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Lack of Normal MR Enhancement of the Pituitary Gland: Findings in Three Siblings with Combined Pituitary Hormone Deficiency

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Summary: We present the MR appearance of the sella turcica in three sibling dwarfs with combined pituitary hormone deficiency in which MR images revealed a peripheral curvilinear band of enhancement about the pituitary gland in all three patients, a normal-size pituitary gland in two siblings, a mildly enlarged pituitary gland in one sibling, and a thin infundibulum and a normal posterior pituitary bright spot in all three siblings. Possible antecedents include an abnormal vascular supply, pituitary gland replacement by a nonfunctioning adenoma, a proteinaceous cyst, or a hamartoma.

Ten percent of all cases of growth retardation are the result of growth hormone deficiency. Growth failure due to growth hormone deficiency represents a heterogeneous group of disorders that may be familial. Familial growth hormone deficiencies may be isolated or accompanied by multiple (combined) pituitary hormone deficiencies. Autosomal recessive, autosomal dominant, and X-linked recessive forms have been described in families with isolated growth hormone deficiency, and autosomal recessive and X-linked recessive forms in those with combined pituitary hormone deficiency (1).

Case Report

A.M., D.M. (both male), and M.M. (female) are three affected siblings of unaffected Jamaican parents in a family of six children. The three affected siblings exhibited severe growth failure, with heights and bone ages well below the norm (see Table). Bone age was estimated from radiographs of the hand and wrist. Physical examination also revealed sexual immaturity. Endocrinologic evaluations revealed growth hormone deficiency in three siblings, prolactin deficiency in two siblings, thyrotropin deficiency in three siblings, and gonadotropin deficiency in three siblings. Stimulation tests supported the diagnosis of pituitary deficiency rather than a hypothalamic disorder in all three siblings.

T1-weighted (550/20/2 [repetition time/echo time/excitations]) magnetic resonance (MR) images of the sella before and after administration of contrast material in all three siblings showed a lack of normal enhancement of the pituitary gland with a curvilinear band of enhancement present around nonenhancing tissue (Fig 1). Delayed images obtained for D.M. 15 minutes after injection of contrast agent showed persistence of this MR appearance (Fig 1C). The pituitary stalk was present but thin in all three siblings (Fig 1). The bright spot of the posterior lobe was visible in all three siblings. The overall size of the pituitary gland was normal in two (A.M. and M.M.) and mildly enlarged in one (D.M.) (Fig 1). M.M. had the additional finding of a nonenhancing suprasellar mass, thought to be most compatible with a hamartoma.

Discussion

Several investigators have described various but inconstant MR findings in patients with pituitary deficiency (1–12). These variable findings include a small pituitary gland (1, 2, 4–7, 10), ectopic posterior lobe (2–9, 12), absent infundibulum (2, 4–6, 12), absent posterior pituitary (5, 6), hypoplastic infundibulum (2, 5, 7), normal pituitary (1, 6, 8, 11), empty sella (6, 12), small sellar volume (2, 7), and normal sellar volume (2, 7). The three siblings with combined pituitary hormone deficiency we describe had an unusual MR appearance and enhancement pattern of the pituitary gland.

Several authors have reported multiple family members with combined pituitary hormone deficiency (10, 11, 13, 14). A subset of these families had combined growth hormone, thyrotropin, and prolactin deficiency, with intact adrenocorticotropin, luteinizing hormone, and follicle-stimulating hormone secretion; the evidence points to a genetic defect. Mutations in the Pit-1 gene (which codes for a pituitary transcription factor) have been found in some of these patients (10, 11, 13, 14). Although our patients are phenotypically similar, evaluation of all six exons in the Pit-1 gene showed no abnormality (unpublished data). Search for a defect in the gene that regulates the function of Pit-1 is ongoing.

The prevalence of morphologic abnormalities in the pituitary gland is greater in patients with combined pituitary hormone deficiency than in those with isolated growth hormone deficiency (5, 6). Cacciari et al (6) reported abnormal morphologic MR findings in all 28 of their patients with combined pituitary hormone deficiency and in only five of 42 patients with isolated growth hormone deficiency. Abrahams et al (5) reported the presence of an ectopic posterior pituitary on MR images in 87% of their 15 patients with combined pituitary hormone deficiency and in only 10% with isolated growth hormone deficiency. Combined data show that in patients with isolated growth hormone deficiency, 135 MR abnormalities were found in 128 patients (2–8). These abnormalities, in decreasing order of frequency, include a hypoplastic anterior lobe (n = 52), an ectopic posterior pituitary (n = 34), a small sella turcica (n = 17), a small infundibulum (n = 14), an absent

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Clinical data for three siblings with combined pituitary hormone deficiency

	M.M.	A.M.	D.M.
Age, y	17	23	23
Bone age, y	8	12	8
Height, cm (SD)	116 (−7.2)	125 (−7.9)	113 (−9.5)
Growth hormone deficiency	+	+	+
Prolactin hormone deficiency	±	+	+
Thyrotropin hormone deficiency	+	+	+
Leutenizing hormone deficiency	+	+	+
Follicle-stimulating hormone deficiency	+	+	+

posterior lobe (n = 10), an absent infundibulum (n = 7), and an empty sella (n = 1). In 55 patients with combined pituitary hormone deficiency examined with MR imaging, 135 abnormalities were found (1, 3, 5–12), including, in decreasing order of frequency, an ectopic posterior pituitary (n = 51), a hypoplastic anterior pituitary (n = 35), an absent infundibulum (n = 31), an absent posterior pituitary (n = 7), an empty sella (n = 4), a small infundibulum (n = 4), and a small sella turcica (n = 3).

Maghnie and coworkers (15, 16) have suggested that the morphologic appearance of the pituitary gland and pituitary gland function as demonstrated by dynamic MR imaging may indicate the patients' endocrinologic status. Patients with idiopathic isolated growth hormone deficiency and reduced anterior pituitary lobe size were found not to be at risk for multiple hormone deficiency (15). Patients with impaired vascular supply with delay in anterior pituitary lobe enhancement showed progressive reduction of anterior pituitary lobe size and multiple hormone dysfunction (16).

Imaging of patients with familial combined pituitary hormone deficiency dates back to 1969 when Ferrier and Stone (17) reported the plain radiographic findings in two siblings, both of whom had evidence of a hypoplastic sella turcica. Similar radiographic findings were subsequently reported by Sipponen et al (18) in two siblings. An enlarged sella turcica as demonstrated by plain radiography or pneumoencephalography was reported by Parks et al (19) in three siblings, by Wit et al (1) in one of two groups of siblings, and by White et al (20) in three siblings with combined pituitary hormone deficiency. Computed tomographic (CT) evaluation of the sella turcica and pituitary in familial combined pituitary hormone deficiency has yielded various findings. In the CT examination of six patients (two sets of three siblings) with familial combined hormone deficiency, Rogol et al (21) found two patients with normal findings, two with an empty sella, one with complete absence of the pituitary gland, and one with a hypoplastic pituitary gland. In the three siblings reported by White et al (20), two had an empty sella on CT studies. One of these siblings had a minimally enhancing intrasellar mass with mild suprasellar extension at 17 years of age that had the appearance of an empty sella 12 months later (20). Of the three siblings reported by Parks et al (19) who had an enlarged sella turcica, two had a CT examination, which reportedly revealed a "full" appearance to the sella turcica. One sibling had no enhancement of the intrasellar contents after intravenous injection of iodinated contrast agent. The three siblings reported by White et al (20) and the three described by Parks et al (19) are of particular interest. The hormonal deficiencies in these siblings are clinically similar to those in our family. It is curious that all six of their patients had an enlarged sella turcica rather than the more commonly encountered hypoplastic sella turcica. In addition, the siblings reported by Parks et al had a "full" appearance to the pituitary by CT. Follow-up MR studies in the three siblings reported by Parks et al revealed the presence of an empty sella (telephone conversation, June 1996). A similar occurrence was reported by White et al. Could the findings in all six of those patients reflect a minimally enlarged nonfunctioning pituitary gland that subsequently underwent necrosis? These observations have led to a postulate that perhaps a form of programmed cell death has occurred (19) or that the cell death was associated with an acute immune response. An alternative explanation might be that negative feedback mechanisms related to exogenous hormone replacement resulted in an empty sella.

The MR findings of the pituitary gland in patients with familial combined pituitary hormone deficiency have been previously reported in five patients (1, 11). Two siblings with growth hormone, prolactin hormone, and thyroid-stimulating hormone deficiencies were found to have a normal-appearing anterior pituitary (11). In three patients with a similar combination of hormone deficiencies, MR imaging revealed a normal pituitary in two patients and a small pituitary in one patient (1). Neither author (1, 11) commented on the use of contrast material or on the appearance of the posterior lobe or infundibulum.

In the three siblings we describe, MR images showed evidence of pituitary dysfunction with lack of normal contrast

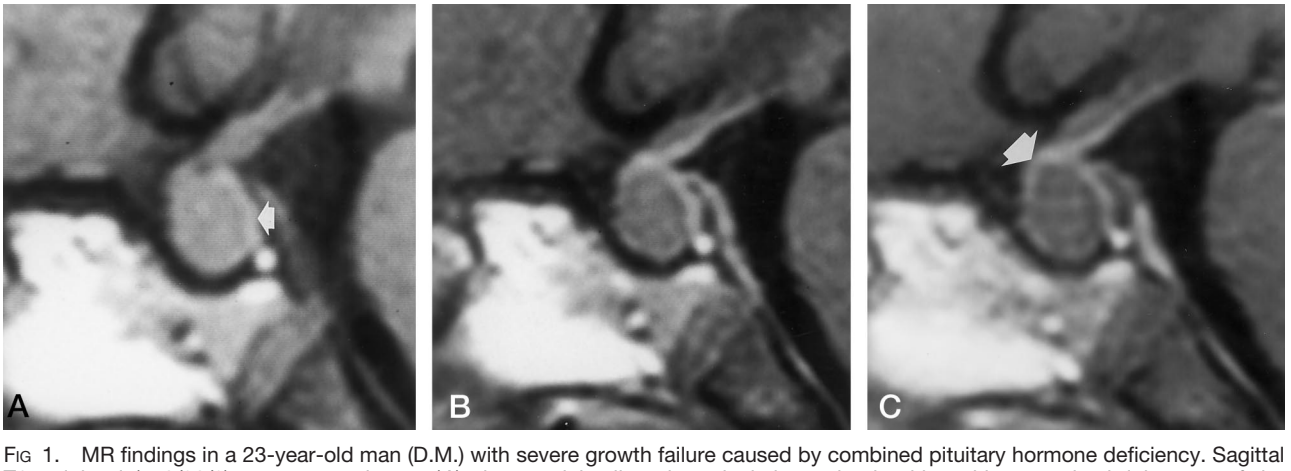

FIG 1. MR findings in a 23-year-old man (D.M.) with severe growth failure caused by combined pituitary hormone deficiency. Sagittal T1-weighted (550/20/2) noncontrast image (*A*) shows minimally enlarged pituitary gland, with a thin posterior bright spot of the neurohypophysis (*arrow*). Immediate (*B*) and delayed (*C*) postcontrast images fail to reveal enhancement within the gland. Only a peripheral rim of enhancement is present (*arrow, C*), which we believe is related to an abnormal vascular supply or to replacement of the pituitary gland by a nonenhancing mass.

enhancement of a minimally enlarged to normal-sized pituitary gland. Delayed postcontrast imaging performed in one sibling showed persistent lack of enhancement. Although no anatomic correlate was evident, possible pathogeneses include an abnormal vascular supply to the pituitary, replacement by a nonenhancing mass such as a proteinaceous cyst, or hamartomatous tissue. An adenoma would be less likely, since no enhancement was seen, even on delayed postcontrast images (Fig 1C).

In conclusion, MR studies of three siblings with familial combined pituitary hormone deficiency revealed a unique feature of rim enhancement of a normal to minimally enlarged pituitary gland. This imaging finding in a patient with growth failure should prompt the search for endocrine abnormalities and encourage genetic screening.

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