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Empty Sella Syndrome, Case Report and Literature Review

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Abstract **Review Article**

Rarely has empty sella syndrome been documented in children, and radiographic imaging frequently identifies subarachnoid herniation through the sellar diaphragm and pituitary gland compression. In this correspondence, we report the discovery of an empty sella turcica on a brain magnetic resonance imaging (MRI) of a short 5-year-old kid. He identified hypopituitarism in form growth hormone deficiency and central adrenocortical insufficiency but normal thyroid function `during neuroendocrine examination of hypothalamic-pituitary function. Before beginning growth hormone therapy, this knowledge is essential to prevent the dangerous effects of an adrenal crisis. This matter was brought to light.

Keywords: Empty Sella, Panhypopitutrism.

INTRODUCTION

Rupture of the diaphragm sellae's subarachnoid space causes empty sella syndrome (ESS) (Fig 1). The degree to which the hypothalamus, pituitary, and optic nerve systems are impacted determines the severity of the signs and symptoms that can accompany this occurrence, which can be an accidental discovery or manifest in ESS in particular [1-3]. Rarely has it been documented in youngsters, and radiographic imaging is typically used to identify it. The phrase "empty sella turcica" is actually misleading because the pituitary gland is always physically and functionally present, even though it is frequently moved downward and influenced by the pressure of the cerebrospinal fluid. The sella turcica is not entirely empty. CSF) is pressed down. The majority of patients with an empty sella are asymptomatic and the abnormal finding may be incidental.

Normally, ESS happens in hefty patients. An Empty sella turcica is frequently connected with hypopituitarism.

They often lack growth hormone, but other pituitary hormones can also malfunction. Patients with empty sella disorder may likewise give hyperpituitarism, for example, precocious puberty [4-10].

In this correspondence, we portray a short 5-year-old kid whose brain magnetic resonance imaging (MRI) revealed an empty sella turcica. Panhypopituitarism in form of growth hormone deficiency and central adrenal insufficiency without diabetes insipidus was uncovered on neuroendocrine assessment of hypothalamic pituitary capability. The significance of a total neuroendocrine assessment of hypothalamic and pituitary hormones is underscored.

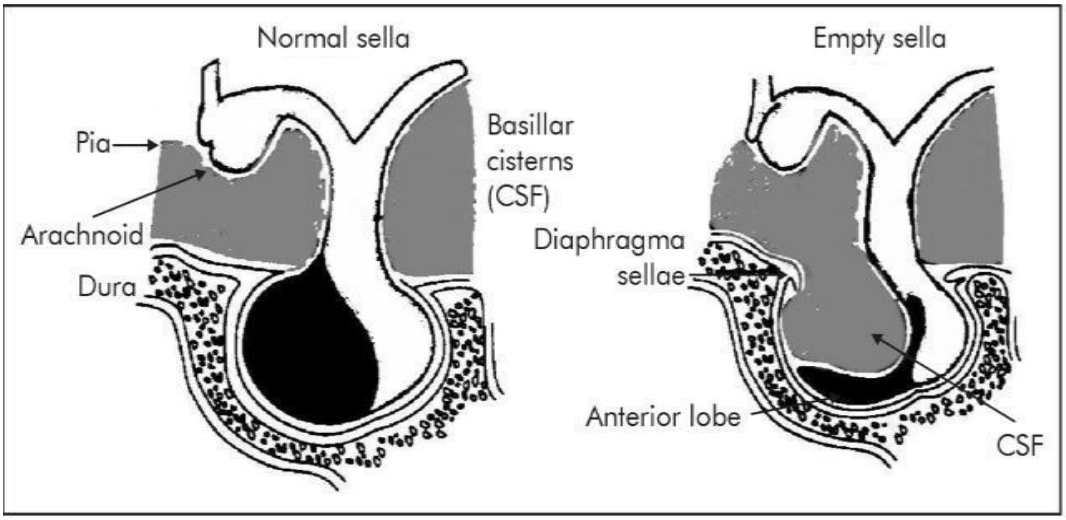

Figure 1: Schematic drawing showing (A) normal anatomic relationship of Sella and (B) arachnoid herniation through an incompetent diaphragm Sellae

Genetics

Combined pituitary hormone deficiency (CPHD) is caused by both genetic and nonheritable factors such as trauma, tumor, and infections. Approximately 50-60% of familial CPHD has a genetic basis and pathogenic variants in a number of different genes are found to cause genetically determined CPHD (De Rienzo *et al.*, 2015. PubMed ID: 26147833). *GLI2*, *HESX1*, *LHX3*, *LHX4*, *OTX2*, *POU1F1*, *PROP1*, *SOX2*, and *SOX3* are the most studied ones (Fang *et al.*, 2016. PubMed ID: 27828722). Of these, *PROP1* pathogenic variants are the most common known cause of this disorder, accounting for approximately 50% of familiar cases, although the incidence in sporadic cases is much lower (de Graaff 2014 PubMed ID: 20301521). These genes all encode transcription factors that are expressed in the developing head, hypothalamus, and/or pituitary, and have been involved in the proper development of the pituitary gland and the specialization of its cell types (Fang *et al.*, 2016. PubMed ID: 27828722). Pathogenic variants in these genes perturb ontogenesis of pituitary gonadotropes, somatotropes, lactotropes, and thyrotropes. These developmental defects result in deficiencies of LH, which is needed for normal growth; FSH and GH, which both play a role in sexual development and fertility; TSH, which helps with thyroid gland function; and ACTH, which influences energy production in the body and maintains normal blood sugar and blood pressure levels. CPHD can be inherited in X-linked (*SOX3*), autosomal dominant (*GLI2, LHX4, HESX1, POU1F1, OTX2, SOX2*), or autosomal recessive (*HESX1, POU1F1, PROP1, LHX3*).

Case Scenario

5 years old boy was evaluated due to his small height. He had poor teeth and grew slowly. He was born weighing 2.5 kg and had an uneventful pregnancy. There were no newborn issues at the time, particularly with regard to hypoglycemia or jaundice. The parents are both of average height. Neither a history of head trauma nor surgery existed.

Aside from a slight, generic headache and sporadic, minor nausea, the systemic examination and the patient's medical and surgical history were ordinary. Polyuria, polydipsia, and constipation are absent. Upon examination, the child's large ears were the only distinguishing characteristic; otherwise, he appeared well-proportioned. 100.5 cm was the height at −3 SD, 18.8 kg was the weight at the 25th percentile, and the blood pressure was normal.

Laboratory investigations revealed normal thyroid function tests (TSH = 2 MU/L, normal range 0.2 – 5.0 and Free T4 = 16 Pmol /L, Normal = 12-25).

LH and FSH were both normal for age and tanner stage of puberty. Serum Sodium was 138 mmol /L, with serum osmolality 287 Mosm /kg and urine osmolality 777 MOsm/kg. Low serum cortisol = 25 nmol and ACTH = 0.22

Base line and post stimulation with 1 microgram tetracosactide (ACTH). Table 1, indicating central adrenal insufficiency. Hydrocortisone was started at a dose of 10 mg /m2/day.

Growth hormone stimulation test were done using clonidine and glucagon and indicated GH deficiency (Peak response of 2.8 ng /ml) which necessitated growth hormone therapy. Bone age was delayed at four years and magnetic resonance imaging (MRI), Fig 2, was suggestive of partial Empty Sella. Patient continues to grow within normal on replacement therapy.

Table 1: Base line and post low ACTH stimulation

Time	Base line 8.00 am 0 time	30 min.	60 min
Cortisol	25 nmol/L (N-150-630)	281 nmol/L	371 nmol/L
ACTH	0.22 Pmol/L (N-1.6-13.9)		

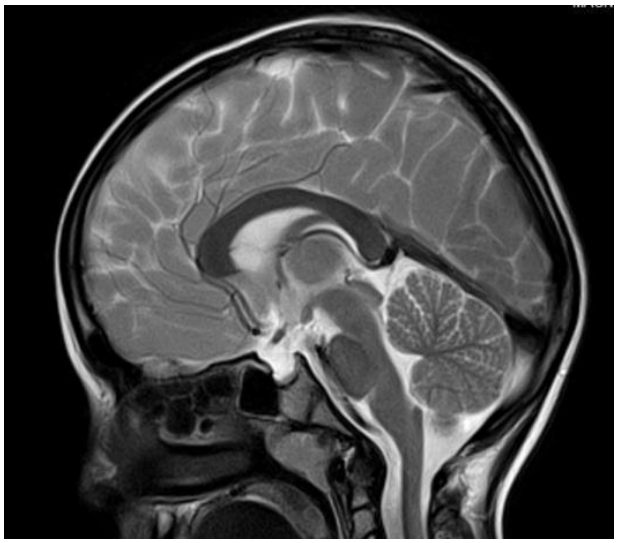

Figure 2: Saggital view of T1 weighted Magnetic Resonance Image (MRI) showing Partial Empty Sella turcica (arrow)

A herniation of the subarachnoid space via the diaphragm sella led to the Empty Sella Syndrome (ESS). Depending on the degree of involvement of the hypothalamus, hypophysis, and optic structures, the phenomena may be an accidental discovery or manifest as a constellation of signs and symptoms [3, 11].

Previous research have shown that females were more likely than males to have empty sella. Of the cases, 24% had obesity. Obesity contributes to obstructive sleep apnea, which increases CSF pressure and increases the risk of hypercapnia and ESS [12].

The high frequency of endocrine irregularities related with empty Sella requires the requirement for brief assessment and early swap of hormones for better personal satisfaction. Isolated GH deficiency is being the commonest [7-15].

Growth hormone testing should be performed only after excluding hypothyroidism and adrenal insufficiency since both could result in false positive test [16-22].

Adrenal crisis induced by Growth hormone treatment as GH can inhibit the expression and activity of 11β-HSD1 in adipose tissues and the liver resulting in reduced local regeneration of cortisol [23, 24].

Other known relationship with Empty sella conditiona are diabetes insipidus (DI) and central hypothyroidism [7, 10, 11, 13].

DI can be masked by coexisting ACTH deficiency (central adrenal insufficiency) as free water clearance at kidney is cortisol dependent and cortisol induce a decrease in AVP release as well as inhibition of action at the level of the kidney has both been reported and initiation of cortisol treatment can unmask preexisted DI [25, 26].

Thyroxine induced adrenal crises by increasing cortisol clearance and increase the metabolic rate and therefore, increase the cortisol requirement that cannot provided by failing adrenals [22].

ESS generally connected with pituitary hypofunction, yet seldom can be tracked down in patients with hyperfunction of the hypothalamic - pituitary - gonadal pivot as precocious puberty.

The pubertal anomaly additionally be incorporated among the endocrine issue possibly connected with the ESS [7, 9, 14].

In Conclusion

Although ESS is uncommon in children it should be included in the differential diagnosis of short children. Knowing adrenal status is crucial before starting growth hormone or thyroxine before hydrocortisone could precipitate uncovered adrenal insufficiency and hence adrenal crises.

Conflict of Interest: The authors have no conflict of interest to declare.

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