Scientific Research Publishing

Open Journal of Endocrine and Metabolic Diseases, 2017, 7, 89-95
http://www.scirp.org/journal/ojemd
ISSN Online: 2165-7432
ISSN Print: 2165-7424

Short Stature due to Ectopic Neurohypophysis: Case Report

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How to cite this paper: Almalki, M.H., Buhary, B.M., Brema, I., Almaghamsi, A. and Al Zahrani, S. (2017) Short Stature due to Ectopic Neurohypophysis: Case Report. *Open Journal of Endocrine and Metabolic Diseases*, **7**, 89-95.
https://doi.org/10.4236/ojemd.2017.72009

Received: February 1, 2017
Accepted: February 25, 2017
Published: February 28, 2017

Abstract

Ectopic posterior pituitary is a disruption in the normal embryogenesis and is one of the rare but common causes of pituitary dwarfism. We report the MRI and clinical findings of a 13.5-year-old Saudi boy who was referred to the endocrine outpatient clinic with no significant complaints except for fatigue, exercise intolerance and short stature. Physical examination revealed short stature (below 2nd centile) with normal body proportion without any dysmorphic features and prepubertal secondary sexual characteristics and genitalia. Hormonal profile revealed: low thyroxine level, low gonadotrophins, low testosterone, low cortisol and blunted growth hormone (GH) response to insulin induced hypoglycaemia. Bone age was of 5 years old. The MRI result concluded with a diagnosis of ectopic posterior pituitary. A diagnosis of posterior pituitary ectopia (PPE) with panhypopituitarism was made.

Keywords

Panhypopituitarism, Posterior Pituitary Ectopia, Growth Hormone Deficiency, Short Stature

1. Introduction

Ectopic posterior pituitary is a rare condition where "bright spot" is not seen at the sella. It can be associated with pituitary stalk transection syndrome and should be suspected when there is lack of pituitary stalk visibility and hypoplasia of the anterior hypophysis in a patient clinically presented with features of isolated growth hormone deficiency (IGHD)/multiple pituitary hormone deficiency (MPHD), but where the posterior pituitary function is usually maintained [1]. Magnetic resonance imaging (MRI) is essential for diagnosis. We present a case of short stature due to combined growth hormone and other anterior pituitary hormone deficiencies with ectopic posterior pituitary.

2. Case Report

A 13.5 years old male Saudi presented to the Endocrine clinic for evaluation of short stature. His medical history revealed that he had fatigue and exercise intolerance. He had a normal birth at 39 weeks and was born with average birth weight (2.6 kg) and height (48 cm). He reached normal milestones till the age of eight months. He was sitting by 7 months of age and crawling at 10 months. He walked at 15 months. Apart from growth retardation, there was no evidence of chronic illness. He had right side undescended testes with surgical correction done three years ago.

He comes from a good socioeconomic status and has 8 siblings who are healthy and have no similar problems. His school performance was average. Physical examination revealed height of 123 cm (below 2nd centile) and a weight of 26 kg (**Figure 1**), with a body mass index of 17.2 kg/m^2. His head circumference was 54 cm and his arm span of 123 cm. He has no goiter, no skin or mucous changes or any pigmentations, no dysmorphic features, no bony deformities and no pubertal changes.

His genitalia are pre pubertal with bilateral testicles felt with less than 3 ml. Systemic examinations are unremarkable.

Laboratory data showed normal complete blood count, urea and electrolytes, liver function test and bone profile. Initial hormone studies showed ACTH 2.8 Pmol/l (1.6 - 13.9 Pmol/l), morning random cortisol 50 nmol/L (170 - 413 nmol/L), Short synathen (250 mcg) test revealed that - baseline ACTH 5.8 Pmol/L (1.6 - 13.9 Pmol/l), and baseline cortisol level 112 nmol/L (170 - 413 nmol/L), 30 minute level 282 nmol/L (170 - 413 nmol/L), and 60 minute level 364 nmol/L (170 - 413 nmol/L). TSH was 4.4 mIU/L (0.270 - 4.200 mIU/L), with free T4 5.7 Pmol/l (12.0 - 22.0 Pmol/L), and free T3 3.8 Pmol/l (3.1 - 6.8 Pmol/L). All normal values of the above parameters are shown in brackets.

LH 0.1 IU/L (1.7 - 8.6 IU/L), FSH 0.1 IU/L (1.5 - 12.4 IU/L), Prolactin 1254 mIU/L (86 - 324 mIU/L). Growth hormone 0.48 mIU/L (0.00 - 9.00 mIU/L), IGF1 3.25 nmol/l (28.6 - 126.4 nmol/L), IGFBP-3 0.9 mg/L (2.2 - 7.8 mg/L) were compatible with GHD. Celiac profile was negative.

Clonidine stimulation test showed: baseline growth hormone at 0.2 mIU/L (0.00 - 9.00 mIU/L), 30 minute level 0.29 mIU/L (0.00 - 9.00 mIU/L), 60 minute level 0.26 mIU/L (0.00 - 9.00 mIU/L) and 90 minute level at 0.56 mIU/L (0.00 - 9.00 mIU/L) resulting in no increase in growth hormone levels.

Insulin tolerance test was abnormal, resulting in confirmation of the diagnosis (**Table 1**).

X-ray left hand showed a bone age of 5 years with delayed bone age more than two standard deviations of the chronological age (**Figure 2**).

The MRI pituitary gland revealed spontaneous high T1 nodule at the median eminence of the third ventricle with absent normal spontaneous T1 hyperintensity of the neurohypophysis indicating ectopic posterior pituitary. The anterior pituitary appears unremarkable. No convincing associated abnormality noted.

The supratentorial and the infratentorial structures appeared essentially

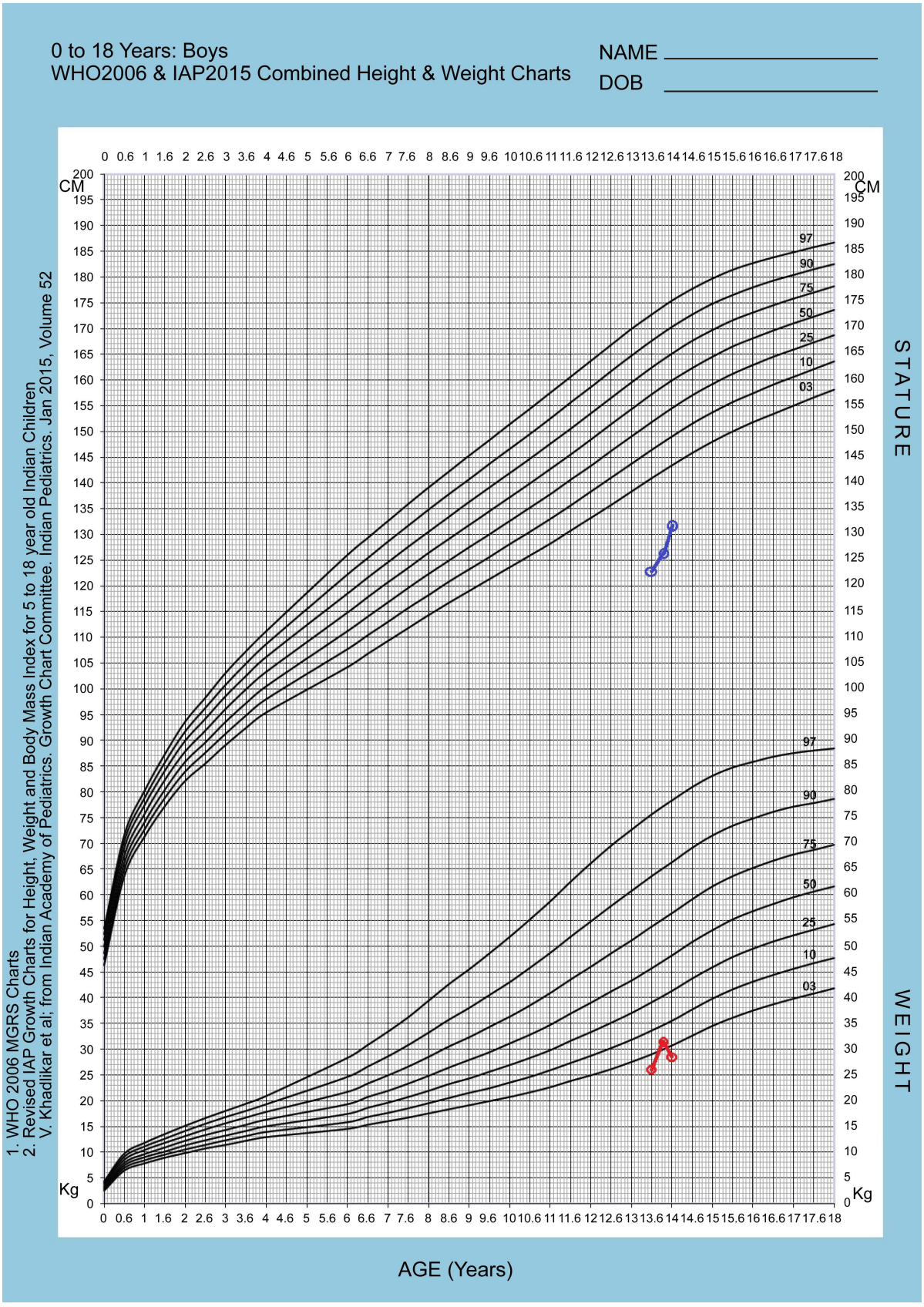

Figure 1. Growth Chart showing data at time of first visit, after 3 months follow up and after 6 months follow up. Height is shown in blue and weight is shown in red.

Table 1. Insulin tolerance test.

Test (normal range)	Baseline values	After IV insulin injection (after 30 minutes)	After IV insulin injection (after 45 minutes)
Blood glucose (4.4 - 7.8 mmol/l)	4.3	2.8	2.1
ACTH (1.6 - 13.9 Pmol/l)	5.9	2.4	2.2
Cortisol (200 - 700 nmol/L)	87	34	32
Growth hormone (0.00 - 9.00 mIU/L)	0.33	0.25	0.41

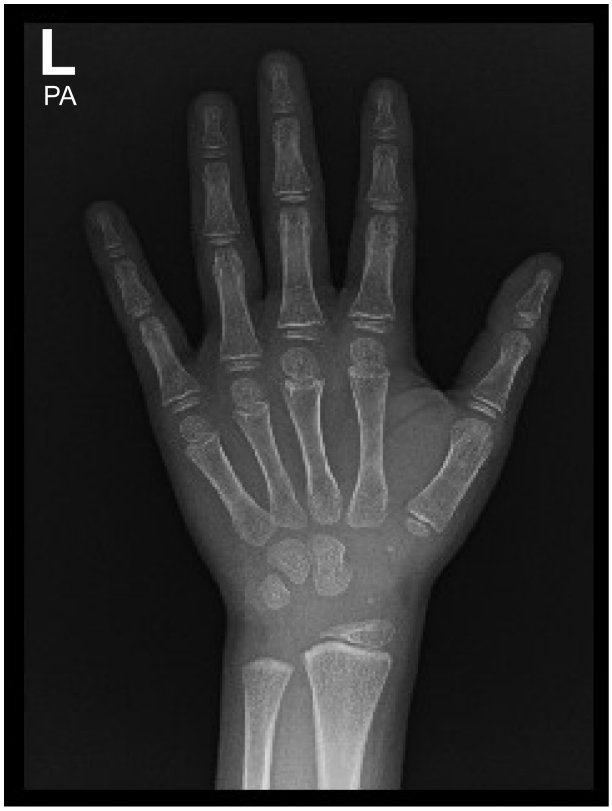

Figure 2. X-ray left hand.

unremarkable. The MRI result concluded with a diagnosis of ectopic posterior pituitary (**Figure 3**). The ectopic pituitary gland is pointed out in **Figure 3(C)**.

From the results of the dynamic tests and pituitary MRI, the patient was diagnosed with Panhypopituitarism with growth hormone deficiency, adrenal insufficiency, secondary hypothyroidism and secondary hypogonadism due to ectopic posterior pituitary. Replacement therapy was started and currently he is on hydrocortisone 2.5 mg tablets twice daily, Levothyroxine 75 mcg tablet daily, recombinant human growth hormone 1 mg injection subcutaneously daily. After 3 months of follow up he has gained height (126.5 cm) and weight (31.8 kg). After 6 months of follow up he has gained height (132 cm) and lost some weight (28.4 kg) (**Figure 1**).

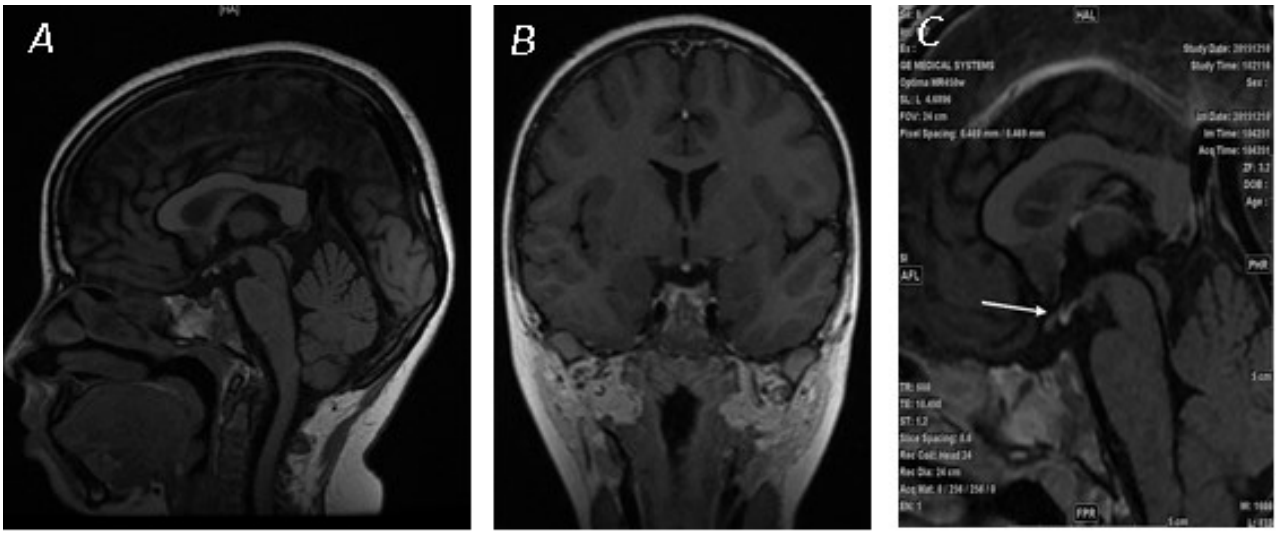

Figure 3. MRI T1-weighted images: (A) Sagittal, (B) Coronal and (C) Sagittal; showed spontaneous high T1 nodule at the median eminence of the third ventricle with absent normal spontaneous T1 hyperintensity of the neurohypophysis indicating ectopic posterior pituitary. The ectopic pituitary gland is pointed out in **Figure 3(C)**.

Informed consent was obtained from the parents to publish this case.

3. Discussion

The ectodermal anterior pituitary evolves from the rathkes pouch while the neuroectodermal posterior pituitary forms from the diencephalon and should be connected with the infundibulum. An ectopic gland forms due to a faulty migration of the posterior lobe during embryogenesis, tumours, trauma, or surgical transection of the pituitary stalk [2] [3]. This rare condition occurs with hypoplasia or absence of the infundibular stalk, an empty pituitary fossa and exhibits features of growth hormone deficiency (short stature/pituitary dwarfism) and may also have features of various related abnormalities like congenital, central nervous system malformations, cardiac abnormality, facial abnormality etc. [4] [5]. Another common malformation is neonatal hypoglycemia [5]. The most common location of the ectopic lobe is along the median eminence in the floor of the third ventricle as in our case; however it can vary [6]. However our patient did not have any dysmorphic features and he had a proportionate body similar in size of a 6 to 7 years old boy.

Multiple hormone deficiencies are commonly associated with the ectopic posterior lobe, the most commonly occurring abnormality is of the anterior gland hormones related to dysfunction of the infundibulum. The neurosecretory cells of the posterior pituitary transport ADH and oxytocin along the infundibular stalk while the anterior pituitary transport hypothalamic releasing hormones via vessels along the infundibulum. This patient was diagnosed with Ectopic posterior pituitary with Panhypopituitarism consisting of Growth hormone deficiency, Adrenal insufficiency, Secondary hypothyroidism and Secondary hypogonadism.

Holoprosencephaly is one of the commonly associated midline anomalies

which usually becomes apparent due to growth failure. Abnormal MRI mostly result with patients that have peak growth hormone levels less than 3 g/L. Research indicates patients with a visible infundibulum after contrast have less severe hormonal problems and are disposed to have isolated growth hormone deficiency [1]. Our patient's MRI study revealed evidence of a spontaneous high T1 nodule at the median eminence of the third ventricle with absent normal spontaneous T1 hyper intensity of the neurohypophysis indicating ectopic posterior pituitary. The anterior pituitary appears unremarkable. No convincing associated abnormality was noted. The supratentorial neither the infratentorial structures appeared essentially unremarkable. No signs of disturbed CSF flow. The mid sagittal images demonstrated a well formed and intact corpus callosum.

In one study evaluating the MRI of 103 patients, 72 patients were with Isolated GHD (IGHD) and 31 with Combined Pituitary Hormone Deficiency (CPHD)] [7]. MRI abnormalities were found in 48.6% patients with IGHD and 93.5% with CPHD. Jaundice, hypoxia, hypoglycemia and breech deliveries were commonly observed in ectopic posterior pituitary (EPP)/thin or interrupted pituitary stalk (PSA) group. EPP/PSA was found in 87.1% patients with severe GHD (peak GH <3 μg/L or <9 mIU/L) as compared to 12.9% with mild to moderate GHD (peak GH: 3 - 10 μg/L). Amongst CPHD, EPP/PSA was present in 80% of subjects with associated hypocortisolism ± hypothyroidism as compared to 18.2% of subjects with hypogonadism.

No treatment is required for the ectopic pituitary as such, but rather for the recurrently associated growth hormone deficiency, or less frequently panhypopituitarism [8]. Growth hormone replacement and other deficient target hormone replacement are available in selected patients and can improve adult height. We replaced the deficient hormones and have observed an improvement in his growth and wellbeing over a period of 6 months.

4. Conclusion

In patients with idiopathic anterior hypopituitarism, they consider to rule out ectopic posterior pituitary and absent pituitary stalk on imaging. We emphasize the association of the absent pituitary stalk in ectopic pituitary gland and low growth hormone levels.

Conflicts of Interest

There are no conflicts of interest to declare in relation to this article.

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