

Original Article

Pituitary imaging in 129 children with growth hormone deficiency: A spectrum of findings

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ABSTRACT

Growth Hormone (GH) deficiency is the most common pituitary hormone deficiency in children. Magnetic Resonance Imaging (MRI) of the brain detects structural pituitary anomalies associated with GH deficiency. This retrospective hospital-based study was conducted at King Khalid University hospital (KKUH), Riyadh, Saudi Arabia, during the period (January 1995–June 2016). The available radiological, clinical and laboratory records of all children with confirmed GH deficiency by dynamic testing who had MRI brain were reviewed. A total of 129 patients were diagnosed with GH deficiency and had MRI brain performed. Isolated GH deficiency (IGHD) was diagnosed in 118 (91.5%) and multiple pituitary hormone deficiency (MPHD) in 11 (8.5%) patients. Most children with IGHD had normal MRI findings ($n = 86/118$), while 14/118 had hypoplasia of the anterior pituitary and 11/118 had aplasia of the anterior pituitary. Most of the children with MPHD (6/11) showed anterior pituitary hypoplasia or (3/11)

aplasia and only 2/11 children with MPHD had normal MRI. In conclusion, our study showed a spectrum of MRI changes in children with GH deficiency.

Keywords:

Magnetic Resonance Imaging; Children; Growth Hormone Deficiency; Pituitary.

INTRODUCTION

Growth hormone deficiency (GHD) is a common endocrine cause of short stature [1]. It may be idiopathic or associated with other causes such as tumors, radiotherapy or surgery [2]. GHD may be isolated (IGHD) or associated with multiple anterior pituitary hormone deficiency (MPHD). Children with IGHD present mainly with short stature while those with MPHD usually present early in infancy with neonatal hypoglycemia, prolonged neonatal jaundice and micro penis and later with short stature [1,2].

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How to cite this article:

AlJurayyan RNA, AlJurayyan NAM, Omer HG,
Alissa SDA, AlOtaibi HMN, AlKhalifah RAH,
Babiker AMI, Mohamed S. Pituitary imaging in
129 children with growth hormone deficiency:
A spectrum of findings. Sudan J Paediatr 2017;
17(1):30–35

Normally, the anterior pituitary and the stalk are well defined and posterior pituitary is easily identified as a hyper tense bright spot on the Magnetic resonance imaging (MRI) studies [3]. MRI brain may show characteristic anatomic pituitary abnormalities in patients with idiopathic GHD including a small or truncated stalk, and an ectopic posterior pituitary [1-3]. A higher frequency of MRI abnormalities was reported in multiple pituitary hormone deficiency (MPHD) compared to IGHD [1-5].

Here in, we present our experience over 20 years with MRI of the hypothalamic pituitary region in Saudi patients with confirmed GHD.

METHODS

This is a retrospective hospital based study, conducted at the pediatric endocrine service, King Khalid University Hospital, Riyadh, Saudi Arabia in the period January 1995 to June 2016, and included patients with biochemically confirmed diagnosis of growth hormone deficiency (GHD) who had MRI brain study available. The diagnosis of GHD was based on suggestive clinical features such as short stature, subnormal growth velocity and delayed bone age [1,2]. In infants and young children, the suggestive clinical features of GHD include hypoglycemia, prolonged neonatal jaundice, micro-penis and other midline defects [1,2]. In addition to these clinical features, the diagnosis of GHD was confirmed in all included patients by growth hormone assay according to the previously published guidelines [2]. These include peak growth hormone response less than 8 ng/ml, on one physiological test (sleep or exercise) and two pharmacological stimulation tests (glucagon, clonidine, L-dopa, propranolol, and arginine). Other hormones routinely assayed included thyroid stimulating hormone (TSH) and free thyroxine (FT4) and a morning cortisol. Also, Luteinizing hormone (LH) and Follicle stimulating hormone (FSH) levels were measured in prepubertal children. Further stimulation testing (e.g. adrenocorticotrophic-hormone, ACTH, and Luteinizing hormone releasing hormone, LHRH) was undertaken when indicated. GHD in neonates was diagnosed by the presence of suggestive clinical features (hypoglycemia, prolonged neonatal jaundice and micro-penis) in association

with a growth hormone level less than 8 ng/ml, at the time of hypoglycemia. Children were diagnosed as having MPHD if two or more pituitary hormones were deficient.

The radiological, clinical and laboratory records of all children with confirmed GHD by dynamic testing who had MRI brain available were reviewed. Relevant clinical data such as age, sex, presenting symptoms and signs, growth parameters, and hormone levels were abstracted by two of the authors using a case report data form.

Magnetic resonance studies were performed with contiguous sagittal and coronal spin-echo T1 weighted images and coronal T2 obtained. Results were retrospectively reviewed by the first author (RNAJ) and analyzed to define one or more of the following abnormalities:

1. Small or absent anterior pituitary
2. Truncated or absent pituitary stalk
3. Ectopic posterior pituitary and other associated anomalies. The findings were correlated with the clinical and biochemical presentation.

STATISTICAL ANALYSIS

Statistical Package for Social Science (SPSS, Version 21) was used for the statistical analysis of the data. Mean and standard deviation were used for categorical data while numbers and percentage were used for numerical data.

RESULTS

During the period under the review, a total of 129 children were diagnosed with GHD (Table 1). Ninety-nine (76.7%) were males and 30 (23.3%) females with a mean age of 10.5 years (range 2-14). IGHD was diagnosed in 118/129 (91.5%) while 11/129 (8.5%) patients had MPHD. There was a spectrum of magnetic resonance imaging abnormalities in patients with IGHD and MPHD (Table 2). Most children, (72.9%, $n = 86/118$), with IGHD had normal MRI findings (Figure 1). However, (11.9%, $n = 14/118$) had hypoplasia of the anterior pituitary and (9.3%, $n = 11/118$) had aplasia of the anterior pituitary. Most of the children with MPHD showed anterior pituitary aplasia 6/11 (54.5%) and anterior pituitary hypoplasia 3/11

(27.3%), while only 2/11 (18.2%) children with MPHD had normal MRI (Figures 2 and 3). Also, other central nervous system (CNS) abnormalities, including optic nerve hypoplasia and Chiari type 1 malformation were seen in both of the IGHD and MPHD groups (Table 3).

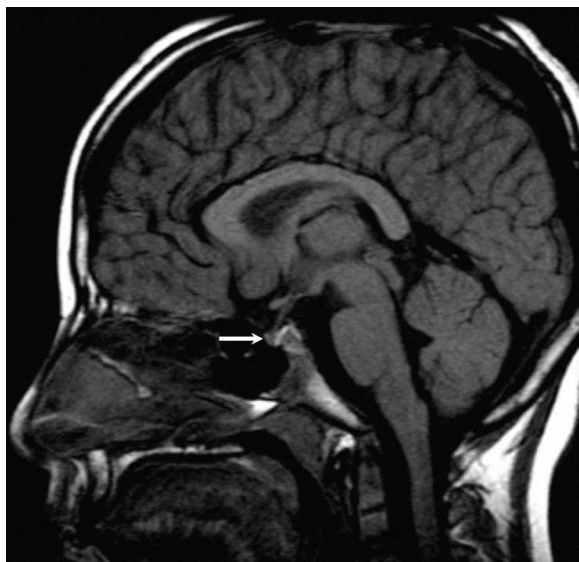


Figure 1- Sagittal T1 weighted Magnetic resonance imaging showing a normal study in an 8-year-old girl with isolated GH

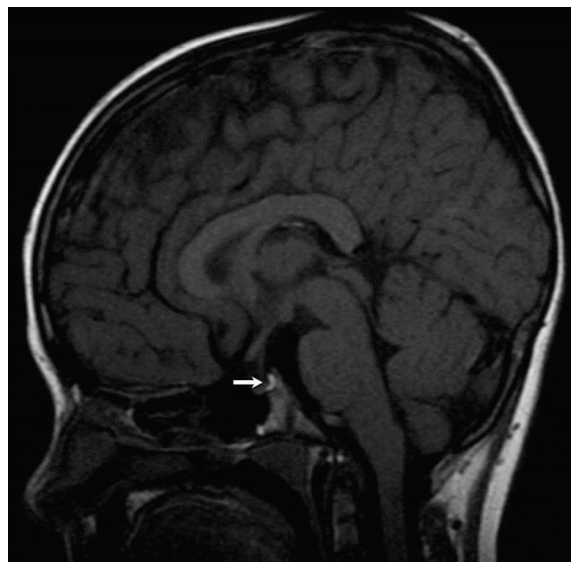


Figure 2- Sagittal T1 weighted Magnetic resonance imaging in a 2-year-old boy with MPHD showing a small anterior pituitary with bright spot of the posterior pituitary in a normal position

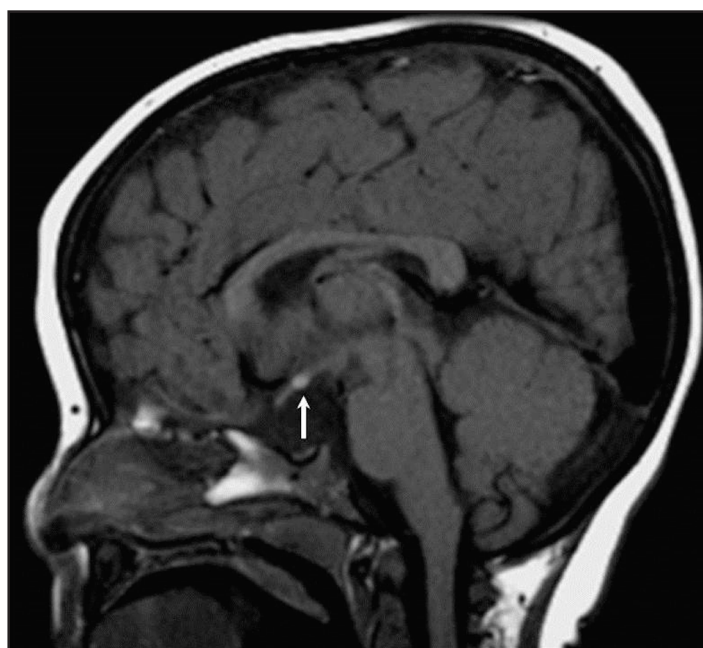


Figure 3- Sagittal T1 weighted Magnetic resonance imaging in a 2.5-year-old girl with multiple pituitary hormone deficiency showing a small anterior pituitary, absent stalk, and ectopic posterior pituitary

Table 1- Demographic characteristics of 129 children with growth hormone deficiency.

Diagnosis	Number (%)	Mean age (range)	Male	Female
Isolated growth hormone deficiency (IGHD)	118 (96.1%)	10.5 years (2-14)	92	26
Multiple pituitary hormone deficiency (MPHD)	11 (3.9%)	2.5 year (1.5-8)	7	4

Table 2- Appearance of hypophysis and stalk in children with growth hormone deficiency.

MRI findings	IGHD No. (%)	MPHD No. (%)
Normal	86 (72.9%)	2 (18.2%)
Empty Sella	1 (0.85%)	–
Bulky pituitary	1 (0.85%)	–
Anterior pituitary hypoplasia with ectopic posterior pituitary and normal stalk	4 (3.4%)	–
Hypoplasia hypophysis with normal stalk	6 (5.1%)	1 (9.1%)
Hypophysial hypoplasia and not visible stalk	4 (3.4%)	2 (18.2%)
Ectopic hypophysis with normal stalk	5 (4.2%)	–
Small or aplastic anterior pituitary with ectopic posterior pituitary and not visible stalk	5 (4.2%)	4 (36.3%)
Aplasia of anterior pituitary with normal posterior pituitary and stalk	6 (5.1%)	–
Aplastic hypophysis with not visible stalk	–	2 (18.2%)
Total (%)	118 (100%)	11 (100%)

IGHD - Isolated growth hormone deficiency, MGHD - Multiple pituitary hormone deficiency

Table 3- Malformations of central nervous system in patients with growth hormone deficiency

CNS malformation	IGHD No. (%)	MPHD No. (%)
Cavernous hemangioma	1 (0.86%)	–
Optic nerve hypoplasia	–	1 (9.1%)
Left eye coloboma	1 (0.86%)	–
Chiari type 1 malformation	1 (0.86%)	1 (9.1%)

CNS - Central nervous system, IGHD - Isolated growth hormone deficiency, MGHD - Multiple pituitary hormones deficiency.

DISCUSSION

Growth hormone deficiency GHD presents with a wide spectrum of findings both clinically and anatomically. The endocrine abnormalities of GHD manifest either as an isolated deficiency (IGHD) or it may be present as multiple hormone deficiency (MPHD).

In this report, we describe the MRI findings of a large cohort of children with GHD attending a single center in Saudi Arabia. Most of our patients had IGHD, which agree with the previous studies conducted in other ethnic groups [4,6,7]. MRI remains the modality of choice for assessing the hypothalamic pituitary region for patients with growth hormone and or other pituitary hormone deficiencies. MRI can precisely diagnose anomalies of the neurohypophysis and adenohypophysis including the stalk [3,6-12]. A Spectrum of findings was observed in our cohort with GHD, ranging from normal to small or completely absent anterior and or posterior pituitary together with an absent or thin stalk. Similar findings were reported in previous studies [7,10-12]. For instance, as in our study, different CNS malformations such Chiari type 1 malformation and optic nerve hypoplasia have been previously found in association with GHD [3,6,7]. It is worth noting that our study findings agree with the report from the major international study conducted

by Pfizer (KIGS study) in which 15043 patients with GHD were recruited from different countries. KIGS study found that most patients had normal pituitary gland, 7.8% had pituitary hypoplasia, 3.0% had empty Sella, and 6.8% had hypoplasia of the anterior pituitary, absent stalk and ectopic posterior pituitary [13].

Our study limitations include: limited number of patient with MPHD, limitation related to the lack of MRI standardization, and finally, lack of molecular testing for transcription factors causing MPHD.

CONCLUSION

There was a spectrum of changes in MRI pituitary in Saudi children with GH deficiency or multiple pituitary deficiencies similar to what has been reported in other ethnic groups.

ACKNOWLEDGEMENT

The authors would like to thank Jumna Khader for typing the manuscript and extend their thanks and appreciation to Miss Hadeel N A AL Jurayyan for her help in preparing the manuscript.

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