

**CASE REPORT****PRIMARY EMPTY SELLA SYNDROME PRESENTING WITH SEVERE HYPONATREMIA AND MINIMAL SALT WASTING****Ishma Aijazi, Fadil Mustafa Abdullah Al Shama, Sara Hussein Adam Mukhtar**

Department of Internal Medicine, Dubai Hospital, Dubai Health Authority-U.A.E

A 41 year old Jordanian gentleman known case of osteogenesis imperfecta presented with vomiting, decreased oral intake followed by confusion. At presentation he was found to have signs of hypogonadism with severe hyponatremia. The hyponatremia responded to intravenous steroid replacement. This alerted the physicians to search for other pituitary hormone deficiencies. Our patient had pneumonia with respiratory failure. He was intubated and mechanically ventilated. Subsequent tracheostomy was done because of failure of weaning. His GCS remained very low despite treatment of infection and correction of electrolyte imbalance. He had multiple hormone deficiencies. He was found to be severely hypothyroid, replacement of thyroxine caused gradual improvement of GCS over a period of six to eight weeks. In the absence of history pituitary adenoma, pituitary, irradiation or surgery, a diagnosis of primary empty Sella syndrome with anterior pituitary dysfunction was made.

**Keywords:** Empty sella; Hyponatremia; Central hypothyroidism

J Ayub Med Coll Abbottabad 2016;28(3):605-8

**INTRODUCTION**

Empty Sella syndrome (ESS) is complete or partial depending whether the Sella turcica is completely or partially filled with cerebrospinal fluid, this results in displacement of the pituitary gland. It has distinct anatomical and radiological characteristics.<sup>1</sup> Endocrine dysfunction has been reported in 25–30% of cases.<sup>2</sup>

In partial empty Sella syndrome pituitary gland thickness is from 3–7 mm and less than 50% of the sella is filled with cerebrospinal fluid. While in total empty sella syndrome pituitary gland thickness is less than 2 mm and more than 50% of the Sella is filled with spinal fluid. Patients of empty sella syndrome have deficiencies of at least one pituitary hormone. However 50% of patients present with multiple hormonal deficiencies and hyperprolactinemia is the most common endocrine abnormality observed.<sup>3</sup>

Primary empty Sella occurs when there is combination of increase cerebro spinal fluid pressure together with a defect in diaphragma sellae. It is seen in pseudo tumour cerebri, obese, multiparous females.<sup>3,4</sup> While surgery, radiation to a pituitary tumour, or any condition that damages a pituitary gland such as an history of pituitary apoplexy, neurosarcoidosis, or hypo physites gives rise to secondary empty sella syndrome.

Our patient was believed to have partial primary empty Sella syndrome since he lived to an age of 41 without hormonal supplementation. He had multiple endocrine abnormalities namely long standing severe hypogonadism. The secondary hypothyroidism and secondary Addison disease were only evident at the time of acute stress.

**CASE REPORT**

Forty-one year old Jordanian gentleman known case of osteogenesis imperfecta with multiple corrective surgeries was admitted with vomiting, poor oral intake and confusion. There was no history of fever, loose motions, chest or urinary symptoms. He was not married till this age. Sexual history could not be taken in detail from family. He had normal intellects and possessed a degree in engineering and designing. On examination (initially in the emergency), he was drowsy but arousable to verbal commands. Pulse 100/min, blood pressure 100/60 mmg HG, afebrile, mildly dehydrated, saturation 93% on room air.

Physical examination revealed a short statured gentleman with kyphoscoliosis, chest bilateral crept and wheeze, cardiovascular and abdominal examination were unremarkable. Fundi were normal and visual fields could not be assessed. Detailed endocrine examination revealed

Short stature, facies of a female with no male pattern of hair growth. No signs of virilisation with female phenotype body pattern with more fat than muscles. Bi lateral gynecomastia. There was no facial or axillary hair and very scant pubic hair. Genital examination revealed a small rudimentary penis and a very small phallus with severe phimosis, micro genitalia with meatal stenosis. Sense of smell could not be assessed. In conclusion all features favoured severe hypogonadism

Arterial blood gases: acidosis with type 2 respiratory failure. WBC 6300 cubic mm (3.6–11), HB 13.7g/dl (11-15), platelets 319,000 cubic mm (150,000–400,000), C-reactive protein >120 mg/l (<10), ESR 90 mm/hour, lactic acid 0.5 mmol/l, procalcitonin 0.17. ng/ml (<0.05)

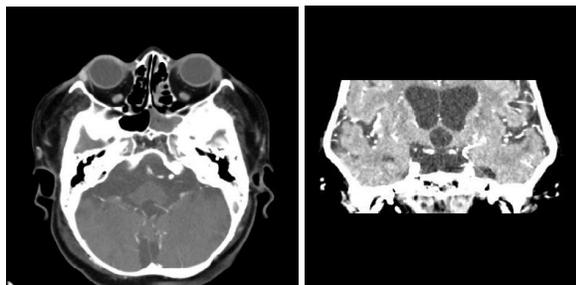
Sodium 101mmol/l (136–145), potassium 3.4 mmol/l (3.3–4.8 ), bicarbonate 22.9 mmol/l (20–28), urea 15 mg/dl, (12–40). Creatinine 0.3 mg/dl. (0.7–1.2), Serum osmolality 217 mosm/kg (275–295), Urine osmolality 250 mosm/kg (50–1200), Urine sodium <10. Calcium 9 mg/dl, phosphate 3.8mg/dl, vitamin B12 and folate levels were normal. Urine culture no growth, Blood culture: no growth. Chest x ray (at admission) revealed thoracic wall deformity with bilateral lung infiltrates.

**Table-1: Detailed endocrine work up**

Endocrine test	Normal value
FSH 0.4 Miu/ml	1.5–2.4 Miu/mL
LH <0.5 MIU/ml	1.7–8.6 Miu/ml
Prolactin 315 Miu/l	86–324Miu/l
Growth hormone <0.1	0–3
Insulin like growth factor (IGF -1) <25	109–284
Free androgen index (FAI) 0.3	40–150
Sex hormone binding Globulin (SHBG) 34 nmol/l	9–55 nmol/l
Testosterone 0.1 nmol/l	9.9–27.8 nmol/l
Cortisol dynamic 127nmol/l	
Cortisol AM 127 nmol/l	138–690 nmol/l
ACTH-AM 7.5 pg/ml	<46
FT4 12.1 pmol/l	11.5–22.7 pmol/l
FT3 1 pmol/l	2.8–7.1 pmol/l
TSH 0.74 Uiu/ml	
HBAIC 5.0% Random blood sugar 100mg/dl	4.8–6



**Figure-1: CT features are of generalized cortical atrophy with pan sinusitis**



**Figure-2: CT (Sella) with contrast**

Reported as No obvious mass lesion in Sella or differential enhancing lesion in the pituitary gland Prominent CSF space density is noted in Sella

suggestive of partially empty Sella .Mucosal thickening is noted in left frontal, ethmoid, and bilateral sphenoid sinus, suggestive of mucosal sinus disease. Incidental note is made of diffuse brain atrophic changes. There is decrease density of the bones of the skull with thinning of the bones (osteogenesis imperfecta)

He was initially assessed by intensivist, given intravenous fluids, antibiotics and intravenous hydrocortisone. Serum sodium improved in next 24 hours but the patient became drowsier and was shifted to ICU, intubated and mechanically ventilated. During subsequent follow up there was difficulty in weaning of the ventilator hence tracheostomy was done. During his ICU stay, despite being weaned off sedation GCS remained 3/15. After prolonged ICU stay he was shifted to medical floor.

Severe hyponatremia together with clinical signs of hypogonadism led us to investigate for all other pituitary hormones. In view of his hormone profile he was initially started on intravenous steroids, followed by meticulous T3 and t4 supplementations. This was followed by low dose Sub cutaneous growth hormone and intramuscular testosterone supplementations for building muscle mass and general wellbeing. After a period of 6 to 8 weeks the patient's GCS started improving. From a GCS of 3 it improved to 11 and attempts were made to wean him off the ventilator. This was an unbelievable observation! However we were unable to wean him off the ventilator due to recurrent episodes of hospital acquired pneumonia, and restrictive chest wall deformity due severe kyphoscoliosis secondary to osteogenesis imperfecta. However unfortunately patient developed septic shock because of recurrent episodes of ventilator acquired pneumonia and subsequently passed away.

**DISCUSSION**

Empty Sella syndrome is an anatomical condition which was first described by Busch in 1951.<sup>5</sup> There is remodelling of Sella turcica and flattening of the pituitary gland resulting from subarachnoid space extension into an intra seller position. Primary empty Sella syndrome is usually found in obese, multiparous women. These patients can have an increase incidence of hypertension, CSF rhinorrhea, pseudo motor cereberi.<sup>5</sup> Our patient had primary empty Sella syndrome with associated anterior pituitary hypofunction. Primary empty Sella syndrome is commonly associated with primary hypothyroidism<sup>6</sup> however our patient presented with severe central hypothyroidism. The prevalence of central hypothyroidism is estimated 1 in 80,000 individuals.<sup>7</sup>

Clinical features (signs of hypo gonadism and brain atrophy on CT scan) suggest that the pituitary hypo function associated with the empty Sella syndrome in our patient was partial. He managed to live till 41 years of age without hormone supplements. He went into Addisonian crises in time of extreme stress and presented with severe hyponatremia, hypotension and severe hypothyroidism. In a majority of patients pituitary functions may remain normal despite extensive arachnoid herniation and severe compression and flattening of pituitary gland. However 25–35% of patients with primary empty sella syndrome are reported to have endocrine abnormalities.<sup>2</sup> Growth hormone deficiency is present in 30–60% of cases. Isolated pituitary deficiencies are infrequent (hypogonadotropic hypogonadism in 6%, central hypoadrenalism in 1% and central hypothyroidism is also seen in 1% of patients). Hyperprolactinemia may occur due to distortion of pituitary stalk in 10–12% of patients.<sup>8</sup> Hyperprolactinemia and diabetes insipidus only occur in primary empty Sella syndrome if the pituitary stalk is compressed by extensive arachnoid herniation. In our patient, there was no compression of pituitary stalk as evidenced by normal prolactin levels and low serum and urine sodium and low serum osmolality.

Central hypothyroidism (like our patient) is very rare to find in primary empty Sella syndrome. The prevalence is 1 in 80,000 to 1 in 120,000 individuals.<sup>9</sup> It occurs in equally in both sexes and is more common in secondary empty sella syndrome due to pituitary macro adenomas, pituitary surgeries or irradiations.<sup>9</sup>

Our patient presented with severe hyponatremia. Severe hyponatremia in the setting of features of severe hypogonadism should warrant immediate screening for hypopituitarism and secondary adrenal insufficiency. Secondary adrenal insufficiency unlike primary adrenal insufficiency is characterized by the absence of hyperkalemia, hyperreninemia and normal or low ACTH levels. Yammato *et al*<sup>10</sup> observed that these patients with hyponatremic hypopituitarism were “mildly dehydrated” with regards to blood pressure, body weight, blood urea nitrogen, total proteins and haematocrit. They are very similar to patients with dilutional hypo natremia who have hypo cortisolism. The hyponatremia in both these group of patients responds very poorly to intravenous fluids and is corrected only by intravenous hydrocortisone administration.

However in our patient severe hyponatremia was multi factorial. It was due to long standing severe hypothyroidism and secondary adrenal insufficiency. It is seen that usually primary, not secondary hypothyroidism is associated with SIADH –like

syndrome.<sup>11</sup> In our case the response of hyponatremia to intravenous steroids suggest that the role of thyroid hormone deficiency in the genesis of hyponatremia was probably very small. This is also supported by the fact that steroid replacement before the replacement of thyroxine resulted in the correction of serum sodium.

The value of low urine sodium (urine sodium <10) can be very misleading. Since usually severe endogenous steroid insufficiency should present with hyponatremia and severe urine salt wasting not dehydration like picture. The main cause of very low urine sodium in this case is due to the severe deficiency of endogenous cortisol resulting in failure of endogenous cortisol to exert a tonic inhibitory effect on the ADH secretion.<sup>12</sup> Hence there is no urinary salt wasting and our patient is presenting with SIADH like biochemical picture, i.e., low plasma and urine osmolality.

In our patient dynamic pituitary function tests were not done because firstly patient was non-affording, secondarily initially with a GCS of 3/15 for more than 2 weeks we were not expecting a very good clinical outcome. Thirdly putting in picture his clinical scenario and initial hormonal work up, pan hypopituitarism was quite evident and did not need any further elaborate laboratory testing. MRI brain could not be done since patient had multiple corrective surgeries and metal prosthesis implants for his osteo-genesis imperfecta.

## CONCLUSION

Severe hyponatremia should alert physicians about Addisonian crises. They should not be misled by the low urine sodium and treat this as simple dehydration.

In conclusion, hypopituitarism should be considered in all patients with SIADH like clinical picture without any apparent cause (eg, bronchogenic carcinoma) and even in patients who have mild dehydration with inappropriately low serum sodium.<sup>10</sup> A careful history and physical examination with regards to symptoms of hypopituitarism should be conducted. This may have to be delayed in patients with mental disturbances associated with severe hyponatremia, just like our patient.

Secondarily if pituitary tropic hormones are inappropriately low in the presence of low target hormones we should screen for secondary endocrine insufficiencies. More over pituitary deficiencies can be easily over looked if only tropic hormones are used for evaluation of hormone deficiencies.

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### Address for Correspondence:

**Dr Ishma Aijazi**, Department of Internal Medicine, Dubai Hospital, Dubai Health Authority-U.A.E

**Email:** engrjaffar@gmail.com