ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 04 | April - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

HYPOPITUITARISM: A CASE REPORT OF OVERLOOKED DIAGNOSIS.

Endocrinology

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ABSTRACT

Hypopituitarism, which has a number of causes, is a severe endocrine condition that needs early diagnosis and treatment to prevent serious consequences. We report a 17-year old male seen in outpatient department for lack of development of secondary sexual characters and short stature. Laboratory investigation showed low total tri-iodothyronine (T3) , low total thyroxine (T4) and slightly elevated thyroid stimulating hormone (TSH) , low basal cortisol, and normal prolactin level. The patient also had low total testosterone, low LH, and FSH values. Magnetic resonance imaging (MRI) of the pituitary revealed a hypoplastic anterior pituitary with ectopic posterior pituitary. This case highlights the notable absence of recognizing the clinical presentation of hypopituitarism which at times is nonspecific and often progress insidiously before a diagnosis is made. The case calls attention to importance of thorough history taking, attention, and observation in making a new diagnosis that has the potential to alter a patient's health care and quality of life.

KEYWORDS

Hypopituitarism, growth hormone deficiency, hypogonadism, hypothyroidism, short stature

INTRODUCTION

Hypopituitarism describes deficiency of one or more hormones of the anterior or posterior pituitary gland. Panhypopituitarism specifies the loss of all pituitary hormones, it's clinical implementation is used to report patients with growth hormone (GH), gonadotropins (LH and FSH), thyrotropin (TSH), and corticotropin (ACTH) deficiencies with intact posterior pituitary function. It is a rare condition, though its prevalence is underestimated [1,2]. An Indian study estimated the total prevalence of pituitary disorder to 4 million in the year 2000 [3]. Neuroendocrine disturbances in anterior pituitary hormone secretion are common, according to numerous studies, post empty Sella [4], cerebrovascular accidents [5], traumatic brain injuries [6], post-radiation [7], autoimmune hypophysitis [8], postpartum pituitary necrosis [9], sarcoidosis [10], and snake bite[11]. Hypopituitarism's clinical effect differs depending on the age at which it arises, the pace at which it manifests, the patient's gender, the underlying cause, and the pattern of hormone deficiencies.

Case presentation

A 17-year-old-male, presented with complaints of lack of secondary sexual characters and growth failure. He was delivered at term by normal vaginal delivery. His data related to consanguinity, birthweight , Apgar score , mental milestones was not available. There was no family history of pituitary or thyroid disease. He has one sibling with normal growth and development. There was no history of any systemic illness, head injury, drug intake, diarrhea, headache and visual disturbance. There is no history of fatigue , lethargy, constipation or irritability. On examination, his height was 107cm (- 9.71 SDS, height age 6 years, target height 171.5cm) upper and lower segment ratio 0.93 , arm span 124 cm, weight 41.7kg (weight age 12.6 years), and a body mass index of 15.7kg/m^2. He had cherubic face with frontal bossing, depressed nasal bridge, mid-facial hypoplasia, and low-set ear . He didn't have a goiter. His blood pressure was 110/70mm of Hg in the right arm supine position. He had bilateral palpable testes with testicular volume of < 2ml and stretched penile length of 1.9 cm (Tanner stage P_1). Systemic examination was un remarkable. On investigations he had a hemoglobin of 11.6 g/dl with normal total and differential counts. Liver and renal function tests, electrolytes, calcium profile, and Ig A tissue transglutaminase (tTg-IgA) were normal. Lipid profile showed increased total cholesterol of 225mg/dl and low density cholesterol 167mg/dl. Hormonal profile showed (Table 1).

Table 1 Serum hormonal profile

Hormone	Observed value	Normal Range
0800 h Cortisol	4.60	5-23 µg/dl
Total T3	65.11	70 – 204 ng/dl
Total T 4	4.43	5.0 - 12.5 µg/dl
TSH	6.86	0.45– 4.5 µIU/ml
LH	< 0.07	1.5 – 9.3 mIU/ml
FSH	0.97	1.4 – 18.1 mIU/ml
Total Testosterone	< 7.00	118.22 – 948.56 ng/dl
IGF-1	36.20	57- 426 ng/ml
Prolactin	12.34	5.18 – 26.53 ng/ml
ACTH	12.40	7.2 – 63.8 pg/mL
Clonidine stimulation test		
GH 0 min	0.13	0.18 – 10.04 ng/mL
GH 60 min	0.11	> 10 ng/mL
GH 90 min	0.10	> 10 ng/mL

Abbreviations: T 3 -triiodothyronine, T4 – thyroxine, TSH – thyrotropin, LH & FSH - gonadotropins, IGF-1- insulin-like growth factor , GH – growth hormone, ACTH – corticotropin.

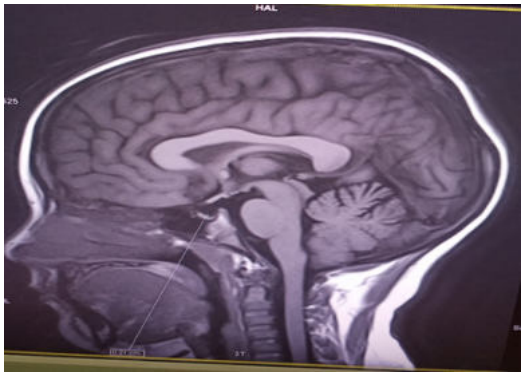

Figure 1 MRI Brain

Following priming with Ethinyl estradiol for three consecutive days and single-dose of testosterone respectively, tablet clonidine was administered and an estimate of GH (basal 0 min), and at 60 and 90 minutes subsequently was done using chemiluminescent immunometric assay. The response of GH was subnormal in all 3 samples. 2-D echocardiography was normal with a left ventricular ejection fraction of 60%. His bone age was 11 years . MR imaging revealed small sella, hypoplastic anterior pituitary , absent pituitary stalk with ectopic posterior pituitary bright spot.(Figure 1).

To mimic natural cortisol secretion, the patient was given T. prednisolone 5 mg in the morning and 2.5 mg in the early evening. Tablet L-thyroxine was started at a dose of 25mcg once daily. The aim of treatment was to achieve a normal serum T4 level. The initial testosterone enanthate regimen should consist of 200 mg every two weeks. To imitate the physiology of GH secretion, recombinant human GH in a dosage of 0.18 – 0.35mg/Kg/week (1mg = 3 IU) is administered by subcutaneous injection once a day, typically between 8 and 9 p.m. The ultimate goal is to find the GH dose that holds serum IGF-1 levels in the normal range.

DISCUSSION:

Our patient was born of full-term normal vaginal delivery thereby mitigating the possibility of intrauterine growth retardation. Stretched penile length of less than 2.5cm or micropenis is a hint to congenital growth hormone deficiency as seen in our patient[12]. There was no history suggestive of persistent physiological jaundice and neonatal hypoglycemia another clues indicative of growth hormone deficiency. Systemic disorders as a cause of short stature is less likely in our patient as weight is more compromised as compared to height, in comparison to endocrine disorders where height is more compromised than weight, as observed in our patient(height age 6 years, weight age 12.6 years). Any patient who has height SDS < - 3 requires urgent screening. Our patient had height of – 9.71 SDS, therefore needing urgent attention. The possibility of Cushing's syndrome was less likely as his weight was < 3rd percentile, and did not have any protein catabolism or moon facies. Primary hypothyroidism was unlikely in our patient as he did not have myxedematous features. Delayed bone age is a usual feature of all endocrine disorders and excludes diagnosis of intrinsic short stature. Our patient had typical features of growth hormone deficiency. Investigations were performed to rule out chronic systemic diseases, hypothyroidism, and pseudohypoparathyroidism before going ahead with GH dynamic research. Our patient had low IGF-1, there are plethora of provocative test to assess GH reserve. GH Research Society Consensus Guidelines recommends two GH provocation tests in suspected isolated GHD [13]. The provocative test should be done in fasting and euthyroidism should be achieved prior to test. Insulin induced hypoglycemia is considered as the " gold standard" test, however is associated with morbidity, such as severe hypoglycemia which can cause seizure and arrhythmias. In patients with structural pituitary defects or multiple pituitary hormone deficiencies a single dynamic test is sufficient. In a recently published paper clonidine stimulation test (CST) , with combined sampling at 60 and 90 minutes is best single sample test to rule out growth hormone deficiency [14]. It is economical , less cumbersome, with minimal compromise on specificity to perform in a government institution. The MRI tetrad of small sella, hypoplastic anterior pituitary, redundant pituitary stalk, and ectopic posterior pituitary bright spot in a patient with short stature is highly suggestive of multiple pituitary hormone deficiency. The final decision to treat adults with GHD necessitates careful clinical judgement and a detailed evaluation of the benefits and risks that are specific to each individual.

CONCLUSION:

Hypopituitarism is a rare chronic condition that causes significant morbidity, shortens life expectancy, and necessitates the use of complex regimens that must be monitored and modified at different stages of life. Early diagnosis and timely initiation of various hormone replacement therapies may be rewarding.

Ethics Approval: Not applicable

Consent Publication: Consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of interests: The authors declare that they have no competing interests.

Funding: None

Author Contributions: Author and co-authors have equally contributed to the manuscript.

Acknowledgements: None

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