3 MRI Lesions in Diabetes Insipidus

Karuna Shekdar

Abbreviations

CP	Craniopharyngioma
DI	Diabetes insipidus
GCT	Germ cell tumor
LCH	Langerhans' cell histiocytosis
MRI	Magnetic resonance imaging
RCC	Rathke cleft cyst
SOD	Septo optic dysplasia

Introduction

A wide spectrum of disease processes can result in central diabetes insipidus in children [1]. Disease processes affecting the neurohypophysis, the pituitary stalk/infundibulum, and the pituitary hypothalamic axis are some of the common causes of central DI [1]. The clinical symptoms from these above-mentioned lesions

K. Shekdar (✉)
Raymond and Ruth Perelman School of Medicine, University of Pennsylvania, Division of Radiology, The Children's Hospital of Philadelphia, Philadelphia, PA, USA
e-mail: shekdar@chop.edu

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can be varied and present a diagnostic challenge to the pediatricians and the endocrinologists. The characteristic MR imaging findings of common conditions that can result in central DI in children have been described in this chapter.

Magnetic resonance imaging (MRI) of the pituitary and the pituitary hypothalamic axis offers excellent soft tissue detail with multiplanar imaging capability which is much superior than CT [2]. MRI offers significant benefits (over CT) such as high signal-to-noise ratio, high spatial resolution, and lack of ionizing radiation which make MR imaging the imaging modality of choice. In some cases both MRI and CT may need to be performed and the information obtained from MRI and CT is complementary.

When evaluating a case of central DI, a pituitary protocol MRI should be performed, which provides thin slices through the pituitary-hypothalamic area, to provide visualization and detailed evaluation. The use of contrast enhancement in MRI is necessary in evaluation of pituitary mass lesions and infectious and inflammatory disorders. For certain indications, it is necessary to image the entire brain. For example, certain tumors (i.e., germinomas) may disseminate and require imaging of the brain and spine, and some developmental pituitary anomalies can be associated with other midline congenital defects such as septo-optic dysplasia [3, 4].

Normal MRI Appearance of the Pituitary Gland (Fig. 3.1)

The pituitary gland is in the sella turcica, within the central skull base. The pituitary gland consists of two lobes, the anterior pituitary (adenohypophysis) and the posterior pituitary (neurohypophysis). The adenohypophysis is isointense to the brain parenchyma, and the neurohypophysis is brighter/hyperintense compared to the brain parenchyma on T1-weighted images. The T1 hyperintensity of the neurohypophysis is attributed to the protein hormone granules within. The pituitary stalk is the inferior continuation of the hypothalamus inserting to the superior aspect of the pituitary gland in the midline. The pituitary stalk is broader superiorly and gradually tapers inferiorly.

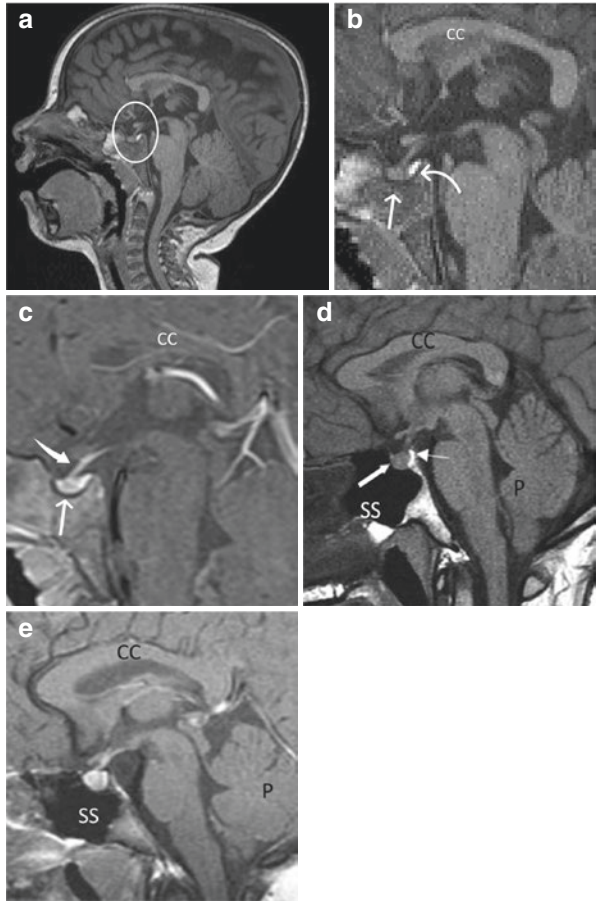

Fig. 3.1 Normal appearance of pituitary gland on MRI. (**a**) Sagittal T1 images through the brain in a 2-year-old boy with white circle marking the area of the sella and the pituitary gland. (**b**) Magnified unenhanced sagittal T1 image demonstrating the pituitary gland (straight arrow) and posterior pituitary bright spot of the neurohypophysis (curved arrow). (**c**) Postcontrast sagittal T1 image shows homogeneously enhancing pituitary gland (straight arrow) with normal enhancing pituitary stalk/infundibulum (thick white arrow). (**d**) Unenhanced T1 sagittal and (**e**) postcontrast T1 sagittal through the pituitary gland in a pubertal 13-year-old female demonstrating the pituitary gland (straight arrow) and posterior pituitary bright spot of the thin white arrow) and homogeneous enhancement. CC corpus callosum, SS sphenoid sinus, P cerebellum

It is important to identify the presence and location of the T1 hyperintensity ("bright spot") of the neurohypophysis. The bright spot may be found in an ectopic location when there is a pituitary developmental abnormality, or it may be absent if there is vasopressin, also known as anti-diuretic hormone (ADH), deficiency due to mass effect or infiltration from space-occupying lesions [2].

A normal pituitary gland enhances diffusely and homogeneously following administration of intravenous gadolinium. There is also enhancement of the pituitary stalk, but the hypothalamus does not show any enhancement.

The MRI imaging protocol for diabetes insipidus at our institute typically includes evaluation of the whole brain. The following sequences are obtained: 3-D volumetric T1 sagittal with axial and coronal reformations obtained pre and postcontrast, axial TSE T2, axial FLAIR, postcontrast spin echo T1 sagittal and coronal with fat suppression through the pituitary gland, axial spin echo T1 with fat saturation through the brain and axial diffusion.

MRI Findings in a Child with Diabetes Insipidus

Most children have a nonspecific finding of non-visualization of the posterior pituitary bright spot. Thickening of either the entire pituitary stalk or just the proximal portion is the second most common abnormality on MRI scans [5]. When present, the thickening suggests infiltration. The most common diagnoses which are associated with DI pituitary stalk thickening are hypophysitis, Langerhans cell histiocytosis (LCH), and germ cell tumors (e.g., germinoma) [5].

If the pituitary stalk is not thickened, follow-up scans should be done, as there can be progression of disease, especially of germinoma; progression is generally seen by 6 months but can occur years later [6].

The common findings on MR imaging in patients with DI are listed in Table 3.1.

When a child is diagnosed with central DI, the endocrinologist's and/or oncologist's goal is to determine whether the child

Table 3.1 Common findings seen on MRI in children with DI

	Common findings on MRI seen in DI	DI causes
1	Non-visualization of the posterior pituitary bright spot	LCH, LH, GCT, CP post-surgery, TB, sarcoidosis
2	Thickening of the pituitary stalk	LCH, LH, GCT, TB, sarcoidosis
3	Mass lesions	GCT, CP, RCC, gliomas
4	Thin pituitary stalk or disruption of pituitary-hypothalamic axis	SOD, other developmental causes, post-surgery, trauma

has hypophysitis or one of the more aggressive conditions (LCH or germ cell tumors).

Langerhans Cell Histiocytosis (LCH)

Studies on the causes of central diabetes insipidus show approximately 5–20% prevalence of Langerhans' cell histiocytosis as the cause [7]. LCH in children commonly affects bones, skin, and the pituitary gland. Central diabetes insipidus is the most frequent central nervous system manifestation of LCH, occurring in 10–50% of all LCH patients [7].

MRI of the pituitary gland in a child with LCH may demonstrate absent T1 hyperintensity of the posterior pituitary/neurohypophysis and a thickened pituitary stalk [8, 9] (Fig. 3.2). In some cases of LCH the posterior pituitary signal may initially be detectable but may disappear over time, hence follow-up MRI may need to be obtained in some cases of LCH. Other MR imaging findings of LCH such as calvarial lesions, foci of T2 hyperintensity in the basal ganglia, thalami, and cerebellum may be noted in some cases [7] (Figs. 3.2 and 3.3).

In children with a new diagnosis of DI, LCH should be considered [10]. Clues might include associated skin lesions and bone lesions.

Typical MRI features are an absent posterior pituitary bright spot and a thickening of the stalk [9]. Additional pituitary hormone deficiencies may be present, such as GH deficiency, or may develop several years later.

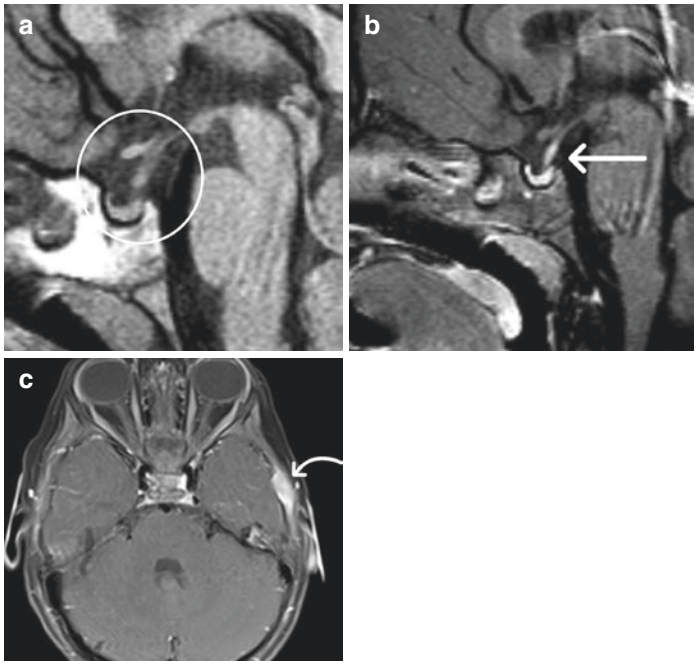

Fig. 3.2 Langerhans' cell histiocytosis (LCH) MRI images of a 5-year-old boy with LCH. (**a**) Unenhanced T1 sagittal image showing absence of the normal posterior pituitary bright spot. (**b**) Postcontrast sagittal T1 with fat saturation demonstrate thickened enhancing pituitary stalk(straight arrow). (**c**) Postcontrast axial T1 with fat saturation shows enhancing left temporal bone lesion of LCH (curved arrow)

Hypophysitis

When there is autoimmune destruction of the pituitary, like what occurs in Hashimoto's thyroiditis, it is termed hypophysitis. Hypophysitis may be associated with both anterior and posterior pituitary deficits. It is presumed that when there is idiopathic diabetes insipidus, it is likely due to hypophysitis [11]. Follow-up MRI scans of patients with hypophysitis as the cause of DI and a

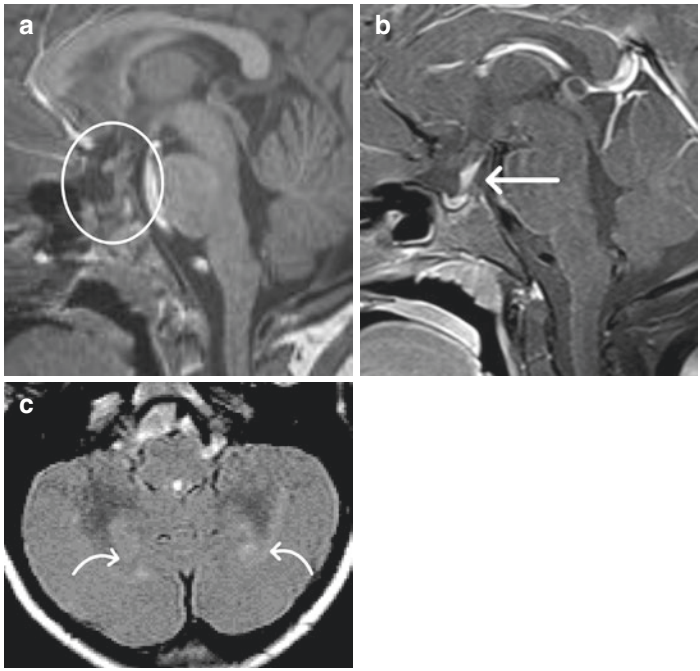

Fig. 3.3 Langerhans' cell histiocytosis (LCH) MRI images of a 9-year-old boy with LCH. (**a**) Unenhanced T1 sagittal image showing absence of the normal posterior pituitary bright spot. (**b**) Postcontrast sagittal T1 with fat saturation demonstrate thickened enhancing pituitary stalk (straight white arrow). (**c**) Axial FLAIR shows hyperintense lesions in the cerebellum (curved arrows)

thickened pituitary stalk show a range of changes, from a spontaneous resolution of the abnormality to no change (Fig. 3.4). Caution must be made as germ cell tumors and hypophysitis have similar presentations. Follow-up MR imaging and other investigations including germ cell tumor markers and, in some cases genetic testing for LCH may need to be performed before arriving at this diagnosis [8].

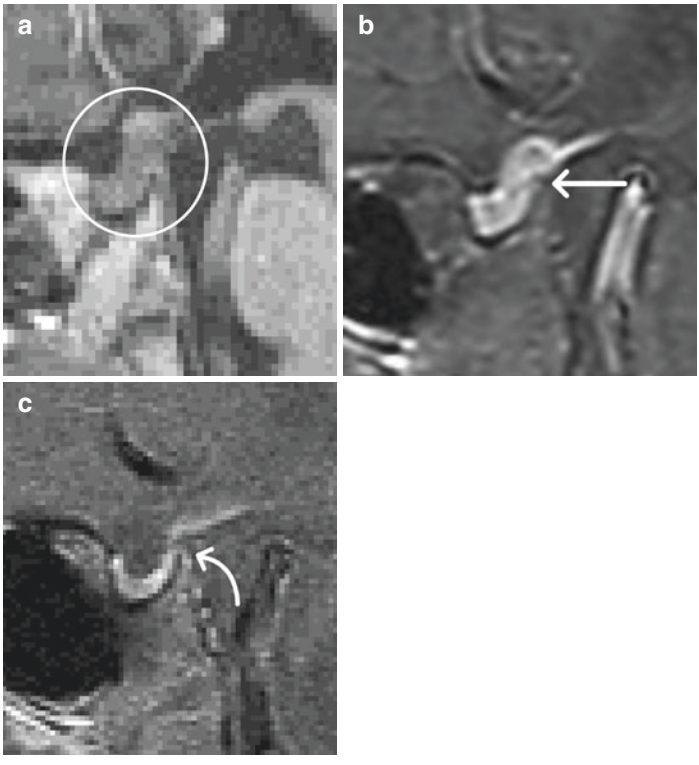

Fig. 3.4 Lymphocytic hypophysitis (LH) MRI images of a 11-year-old girl with LH. (**a**) Unenhanced T1 sagittal image showing absence of the normal posterior pituitary bright spot and thickened pituitary stalk. (**b**) Postcontrast sagittal T1 with fat saturation demonstrate thickened enhancing pituitary stalk (straight white arrow) MRI image three years following treatment. (**c**) Postcontrast sagittal T1 with fat saturation demonstrates resolution of the previously noted pituitary stalk thickening (curved arrow)

Germ Cell Tumors (GCT)

Germ cell tumors include germinoma, as well as non–germinomatous tumors such as teratoma, yolk sac tumor, and embryonal carcinoma. Central nervous system (CNS) germ cell tumors (GCTs)

represent approximately 3% of primary pediatric brain tumors. The clinical presentation varies by location and size, and it frequently includes endocrine abnormalities including central DI, visual changes, and signs of increased intracranial pressure [12]. A small percentage of those with germ cell tumors have tumor markers alpha-feto protein and/or human chorionic gonadotropin (HCG) in the serum and/or CSF, and both blood and CSF should be evaluated [12]. In this group of germ cell tumors the MR imaging findings along with the tumor marker elevation may be diagnostic in themselves without the need for tissue confirmation [13].

Essentially, when a child is diagnosed with central DI, the endocrinologist's and/or oncologist's goal is to determine the cause and to assess if the child has any of the more aggressive conditions which includes germ cell tumors [14].

MR imaging findings in suprasellar GCTs include absent posterior pituitary bright spot and thickened pituitary stalk with enhancement [3] (Fig. 3.5).

DI can present for extended period prior to MR abnormalities which become evident in cases of suprasellar germinomas. Some of the GCTs have a tendency for dissemination through the CSF; therefore, it is essential to scan the whole brain and the entire spinal axis to exclude dissemination. It is not possible by MR imaging to differentiate between the different types of germ cell tumors.

Majority of the GCTs are noted to be very sensitive to radiation treatment. Serial MR imaging is useful in assessing response to treatment [12] (Fig. 3.5).

Rathke Cleft Cysts (RCC)

Rathke cleft cysts (Fig. 3.3) are incidental pituitary cysts that arise from the non-obliterated intrasellar lumen of Rathke pouch. RCCs are benign, sellar region endodermal cysts lined by ciliated, mucus-producing epithelium [15]. When RCCs are large, they become symptomatic, because of the exerted mass effect. Larger RCCs can result in pituitary dysfunction (70%) and central diabetes insipidus [16].

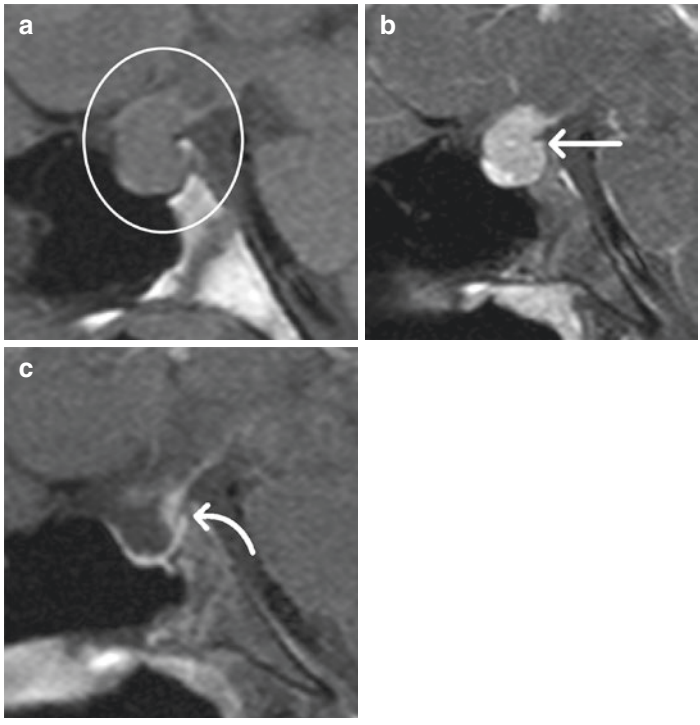

Fig. 3.5 Suprasellar germinoma (SG) MRI images of a 12-year-old boy with SG presenting with new-onset diabetes insipidus and panhypopituitarism. (**a**) Unenhanced T1 sagittal image showing absence of the normal posterior pituitary bright spot and thickened pituitary stalk. (**b**) Postcontrast sagittal T1 with fat saturation demonstrate thickened enhancing pituitary stalk (straight white arrow) MRI image two years following treatment. (**c**) Postcontrast sagittal T1 with fat saturation demonstrates resolution of the previously noted pituitary stalk thickening (curved arrow)

RCCs are smoothly lobulated well-delineated intrasellar/suprasellar cystic masses, typically without enhancement. MR imaging findings of RCCs depend on the cyst content (Fig. 3.6). Typically, RCCs with proteinaceous content are hyperintense on T1 and hypointense on T2 in 50% of cases and the remainder may be T1 hypointense and T2 hyperintense [17]. Small non-enhancing intra-cystic nodule is seen in 75% of cases [17]. When they are T1 bright no enhancement is appreciated.

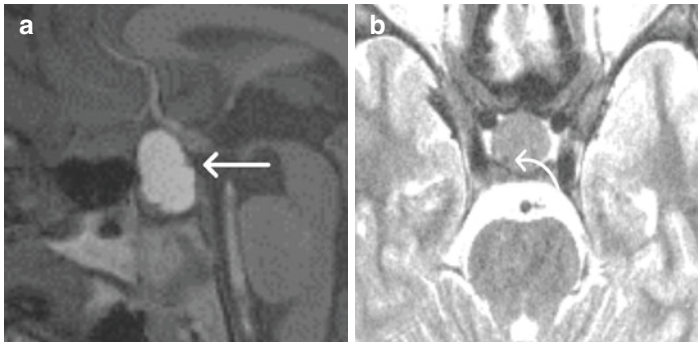

Fig. 3.6 Rathke cleft cyst (RCC) MRI images of a 10-year-old boy with RCC presenting with new onset diabetes insipidus. (**a**) Unenhanced T1 sagittal image showing hyperintense cyst in the sella and suprasellar region (straight white arrow). (**b**) Axial T2-weighted imaging showing hypointense / dark content within the cyst with a peripheral hypointense/dark nodule (curved arrow)

Craniopharyngioma

Craniopharyngiomas (CP) (Fig. 3.4) account for 1.2–4.6% of all central nervous system tumors and about 6% of pediatric brain tumors [18, 19]. Childhood CP almost always have an adamantinomatous pathology, may be cystic and may have calcifications (Fig. 3.4B) [20].

Craniopharyngiomas are thought to arise from neoplastic transformation of ectopic embryonal remnants along the hypophyseal duct through which the Rathke pouch migrates to form the anterior pituitary gland [18]. Because they arise along the hypophyseal duct, they may be in an infradiaphragmatic location (below the dura mater through which the pituitary stalk passes) and/or a suprasellar location above the pituitary gland to the floor of third ventricle. Because craniopharyngiomas are located close to and can invade the pituitary gland, pituitary stalk, and the hypothalamus, they can present with pituitary hormone deficiencies; and when suprasellar, they are more likely to present with hypothalamic dysfunction including DI [21].

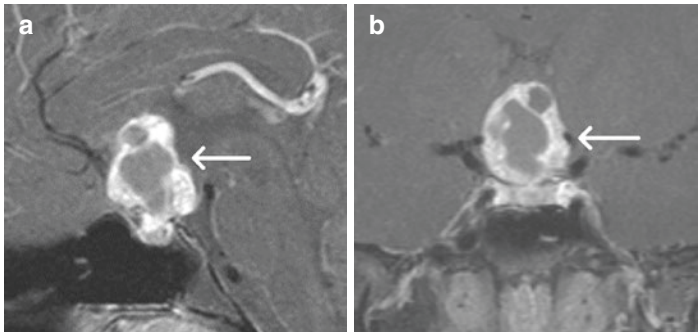

Fig. 3.7 Craniopharyngioma (CP) MRI images of a 6-year-old girl with CP. (**a**) Postcontrast sagittal T1 with fat saturation image. (**b**) Postcontrast coronal T1 with fat saturation showing mixed cystic and solid mass with heterogeneous enhancement extending to the suprasellar region (straight white arrow)

On MR imaging typically the craniopharyngiomas are a heterogeneous solid and cystic mass in the sellar and suprasellar region with heterogeneous enhancement of the solid components. The appearance of the cysts on MRI is variable depending on the content and can be hyperintense on T1. The presence of calcifications is a hallmark of craniopharyngioma and can be identified easily on CT scan compared to MRI (Fig. 3.7).

Major morbidity can occur during surgical resection of the craniopharyngioma with injury to the surrounding structures, as well as due to scarring and reactive changes after resection and radiation therapy (Fig. 3.8). These complications include DI in addition to hypopituitarism, hypothalamic (morbid) obesity, visual, and neurological deficits [22].

Other Tumors

Gliomas and lymphoma are tumors that may rarely grow in the region of the pituitary [23]. Gliomas are sometimes seen in children with neurofibromatosis type 1 (NF1). Large hypothalamic-chiasmatic gliomas (seen in NF1) and meningiomas (seen in NF2) can cause DI [24].

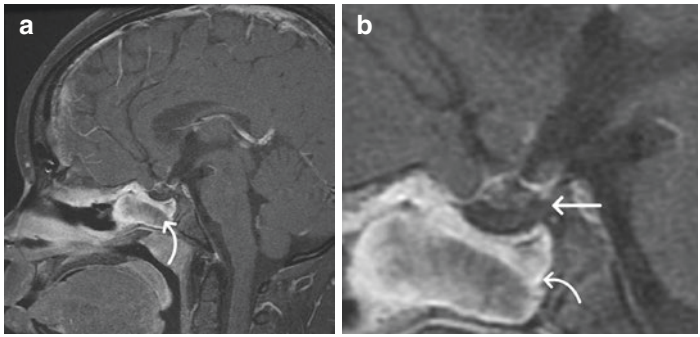

Fig. 3.8 Posttreatment craniopharyngioma (CP) MRI images of a 13-year-old boy with recurrent craniopharyngioma with pan hypopituitarism and central DI. (**a**, **b**) Postcontrast sagittal T1 with fat saturation showing post-surgical distortion in the sella following endoscopic endonasal resection and radiation therapy. The pituitary gland, posterior pituitary bright spot, and the pituitary stalk are not well visualized (straight white arrow). There is enhancement of the mucosal flap in the sphenoid sinus (curved arrow)

Rarely, large pituitary adenomas can surround and compress the pituitary stalk, resulting in DI.

Metastases to the pituitary-hypothalamic axis can present clinically, with DI as the main presenting symptom mainly in adults. DI of a transient nature may occur from metastases to the posterior lobe of the pituitary.

Congenital Abnormalities in the Pituitary/Hypothalamic Region Causing DI

Ectopic Posterior Pituitary (EPP)

Occasionally, in the workup for a child with a new diagnosis of GH deficiency, an MRI that shows the bright spot is located either on the stalk or even above the stalk (Fig. 3.9). The presence of an EPP is usually associated with anterior pituitary hormone deficiencies, and occasionally DI [14, 25].

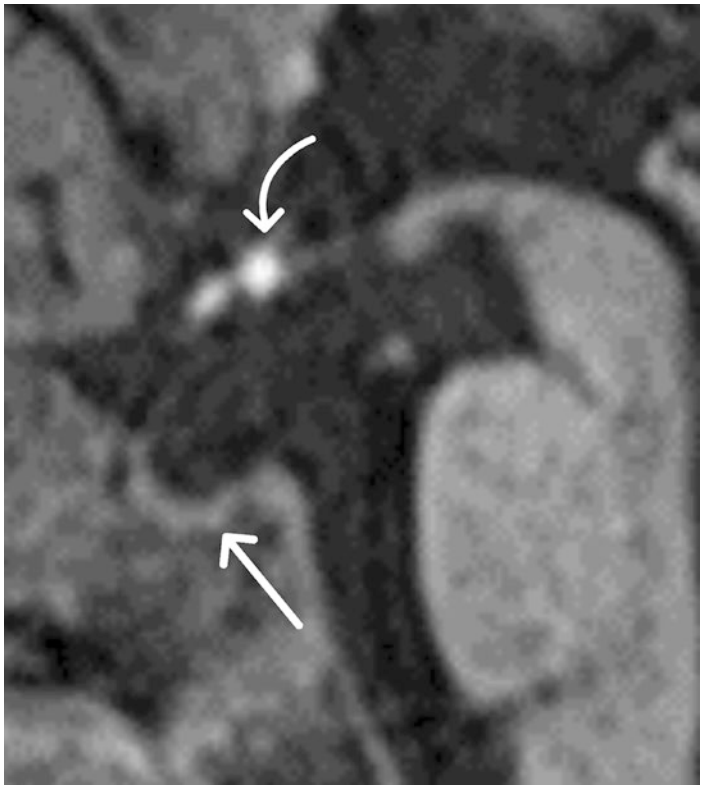

Fig. 3.9 Ectopic neurohypophysis in a 7-month-old boy with DI. Unenhanced sagittal T1 image showing diminutive pituitary gland (straight arrow). The pituitary stalk cannot be identified and note ectopic location of the neurohypophysis (curved arrow)

Septo-optic Dysplasia (SOD)

SOD is a congenital malformation where there is a small pituitary, underdevelopment of the optic nerves, and absence of midline brain structures such as the septum pellucidum and corpus callosum. Children with SOD may present with features secondary to anterior and posterior hormone deficiencies including DI [4]. SOD is diagnosed by MRI identification of small pituitary

gland and an absent infundibulum in addition to absence of septum pellucidum and other midline and optic nerve anomalies [25, 26] (Figure included in the chapter on pituitary causes of short stature).

Inflammatory and Infectious Conditions

Granulomatous diseases like sarcoidosis can involve the hypothalamic-pituitary axis, and result in central DI. MR imaging reveals a smooth thickening of the pituitary stalk, with occasional involvement of the adjacent hypothalamus or pituitary gland [27, 28].

Among infectious causes of central DI, the most common infection is tuberculosis [28]. MR imaging reveals a smooth thickening of the pituitary stalk, like sarcoidosis, associated with diffuse leptomeningeal enhancement, especially in the basal cisterns [29].

Rarely trauma and following surgery disruption of the pituitary–hypothalamic axis result in DI. The MRI findings would reflect changes related to trauma and pituitary findings include non-visualization of the T1 hyperintensity of the neurohypophysis with or without imaging evidence of disruption of the pituitary infundibulum [16].

Summary

A wide spectrum of disease processes can result in central diabetes insipidus. MR imaging plays an important role in the assessment of pituitary-hypothalamic axis and in identifying lesions that can cause central DI. The high spatial resolution, multiplanar imaging capability, and lack of ionizing radiation make MR imaging the investigation of choice in the workup of diabetes insipidus in children.

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