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Review Article

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EMPTY SELLA SYNDROME IN CHILDREN: THE IMPORTANCE OF EARLY DIAGNOSIS AND PROPER NEUROENDOCRINE ASSESSMENT

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ABSTRACT

Empty Sella Syndrome has been rarely reported in children and commonly detected on radiological imaging as a herniation of the subarachnoid space through the diaphragm sella with compression of the pituitary gland. In this communication, we present an eight years old boy with short stature who proved to have an Empty Sella on Magnetic resonance imaging (MRI) of the brain. He revealed hypopituitarism (Growth Hormone deficiency and central adrenal insufficiency without Diabetes insipidus on neuroendocrine assessment of the hypothalamic pituitary function. Such information is crucial before initiating Growth Hormone therapy, to avoid the major consequence of adrenal crises. This issue is highlighted.

KEYWORDS: Children, Empty Sella, Panhypopitutrism, Syndrome.

INTRODUCTION

The Empty Sella Syndrome (ESS), results from herniation of the subarachnoid space through the diaphragm Sellae (Fig 1). The phenomenon may be an incidental finding or present with constellation of signs and symptoms namely the ESS, whose severity depends on the extent to which the hypothalamus, hypophysis and optic structure are involved.[1-3]

It has been rarely reported in children and commonly detected on radiological imaging. However the term Empty Sella in fact is a misnorm as the Sella is not completely Empty but the pituitary is always present both anatomically and functionally, though often it is displaced downwards and compressed by cerebrospinal fluid (CSF)pressure .Most persons with Empty Sella are asymptomatic and the detection of this abnormality may be incidental .

Typically, ESS occurs in obese patients. Empty Sella is usually associated with pituitary hypofunction. They commonly have Growth hormone deficiency, although other pituitary hormones dysfunction may occur. Patients with Empty Sella syndrome also may manifest with pituitary hyperfunction as in precocious puberty.[4-10]

In this communication, we present an eight years old boy with short stature who proved to have an Empty Sella on Magnetic resonance imaging (MRI) of the brain. He revealed panhypopituitarism (Growth Hormone deficiency and central adrenal insufficiency without Diabetic insipidus on neuroendocrine assessment of the hypothalamic pituitary function. The importance of full neuroendocrine assessment of the hypthalemic and pituitary hormones are highlighted.

Case scenario

An 8 year old boy was evaluated for short stature. He was growing, but slowly with poor dentition. He was a product of full term uncomplicated pregnancy, with a birth weight of 3 Kg. No immediate neonatal problems especially hypoglycemia or jaundice. Both parents were normal and average in height. No history of surgery or head trauma.

Apart from mild non-specific headache and on and off mild nausea, systemic review and past medical surgical history were unremarkable. No constipation, polyuria, polydipsia. Physical examination showed a well proportionate child with no distinctive features other than big ear. The height was 114.5 Cm at – 3 SD and weight of 24.8 Kg, 25th centile, with normal blood pressure.

No thyromegally and genitalia was normal prepubertal. Vision and hearing were normal. The rest of physical examination was normal.

Laboratory investigations revealed normal thyroid function tests (TSH = 3 MU/L, normal range 0.2 – 5.0 and Free T4 = 18 Pmol /L, Normal = 12-25).

LH and FSH were both normal for age and tanner stage of puberty .Serum Sodium was 140 mmol /L , with serum osmolality 277 Mosm /kg and urine osmolality 677 MOsm/kg.

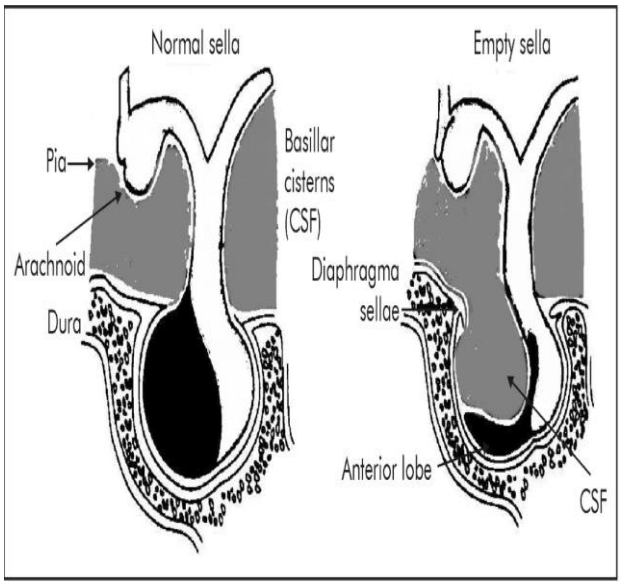
Low serum cortisol and ACTH.

Base line and post stimulation with 1 microgram tetracosactide (ACTH).

Tabel 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.



(A) **(B)**

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

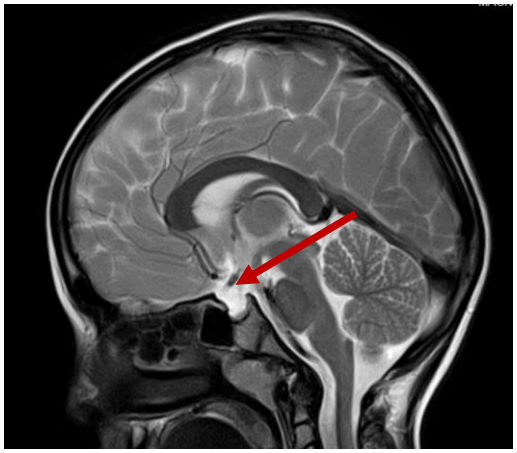


Figure 2 Saggital view of T1 weighted Magnetic Resonance Image (MRI) showing Partial Empty Sella turcica(arrow).

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)	————	————

DISCUSSION

The Empty Sella Syndrome (ESS), resulted from herniation of the subarachnoid space through the diaphragm sella. The phenomenon may be an incidental finding or present with constellation of signs and symptoms depend on the extent to which the hypothalamus, hypophysis and optic structures are involved.[3,11]

Empty Sella were more prevalent in females than males as seen in earlier studies .Obesity was noted in 24% of cases. Obesity causes obstructive sleep apnea predisposing to hypercapnia and increased CSF pressure, leading to ESS.[12]

The high incidence of endocrine abnormalities associated with Empty Sella necessitates the need for prompt evaluation and early replacement of hormones for better quality of life. 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 association with Empty Sella syndrome are diabetes insipidus (DI) and primary 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 usually associated with pituitary hypofunction, but rarely can be found in patients with hyperfunction of the hypothalamic -pituitary – gonadal axis as precocious puberty. The pubertal abnormality also be included among the endocrine disorder potentially associated 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 before hydrocortisone could precipitate uncovered adrenal insufficiency and hence adrenal crises.

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