

## **Hypothalamic-Pituitary MRI Imaging : Normal And Abnormal Features In GH Deficiency**

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### **Introduction**

The accurate investigation of the hypothalamic-pituitary area is essential in the diagnosis of endocrine-related diseases. High quality magnetic resonance imaging (MRI) represents the examination modality of choice in the evaluation of hypothalamic-pituitary morphology. MRI is advisable in all patients with GH deficiency (GHD), although hypothalamic-pituitary abnormalities are more common in severe GHD. MRI pituitary morphology has important clinical implications, both in terms of diagnostic accuracy and long-term prognosis; indeed, when MRI findings are appropriately interpreted, they clearly represent a gold standard in the work-up of children with GHD. Establishing endocrine and MRI phenotypes is extremely helpful in the selection and management of patients with hypopituitarism, both in terms of possible genetic counselling and of early diagnosis of evolving anterior pituitary hormone deficiencies.

### **A. Normal pituitary appearance**

In normal newborns, the gland is typically convex, sometimes pear-shaped, with very high signal intensity on T1-weighted images. This appearance persists for the first month but changes during the second month as it progresses towards adult appearance, i.e. with a flat superior surface and isointensity of the anterior lobe and of the white matter on T1- and T2-weighted images. The gland

may have a slightly concave superior margin throughout childhood and is not expected to reach a height of less than 3 mm or greater than 6 mm prior to puberty. At puberty, the pituitary gland undergoes profound changes in size and shape, basically represented by marked enlargement. In girls, the gland may enlarge symmetrically to a height of 10 mm, appearing nearly spherical, whereas in pubertal boys it may reach 7-8 mm. In addition, in preterm babies a bright anterior pituitary gland has recently been reported during the first age-corrected 2 months (1).

## **B. Standard MRI in GHD**

Patients with idiopathic isolated GH deficiency (IGHD) may show an anterior pituitary gland that is normal size or “reduced” at MRI examination; ectopic posterior pituitary and anterior pituitary hypoplasia are also common features. A finding of empty sella has been reported in 9% of patients with IGHD. On the contrary, in cases of idiopathic multiple pituitary hormone deficiencies (MPHD), the most frequent MRI findings included:

**a-**moderate to severe anterior pituitary hypoplasia or anterior pituitary aplasia, frequently associated with a sella turcica of reduced size or flattened sella;

**b-**ectopic posterior pituitary at the median eminence or along the stalk projection up to its distal extremity, the hypoplastic stalk, (the maintenance of neurohypophyseal function in these types of patients is demonstrated by the presence, albeit in the ectopic site, of an area of hyperintense signal and by a lack of clinical signs suggestive of water metabolism dysfunction);

**c-**complete agenesis of the pituitary stalk (both nervous and vascular components); cerebral malformations like Arnold-Chiari I, Arnold-Chiari II, agenesis of the septum pellucidum, septo-optic dysplasia, vermis dysplasia, syringomyelia, absence of the internal carotid artery, dysgenesis of the corpus callosum, arachnoid cysts, and tentorium anomalies with basilar impression (2-4).

The frequency of these radiological findings and their distribution between isolated GHD and MPHD varies among reports. The variability between different studies could be attributed variously to the degree of restriction in the studies’ diagnostic criteria, to the diagnostic limits of GHD

(transitory deficits, recovery, false positives, etc.), and/or to the lack of a convincing standard normal size of pituitary gland among the pre-pubertal pediatric population.

Idiopathic MPHD may be less often associated with anterior pituitary hypoplasia but more frequently with normal posterior pituitary and pituitary stalk. Under such conditions, the search for gene involvement becomes mandatory (5). MR imaging evidence of normal or small anterior pituitary gland, enlarged empty sella, pituitary hyperplasia and/or intrasellar or suprasellar mass when associated with combined pituitary hormone deficiency or MPHD call for molecular analysis of POUF1F1, PROP-1, HESX-1, or LHX-3 while LHX4, SOX3 and GLI2 may be associated with ectopic posterior pituitary (Table 1).

### **C. MRI after Gadolinium**

A detailed study of the pituitary stalk should be carried out following the administration of contrast medium (Gd-DTPA). A finding of a vascular component of the stalk has a great deal of prognostic significance since patients with agenesis of the pituitary stalk run a greater risk of developing MPHD than those who show a vascular residue of the stalk (2,3,6).

### **D. Key issues and Flow-chart**

- MRI is the technique of choice in the diagnosis of children with hypopituitarism. Marked differences in MR pituitary gland morphology suggest different etiologies of GHD and different prognoses (Figure 1).
- Pituitary stalk agenesis and ectopic posterior pituitary are specific markers of permanent GHD and show a different clinical and endocrine outcome between patients identified after Gd-DTPA administration as having partial (IGHD) or having complete pituitary stalk agenesis (MPHD).
- Patients which do not have POUF1F1, PROP1 or LHX3 mutations and should be carefully monitored for evolving pituitary hormone defects; although exceedingly rare, mutations in other genes encoding transcription factors such as HESX1, LHX4, GLI2

and SOX3 in selected cases can be investigated.

- The next major challenge to image structural hypothalamic-pituitary abnormalities in more detail and to obtain a better definition of normal standards of anterior pituitary size.

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