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Review Article

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ISOLATED GROWTH HORMONE DEFICIENCY SECONDARY TO EMPTY SELLA SYNDROME

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ABSTRACT

Empty Sella Syndrome describe as a herniation of the subarachnoid space through the diaphragm Sella and it might compresses the pituitary gland and affect its function leading to, either isolated or combined hormones deficiencies. Screening of all pituitary hormones is important, since early diagnosis and proper replacement therapy can save life and improve quality of life. We report here a 11 years boy with short stature with isolated Growth hormone deficiency and Magnetic Resonance Imaging (MRI) of the brain show Empty Sella Syndrome. Evaluation of adrenal function show normal response and that is critical prior to start Growth hormone treatment due to the fact that GH might precipitate Adrenal crises in patient with combined subclinical adrenal failure. This point is highlighted in our paper.

KEYWORDS: Children, Empty Sella, shrinked Pituitary Panhypopitutrism.

INTRODUCTION

The Empty Sella Syndrome (ESS), results from herniation of the subarachnoid space through the diaphragm Sellae (Fig 1). It might be an incidental finding with no pituitary dysfunction or present with Hypopituitarism, whose severity depends on the extent to which the hypothalamus, hypophysis and optic structure are involved.[1,2,5-9]

It has been rarely reported in children and commonly detected on radiological imaging as part of short stature workup. 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.[3]

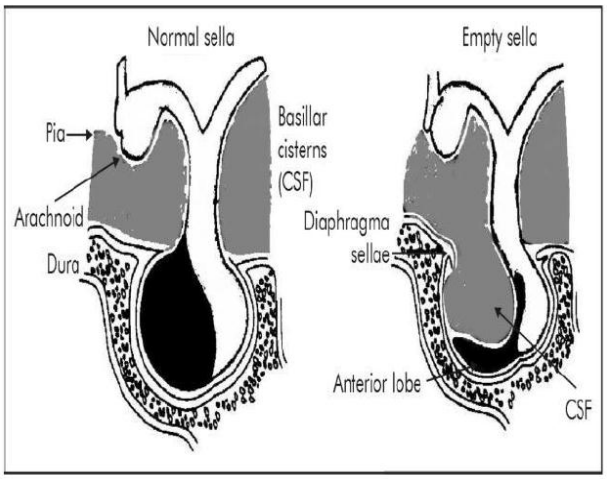

Figure 1: Schematic drawing showing (A) normal anatomic relationship of Sella and (B) arachnoid herniation through an incompetent diaphragm Sellae.

ESS might be idiopathic (unrecognized pituitary Infarction) Or secondary To increase intracranial pressure due to CNC insult caused by: head trauma, infection, congenital malformation (Hydrocephalus), CNS surgery, radiation or associated with syndromes e,g. DIDMOD, Laurance Moon Biedle.[4-8] and rarely it can be secondary to obesity and high blood pressure.[9]

Case scenario

11 years old Saudi boy came to OPD with short stature notice since early childhood.

His birth Wight was 2.8 Kg, with uncomplicated neonatal history, no history of neonatal hypoglycemia or jaundice, with adequate nutrition. No neurological complaint, no history of head trauma, No history of chronic constipation, polyuria, polydipsia. He is unknown to have any chronic medical diseases, was never on any chronic medication, his parents are average in Hight (MPH = 175cm), with no family history of short stature or delayed puberty or any significant endocrine disorders.

Physical examination showed a well proportionate child with no distinctive features.
The height was – 3 SD and weight at 25th centile, with normal blood pressure.
No thyromegally and genitalia was normal prepubertal boy. The rest of physical examination was unremarkable.

Laboratory investigations revealed normal thyroid function tests, prepubertal LH and FSH level. Negative celiac screening.

Serum electrolyte was normal. serum osmolality 277 Mosm /kg and urine osmolality 677 MOsm/kg.

Basal cortisol was 110 nmol /L and ACTH = 5 Pmol/l.

ACTH stimulation test using 1 microgram tetracosactide (ACTH), show adequate cortisol response of 550 nmol/L.

After Normal adrenal and Thyroid function is ensured then Growth hormone stimulation test was done using clonidine and glucagon and show sever GH deficiency (Peak response of 4 ng /ml). Bone age was delayed by 5 years and magnetic resonance imaging (MRI), Fig 2, show Empty Sella.

Diagnosis: Isolated GH deficiency secondary to ESS.

Treatment: GH injection was started dose of 0.035 mg /kg /day, daily, and his Hight velocity was increased from 2 cm /year to 9 cm /year.

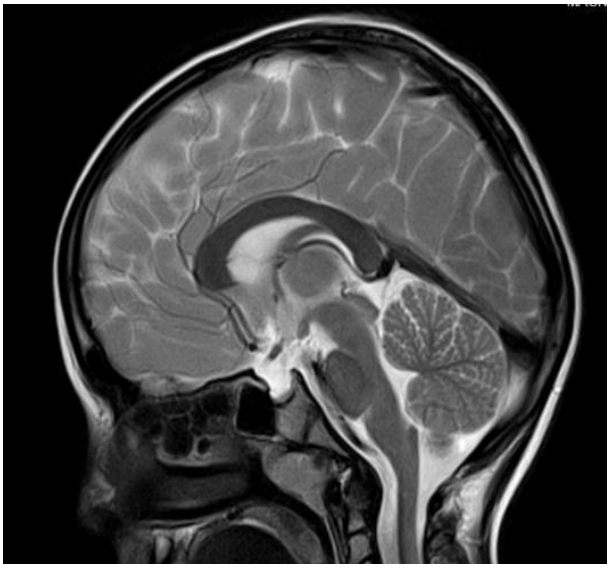

Fig 2: MRI showing Shrinked Pituitary Gland.

DISCUSSION

The Empty Sella Syndrome (ESS), although is rare in kids, but it should be kept in mind upon evaluating patient with short stature.

ESS can be associated with no Pituitary hormones dysfunction, but dysfunction might develop over time. Commonest hormone being affected is the GH but other hormones might be affected also including, TSH, ACTH, FSH, LH and ADH.[10,11]

Interestingly few case report show that ESS association with hyperfunction leading to Precocious puberty with unknown mechanism.[12]

The importance of diagnosing ESS is that carful Hormonal replacement is critical especially replacement of thyroxine and GH since both might uncover preexisting subclinical adrenal dysfunction and might precipitate adrenal crises. Mechanism of thyroxine inducing adrenal crises is that thyroxine lead to increasing cortisol clearance and increase the metabolic rate and therefore, increase the cortisol requirement that can not provided by failing adrenals.[13]

While GH theoretically might cause adrenal crises because GH can inhibit the expression and activity of 11β-HSD1 in adipose tissues and the liver resulting in reduced local regeneration of cortisol from cortisone.[14]

Other important fact that should be kept in mind while treating patient with ESS is that in patient with DI, its polyurea symptoms can be masked by coexisting ACTH deficiency (central adrenal insufficiency) as free water clearance at kidney is cortisol dependent and cortisol physiologically induce a decrease in AVP release from Hypothalmus as well as inhibition of its action at the level of the kidney has both been reported and initiation of cortisol treatment can unmask preexisted DI.[15,16]

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 adrenal crises in patient with coexisting subclinical adrenal insufficiency.

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

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