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MR in Idiopathic Central Diabetes Insipidus of Childhood

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Summary: We present the cases of two children with presumed idiopathic central diabetes insipidus whose follow-up MR studies eventually revealed hypothalamic tumors. Thin-section sagittal T1-weighted MR with gadolinium administration is important in the evaluation of these children, and serial examinations are probably necessary.

Index terms: Diabetes insipidus; Hypothalamus; Pituitary gland, magnetic resonance; Sella turcica, magnetic resonance; Pediatric neuroradiology

We recently have encountered two patients with central diabetes insipidus (CDI), each with symptoms of several months duration, in which no abnormality, other than absence of the normal posterior pituitary bright spot (PPBS), was demonstrated on magnetic resonance (MR) without gadolinium enhancement at the time of initial diagnosis. In each case, follow-up MR with gadolinium enhancement eventually demonstrated a hypothalamic tumor.

Case 1

A 7-year-old girl developed CDI in 1988. MR without gadolinium enhancement at another institution (Fig 1) was interpreted as normal except for absence of the normal PPBS. The patient was presumed to have idiopathic CDI. Subsequent clinical evaluations revealed that the child also had growth hormone deficiency and borderline low levels of adrenocorticotropin and thyroid-stimulating hormone. A repeat MR with gadolinium administration was obtained 20 months later and demonstrated a large enhancing suprasellar mass (Fig 1). Pineal region enhancement was also evident but interpreted to be within normal limits. Spinal MR with gadolinium enhancement was also negative for seeding. A cerebrospinal fluid sample was normal and negative for human chorionic gonadotropin. The patient was treated empirically with radiotherapy, because a biopsy was refused. Within 2 months of treatment, MR showed a complete response. The clinical picture and therapeutic response suggested, although not conclusively, that this was likely a germinoma.

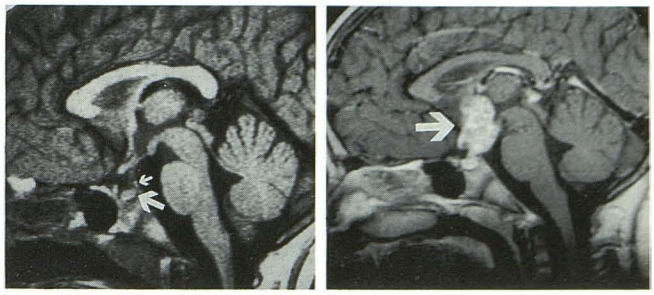

Fig. 1. Case 1, 7-year-old girl with CDI.

A, Initial sagittal T1-weighted MR of December 1988 (1.5 T) (500/20/2) (repetition time/echo time/excitations) (section thickness, 3 mm; gap, 1 mm; matrix, 256 × 256) without gadolinium administration shows absence of the normal PPBS (*large white arrow*), fatty marrow hyperintensity at the tip of the dorsum sella (*small white arrow*), and no evidence of a hypothalamic mass.

B, Follow-up sagittal T1-weighted MR (1.5 T) (600/15) (section thickness, 3 mm; gap, 1 mm; matrix, 256 × 192) of October 1990 with gadolinium administration shows a large, enhancing hypothalamic mass (*large white arrow*), a presumed germinoma.

Case 2

A 12.5-year-old boy presented in November 1989 with a 4-month history of polydipsia and polyuria. Clinical testing confirmed the diagnosis of CDI and also showed evidence of growth hormone deficiency. A cerebrospinal fluid specimen at that time was normal. An MR done without gadolinium enhancement at another institution was interpreted as normal (Fig 2). The posterior sellar laminar hyperintensity on that study was interpreted to represent the normal PPBS. Follow-up MR 6 months later (May 1990) demonstrated definite fading of the PPBS along with questionable thickening of the enhancing proximal stalk and posterior hypothalamus (Fig 2). The next MR (December 1990), 13 months after the onset of symptoms, revealed definite thickening of the gadolinium-enhancing pituitary

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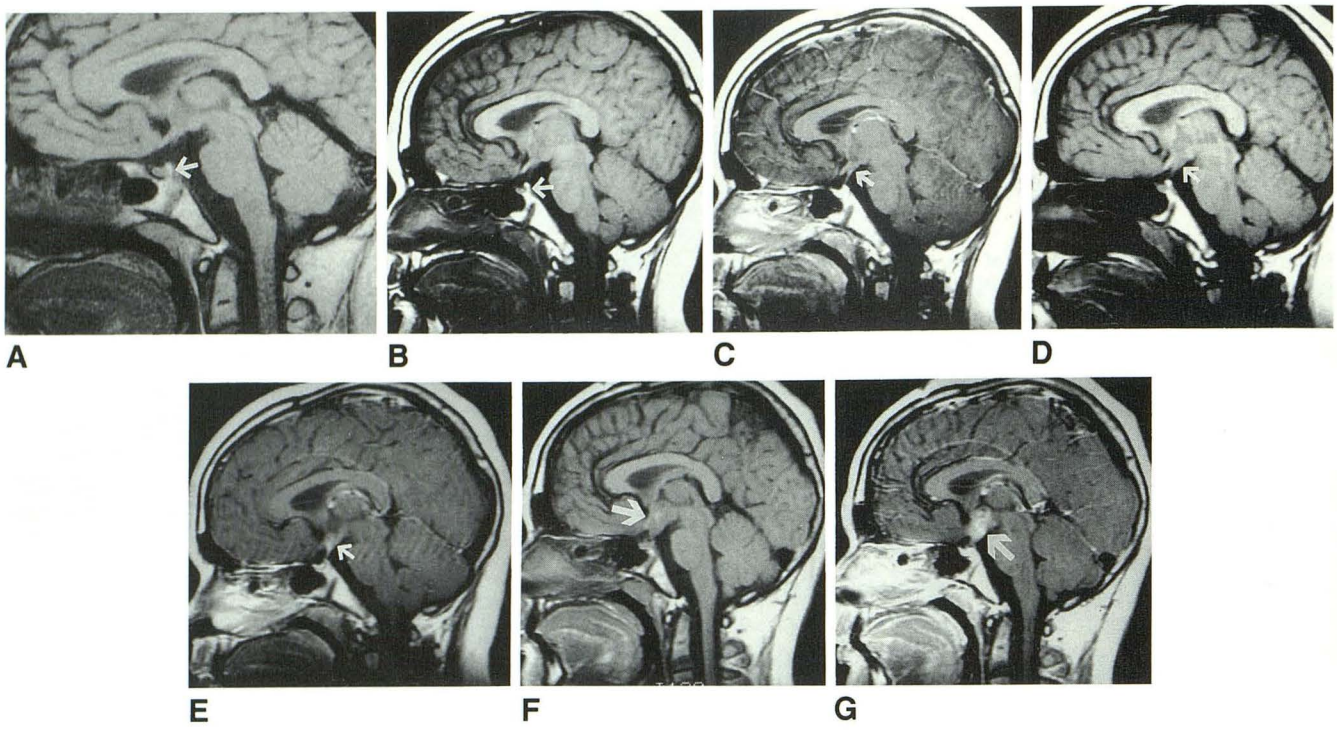

Fig. 2. Case 2, 12-year-old boy with CDI.

A, Initial sagittal T1-weighted MR of November 1989 (0.3 T) (430/30) (section thickness, 4 mm; gap, 1 mm; matrix, 256 × 256) without gadolinium administration reveals no evidence of hypothalamic abnormality and shows a posterior sellar laminar hyperintensity interpreted as a normal PPBS (*white arrow*) rather than representing fatty marrow intensities of the dorsum sellae.

B and *C*, Follow-up sagittal T1-weighted MR (1.5 T) (500/15) (section thickness, 5 mm; gap, 1 mm; matrix, 256 × 192) of May 1990 before (*B*) and after (*C*) the administration of gadolinium shows fading or absence of the normal PPBS with fatty hyperintensity at the dorsum (*white arrow* in *B*) and questionable thickening of the enhancing proximal stalk and posterior hypothalamus (*white arrow* in *C*).

D and *E*, Sagittal T1-weighted MR of December 1990 (1.5 T) (600/15) (section thickness, 5 mm; gap, 1 mm; matrix, 256 × 128) before (*D*) and after (*E*) gadolinium administration shows absent PPBS and definite thickening of the enhancing infundibulum and posterior hypothalamus (*white arrows*). Biopsy was refused at this time.

F and *G*, Subsequent serial MR studies demonstrated no change until October 1991, when sagittal T1-weighted MR (1.5 T) (600/15) (section thickness, 5 mm; gap, 1 mm; matrix, 256 × 128 matrix) before (*F*) and after (*G*) gadolinium administration showed a large hypothalamic mass (*white arrows*) with central hyperintensity and marked enhancement, a biopsy-proved germinoma.

stalk and posterior hypothalamus (Fig 2). At that time, a biopsy was refused. The abnormal finding was stable on the next MR about 3 months later, but by October 1991, an enhancing hypothalamic mass approximately 2 cm in maximal dimension was evident (Fig 2). A high-intensity focus of suspected hemorrhage was also seen within the mass. Craniospinal MR with gadolinium enhancement was negative for seeding. At that time, serum and cerebrospinal fluid specimens were positive for human chorionic gonadotropin. Additional endocrine abnormalities were discovered, including adrenocorticotropin deficiency, hyperprolactinemia, hypothyroidism, and gonadotropin deficiency. An open biopsy was done, and histopathologic study revealed findings characteristic of germinoma. A gradual but complete response to chemotherapy and radiotherapy over 6 months was observed on follow-up MR.

Discussion

Diabetes insipidus is a clinical condition recognized primarily by symptoms of excessive thirst, polydipsia, and polyuria. CDI refers to a deficiency of vasopressin (antidiuretic hormone) as a result of hypothalamic or pituitary dysfunction. This form of DI is distinguished from nephrogenic DI, which results from renal insensitivity to antidiuretic hormone, and from psychogenic DI.

MR of the normal pituitary gland demonstrates an anterior lobe that is roughly isointense to brain and a hyperintense posterior lobe that is as bright as fat on spin-echo T1-weighted images and brighter than fat on spin-echo T2-weighted images. This posterior pituitary bright spot (PPBS) probably represents compartmentalization of the ADH neurosecretory granules. Several reports in the radiologic literature have described a specific MR finding in CDI, that is, absence of the normal PPBS (1–4). This phenomenon is not well under-

stood but is probably related to interruption of synthesis or axonal transport of vasopressin neurosecretory granules along the hypothalamic-infundibular-neurohypophyseal pathway.

In contrast to adults, the PPBS is uniformly present on MR in healthy children (1, 3). Thin closely spaced sections (3- to 5-mm section thickness and 0- to 1-mm intersection gap) are often necessary to capture this small structure in the imaging field (5, 6). Although the expected location of the bright spot is in the posterior portion of the sella, occasionally it is found inferiorly within the sella, or superiorly (7, 8). Therefore, if the PPBS is not seen within the sella, pathologic absence or an ectopic location should be considered. In patients with ectopic posterior pituitary, the PPBS is relocated to the hypothalamus or proximal stalk, the pituitary stalk is often deficient or absent, hypopituitarism is often present (especially growth hormone deficiency), and DI is usually not present. Other small focal T1-weighted bright spots occurring about the sella, which may be mistaken for the PPBS or an ectopic PPBS, include hypothalamic or infundibular lipomas and fatty marrow within the dorsum or floor of the sella.

CDI and absence of the PPBS on MR has been observed with various etiologies including suprasellar tumors, Langerhans cell histiocytosis, granulomatous disease, trauma, and familial forms (4, 9, 10). Most of these produce structural abnormalities on MR, familial DI being the exception. Unexplained cases of CDI are categorized as idiopathic, or primary, after all diagnosable etiologies are excluded. It is difficult to be certain of the incidence of primary CDI. As an isolated clinical finding, CDI often suggests a functional abnormality of the hypothalamic-neurohypophyseal complex. When additional neuroendocrinopathies are present, however, there is a greater likelihood that a structural lesion of the hypothalamic-pituitary axis is present. In about 60% of the cases, tumors or infiltrative lesions producing CDI result in anterior pituitary dysfunction (8). For this reason, clinical suspicion of a mass should be high in cases with multiple neuroendocrinopathies.

A few case reports have described the delayed appearance of intracranial disease in children who spontaneously develop CDI. In two recently reported cases, the diagnoses of a suprasellar mass were made 11 years and 20 years after the onset of symptoms (11, 12). Imaging methods used to examine these patients included computed tomography but not MR. Such lengthy delays in diagnosis might have been averted had MR been available. However, our two current cases demonstrate that a tumor cause of CDI cannot be excluded by MR when the only finding is absence of the normal PPBS and when gadolinium is not administered.

Several studies have considered the utility of MR in the evaluation of hypothalamic-pituitary dysfunction (2, 4, 5, 9). Absence of the normal PPBS was observed on imaging studies in nearly all patients with CDI. In 26 cases of CDI reported by Tien et al (2), a structural abnormality of the hypothalamic-pituitary system and absence of the normal PPBS were shown by MR in every case. Nineteen of the 26 patients, including 10 between the ages of 1 and 20 years, had suprasellar tumors including histiocytosis, germinoma, craniopharyngioma, and hypothalamic glioma. Sagittal T1-weighted images without gadolinium administration demonstrated stalk thickening or a hypothalamic mass in all (19 of 19). Abnormal enhancement was shown in all of the 10 patients who received gadolinium (10 of 19).

In contrast, Cacciari et al, who studied patients with hypothalamic-pituitary disorders with and without CDI, failed to find a consistent relationship between the MR appearance and various neuroendocrinopathies (9). Although most of their cases of CDI demonstrated absence of the normal PPBS, a structural abnormality of the hypothalamus or pituitary was not always seen. However, gadolinium was not used in that study. There are occasional reports of patients with CDI in which the MR demonstrates only absence of the PPBS (1, 4, 6, 9). In all of these studies, only one of a total of 289 patients received gadolinium.

Guidindet et al (1) evaluated the usefulness of MR in determining the cause of pediatric CDI. All 13 children who were studied showed posterior pituitary signal loss. In eight of these patients, MR failed to reveal a structural abnormality that could account for CDI. Again, gadolinium was not used. The authors state that these patients were given the diagnosis of primary CDI only after 4 years of surveillance. Although no details about the frequency of clinical or MR follow up were provided, this is the only report that addresses continued evaluation of patients with unexplained CDI.

In conclusion, it is unclear to what degree MR contributes to the diagnosis of idiopathic CDI in children. However, as a result of our experience with the two children presented in this report, it

is our opinion that no child with unexplained CDI should simply be considered idiopathic, even when the initial MR, including MR with gadolinium administration, is normal or shows only absence of the normal PPBS. Although adequate data are not yet available to establish guidelines for clinical and imaging follow up in such patients, we recommend that serial follow-up MR studies be done. Closely spaced thin sections should be done, and gadolinium, now readily available, should be administered in all cases.

Acknowledgments

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