confirmed diagnosis of hypophysitis.
Fig. 9—36-year-old man with sarcoidosis. (Reprinted with permission from Harnsberger H. *Head and neck digital teaching file.* Salt Lake City, UT: Amirsys, 2002 [16])

A and B, Axial (A) and coronal (B) contrast-enhanced T1-weighted images through pituitary stalk (arrow).

Fig. 10—42-year-old man with Whipple’s disease. (Reprinted with permission from Harnsberger H. *Head and neck digital teaching file.* Salt Lake City, UT: Amirsys, 2002 [16])

A and B, Axial (A) and sagittal (B) contrast-enhanced T1-weighted images show isolated thickening and enhancement of median eminence and pituitary infundibulum (arrow), subsequently proven at histopathology to be Whipple’s disease.
Anatomy and Pathology of Pituitary Lesions

Fig. 11—14-year-old boy with Langerhans cell histiocytosis (LCH). (Reprinted with permission from Harnsberger H. Head and neck digital teaching file. Salt Lake City, UT: Amirsys, 2002 [16])

A and B, Sagittal (A) and coronal (B) contrast-enhanced T1-weighted images reveal focal infundibular thickening in LCH, which was most common pediatric cause of infundibular masslike thickening in this series (arrow). Posterior pituitary ectopia was seen in all patients.

Fig. 12—Sagittal contrast-enhanced T1-weighted image in 40-year-old woman reveals masslike thickening of pituitary infundibulum in intracranial germinoma (straight arrow). Recognition of subtle secondary pineal mass (curved arrow) is highly suggestive of diagnosis. (Reprinted with permission from Harnsberger H. Head and neck digital teaching file. Salt Lake City, UT: Amirsys, 2002 [16])

Fig. 13—Axial contrast-enhanced T1-weighted image in 62-year-old man shows lymphoma of pituitary infundibulum (solid arrow). Although isolated stalk involvement may be seen, enhancing periventricular masses in this patient improved diagnostic specificity (open arrow). (Reprinted with permission from Harnsberger H. Head and neck digital teaching file. Salt Lake City, UT: Amirsys, 2002 [16])
Fig. 14—34-year-old woman with elevated prolactin. (Reprinted with permission from Harnsberger H. *Head and neck digital teaching file*. Salt Lake City, UT: Amirsys, 2002 [16])

A, Sagittal contrast-enhanced T1-weighted image of infundibular adenoma shows that, superiorly, mass (open arrow) is inseparable from pituitary infundibulum (solid arrow).

B, Coronal contrast-enhanced T1-weighted image shows prolactinoma (white arrow) arising from stalk (black arrow).

Fig. 15—35-year-old man with pituicytoma. (Reprinted with permission from Harnsberger H. *Head and neck digital teaching file*. Salt Lake City, UT: Amirsys, 2002 [16])

A and B, Sagittal (A) and coronal (B) contrast-enhanced T1-weighted images show that pituitary infundibulum (arrows) is closely associated with mass.