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RESEARCH ARTICLE

Hypopituitarism in children: The role of Magnetic resonance Imaging (MRI)

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ABSTRACT

Background: Childhood hypopituitarism is a clinical syndrome of deficiency in pituitary hormone production. Presentation varies from asymptomatic to acute collapse depending on the etiology, rapidity of onset, and predominant hormone involved.

Objective: To study the frequency, and type of hypothalamic-pituitary axis abnormalities observed on MRI in patients with hypopituitarism and correlate it with MRI findings.

Design and setting: A retrospective hospital based cohort study was conducted at the pediatric and radiology departments, King Khalid University Hospital (KKUH) Riyadh, Saudi Arabia.

Materials and methods: The medical records of 202 patients who were diagnosed to have hypopituitarism were retrospectively reviewed. Data included were age, sex, clinical presentation, and results of the relevant laboratory investigations and radiological images.

Results: During the period under review, a total of 202 patients were diagnosed with hypopituitarism, of these 142 (70.3%) were males and 60 (29.7%) were females. The mean age was 8.9 years (range 0-18 years). The clinical presentation varies from asymptomatic to symptomatic the severity of which depend on hormone deficiency and the etiology. Beside the congenital causes, a diversity of acquired causes were encountered with a non-tumor causes being the commonest. Magnetic resonance imaging (MRI) of the brain was performed in 173 (85.6%) of patients. Single hormone deficiency [growth hormone (GH), and adrenocorticotropic hormone (A.C.T.H)], thyroid stimulating hormone (TSH), luteinizing hormone (LH) and follicle stimulating hormone[FSH], i.e partial hypopituitarism, in 125 (72.3%) patients while, multiple pituitary hormone deficiency (MPHD) in 48 (27.7%) patients. Diabetes insipidus was found in 17(9.8%). Among those patients with magnetic resonance imaging (MRI) were done, the majority (95%) of patients with isolated hormone deficiency had normal MRI findings, while in those patients with MPHD (>50%) revealed abnormal findings varies from empty sella syndrome to anterior pituitary hypoplasia or aplasia. The hypophyseal stalk abnormalities were also evident (thin or interruption). Central diabetes insipidus is rare in children and characterized by the loss of the posterior pituitary bright spot, and thickening of the pituitary stalk were commonly associated.

Conclusion: Magnetic resonance imaging (MRI) is useful tool in evaluating the hypothalamic-pituitary axis in children. Wide spectrum of MRI findings were encountered. The majority were isolated hormone deficiency (partial hypopituitarism), who had normal MRI findings. The majority of MPHD patients were associated with variable defects (anterior pituitary gland hypoplasia or aplasia and stalk interruptions or thinning). Lack of posterior pituitary gland bright spot, and thickening of the pituitary stalk are commonly associated with central diabetes insipidus (CDI). MRI provide high resolution images of the pituitary gland, pituitary stalk and adjacent structures. It delineated the various neoplastic conditions such as hypothalamic glioma, germinoma, teratoma, langerhans cell, histiocytosis, leukemic infiltrates, and granulomatosis such as sarcoidosis.

Keywords: Anterior pituitary gland, aplasia or hypoplasia, children, central diabetes insipidus (CDI), hypopituitarism, magnetic resonance (MR), posterior pituitary gland, ectopy.

Introduction

Childhood hypopituitarism is a rare clinical syndrome resulting from the deficiency in pituitary hormone production. The pituitary gland is a midline structure located just beneath the optic chiasm. It is composed of two main lobes, the predominant anterior lobe, also known as adenohypophysis and the posterior lobe, also known as neurohypophysis, in addition to the vestigial intermediate lobe. Hypopituitarism might be a life threating condition. It can result from disorders involving the pituitary gland, the hypothalamus or the surrounding structures, such as tumor, inflammation, infection, surgical destruction, radiation, traumatic or vascular insult. Hypopituitarism might be associated with birth trauma, perinatal asphyxia or midline defects such as cleft lip, septo-optic hypoplasia and encephalocele. Hypopituitarism could be partial or complete Insufficiency of pituitary hormones. Panhypopituitarism refer to involvement of two or more pituitary hormones. However, involvement of one hormone only refer to isolated or partial hypopituitarism. The younger the child is at the time of presentation the more likely the etiology is to be congenital. However, on occasions, congenital forms may present or get diagnosed later in childhood, while some acquired forms can be detected relatively early in life[1-8]. Magnetic resonance imaging (MRI) scan is the imaging method of choice for evaluating the hypothalamic pituitary axis with paramount importance to detect various pathologies. MRI is non-invasive and offers greater sensitive for identification of abnormalities in the hypothalamic pituitary region compared to other imaging modalities such as computerized tomography (CT) scan[9-11]. This study aims to investigate the prevalence and patterns of abnormalities identified on MRI in patients with hypopituitarism, with particular emphasis on their association with the clinical severity of the condition.

Materials and methods:

The medical records of patients diagnosed with hypopituitarism were retrospectively reviewed. Collected data included patient age, sex, clinical presentation, results of relevant laboratory investigations, and radiological imaging findings. All patients underwent magnetic resonance imaging (MRI) of the hypothalamic–pituitary region. The diagnosis of hypopituitarism was established based on clinical suspicion and confirmed by appropriate hormonal evaluation. Comprehensive hormonal testing assessing both anterior and posterior pituitary function was performed according to standardized institutional protocols[12]. Pituitary function assessment was conducted 1–2 months following any neurological procedure to avoid transient postoperative hormonal alterations. Thyroid function was evaluated periodically to monitor for the development of thyroid dysfunction.

Statistical analysis

Descriptive data is provided. Dichotomous data is presented as frequencies and percentage. Statistical packages for social service (SPSS version 21) was used for the statistical analysis of the data.

Results

During the period under review, there were 202 patients with hypopituitarism, of these, 142 (70.3%) were males and 60 (29.7%) females. The mean age was 8.9 years (range 0-18 years). The clinical presentation varied from asymptomatic to symptomatic, the severity of which depends on the hormone deficient and the cause of the disorder. Midline defects where clues to the diagnosis. Beside congenital causes, a diversity of acquired causes were encountered with a non-tumor causes being the commonest. MRI brain was performed in 173 (85.6%) of patients, table 1. This included brain tumors (23), congenital hypopituitarism (10), septo-optic dysplasia (6), traumatic brain injury (TBI) (3), and Langerhans cell histiocytosis, post infectious (streptococcal) and empty sella syndrome in two patients each. Central diabetes insipidus (CDI), table 2, associated with Panhypopituitarism were seen in 17 (9.8%) patients.

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Table 1: Etiology of hypopituitarism in 173 patients with MRI

Diagnosis	Number (%)
Isolated hormone deficiency	125 (72.3%)
Multiple pituitary hormone deficiency (MPHD)	48 (27.7%)
Brain tumor	23
Congenital Hypopituitarism	10
Sept-optic dysplasia	6
Traumatic Brain Injury (TBI)	3
Post-infectious	2
Empty sella Syndrome	2
Langerhans cell histiocytosis	2

Table 2. Etiology of Central Diabetes Insipidus (CDI) in 17 patients with abnormal MRI findings

Diagnosis	Number and (%) percentage of patients
Brain tumor	8 (47.1%)
Congenital Hypopituitarism	4 (23.5%)
Traumatic-brain (TBI)	3 (17.6%)
Langerhans Cell histiocytosis	2(11.8%)

Discussion

Hypopituitarism is not that rare in children. There are limited studies on the incidence and prevalence of the disease in the English literature. A study from Spain documented an incidence and prevalence of hypopituitarism to be 4.21 and 45.5 case per 100000 population respectively. Hypopituitarism follows a smoldering course, unless it has an onset with pituitary apoplexy, hence, more often it is likely to be missed. Hypopituitarism is often associated with increased mortality[13,14].

Magnetic resonance imaging (MRI) scan is the imaging method of choice for evaluating the hypothalamic pituitary axis. It is of paramount importance with hypopituitarism among children to detect the varying pathology. It is a non- invasive which offers greater sensitivity than computerized tomography (CT) for identification of abnormalities in the hypothalamic-pituitary region. Normal pituitary MRI shows the anterior pituitary gland as a dark structure equal in intensity to gray matter on T1-weighted imaging, while the posterior pituitary gland appears as a white structure, "bright spot", Figure 1. MRI with gadiolinium injection is more sensitive for the demonstration of the pituitary stalk. The "bright spot" correlates well with the clinical presence of diabetes insipidus (DI) and it is completely absent in some cases of congenital hypopituitarism or it can be found ectopically located ,figure 2, in which case DI is usually absent. Such radiological findings are sometimes helpful in securing the congenital nature of hypopituitarism.[9-11]

In this series the hypothalamic-pituitary tumors were the second most common, with craniopharyngioma being the most frequently encountered. Direct destruction, invasion, necrosis, and surgery are

common factors. Cranial radiotherapy frequently cause abnormal hypothalamic-pituitary dysfunctions. The most frequent changes are the hypothyroidism, and gonadal dysfunctions. Although, subtle abnormalities in adrenal function may occur.[15-18]

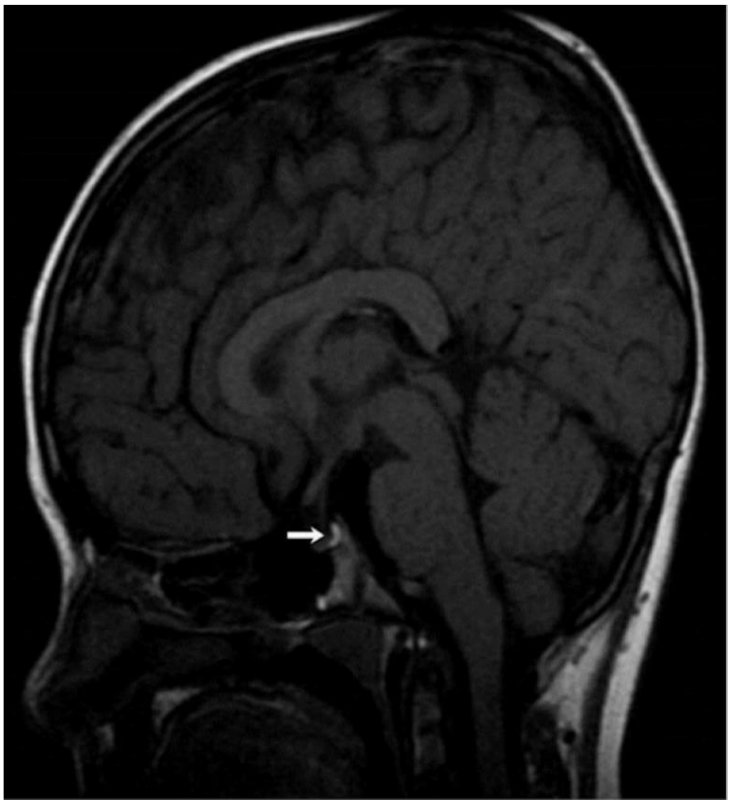

Figure 1. Sagittal T1 weighted Magnetic resonance imaging (MRI) showing a normal anterior pituitary, posterior pituitary and pituitary stalk study.

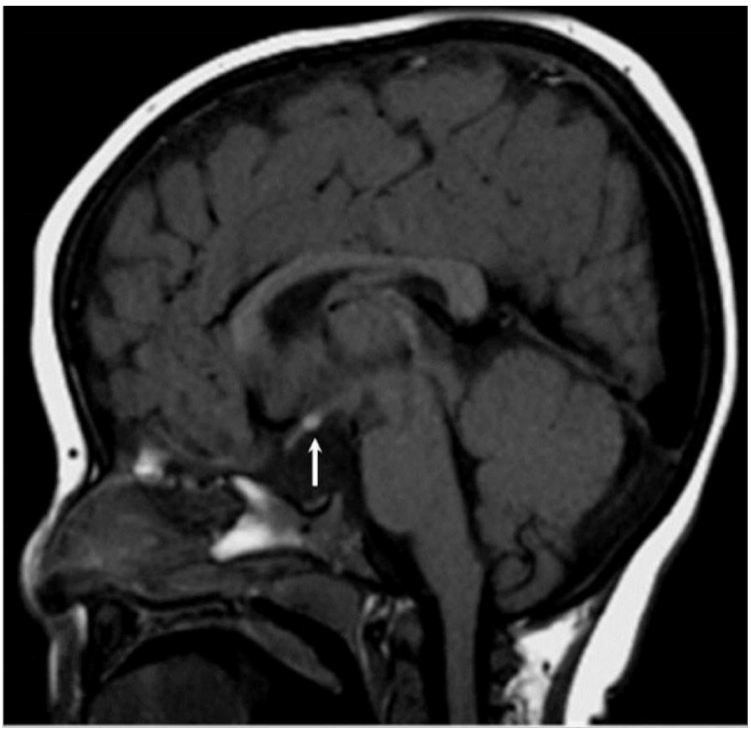

Figure 2. Sagittal T1 weighted Magnetic resonance imaging (MRI) in a girl with multiple pituitary hormone deficiency (MPHD) showing a small anterior pituitary, absent stalk, and ectopic posterior pituitary.

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Idiopathic isolated hormonal deficiency were found in the majority (72.3%) and revealed normal hypothalamic-pituitary MRI studies. Only five patients showed abnormal studies. Three patients revealed anterior pituitary gland hypoplasia and two were aplastic with variable degrees of pituitary stalk abnormalities.[19,20]. MPHD were found in 48 patients included brain tumor (23), congenital hypopituitarism (10), septo-optic dysplasia (6), traumatic brain injury (TBI) (3), post-infectious (2), empty sella syndrome (2), and Langerhans cell histiocytosis (2), and showed greater frequency of MRI abnormalities in more than 50%, which is fairly well correlate positively with the sensitivity.

MRI abnormalities needs to be correlate with the clinical findings and hormonal findings. These included empty sella syndrome, variability of the shape and size of anterior pituitary glands, and pituitary stalk thinning, interruption and transaction. Ectopic posterior pituitary gland or absence of the bright spot, associated with the absence of the pituitary stalk or thickening (PST) were also common finding.[21-28]

Central diabetes insipidus (CDI) is a rare in children, found in 17 patients in this series, associated with MPHD. This includes, brain tumors (8 patients), congenital hypopituitarism (4 patients), post-traumatic-brain injury (3 patients), and langerhen's cell histiocytosis in two, Table 2.

The absence of the bright spot of the posterior pituitary on MR is of valuable. It is used as a sensitive marker for the diagnosis of central diabetes insipidus. The pituitary stalk thickening (PST) was also noted. The shape and size of the anterior pituitary "adenohypophysis" was variable and correlated with multiple pituitary hormone deficiency.[29-32]

Conclusion

In children with hypopituitarism, magnetic resonance imaging (MRI) of the hypothalamic pituitary region in of great value in successful assessment. It delineates the pituitary anatomic features, including the anterior pituitary, infundibulum, and the posterior pituitary bright spot, normally located in the posterior aspect of the sella. The posterior pituitary appears hyper-intense on T1-weighted image as a results of the composition of the neurosecretory granules. Pituitary abnormalities positively correlate with endocrinologic dysfunctions. Structural pituitary abnormalities were encountered more frequently with MPHD. Also, the findings of an ectopic or absent neurohypophysis together with an abnormal pituitary gland were seen specific of MPHD.

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Conflict of interest:

The authors have no conflicts of interest to declare.

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