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Case Report

Primary empty sella syndrome presenting as adrenal insufficiency and without raised intracranial tension

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ABSTRACT

Empty sella syndrome (ESS) based on pathophysiology can be either primary empty sella syndrome (PES) or secondary empty sella syndrome (SES). Patients of PES have no known pituitary pathology and have varying degrees of pituitary gland flattening. We present a 65-year-old female who came with complaints of generalised swelling over the body, generalised weakness, altered sensorium and low-grade fever. Patient had history of ischaemic heart disease 3 years back without any other known co-morbidities. Patient presented in hypoglycaemia and hypotension with facial puffiness and oedema feet with basal crepitations indicating fluid overload state. Patient was stabilised and evaluated. Patient was found to have hyponatremia and urinary tract Infection and associated acute kidney injury. Patient's morning cortisol and adrenocorticotropic hormone (ACTH) levels were also low with associated low insulin-like growth factor 1 (IGF-1) and normal thyroid stimulating hormone (TSH) levels but low T3 and low T4 levels. Patient's magnetic resonance imaging (MRI) brain was done which was suggestive of PES. The cause of empty sella remained unclear but the adrenal insufficiency was treated with hydrocortisone and the patient became asymptomatic and was discharged subsequently.

Keywords: Adrenal insufficiency, Cortisol, ACTH, IGF-1, TSH, Primary empty sella syndrome

INTRODUCTION

Empty sella is a pituitary disorder characterized by the herniation of the subarachnoid space within the sella turcica.[1] Empty sella syndrome (ESS) based on pathophysiology can be either primary empty sella syndrome (PES) or secondary empty sella syndrome (SES).[2]

PES is characterized by variable degrees of flattening of the pituitary gland in patients without any previous pituitary pathologies. PES pathogenetic mechanisms are not well known but seem to be due to a sellar diaphragm incompetence, intracranial hypertension and change of pituitary volume.[4] The resolution of empty sella on imaging after treatment of intracranial hypertension suggests that intracranial hypertension can cause empty sella.[5] The last proposed mechanism causing empty sella involves an initial enlargement of the pituitary gland followed by a later decrease in gland size which creates an empty space in which cerebrospinal fluid (CSF) can accumulate.[2] Majority of patients are asymptomatic, those symptomatic are usually middle aged women who are overweight and hypertensive.[3]

Secondary empty sella is more common and can be attributed to various pathological processes of the sellar region. Causes of SES are pituitary tumour shrinkage secondary to medical treatment, radiotherapy, surgery and apoplexy of a pituitary adenoma, postpartum pituitary necrosis, pituitary infection, hypophysitis, and trauma may lead to pituitary atrophy.[6]

PES patients show an increased cardiovascular mortality risk. Risk factors for cardiovascular diseases identified

among the patients deranged lipid and glucose profiles, and higher Framingham score and secondary hypothyroidism.[8]

Table 1: Associated risk factors for primary and secondary empty sella.[6]

Primary empty sella	Secondary empty sella
Female sex	Medical therapy
Multiple pregnancies	Pituitary surgery
Obesity and sleep apnea	Irradiation
Arterial hypertension	Pituitary apoplexy
Benign intracranial hypertension	Sheehan's syndrome
	Traumatic brain injury
	Congenital hypopituitarism

We report a case of primary empty sella syndrome leading to low IGF-1, low morning cortisol levels but normal TSH level, low total T3 and low total T4.

CASE REPORT

A 65-year-old female was referred from peripheral hospital with documentation of hypoglycaemia and presented with complaints of generalised swelling over the body, generalised weakness and altered sensorium. Patient had history of ischemic heart disease 3 years back, no other known co-morbidities, she had history of menopause 20 years back &is a mother of four children. No significant family history is present.

On presentation the patient was 152 cm and 64 kg (BMI 28-overweight according to WHO classification). Her vitals were unstable with blood pressure of 80/60 mmHg and random blood sugar was 58 mg/dl, pulse rate was 82/minute, respiratory rate was 24/minute. Patients GCS on presentation was 10/15 (E3 V3 M4). Patient had facial puffiness with minimal oedema feet. Patient's skin was dry, fair and white, with ichthyotic patches with brownish polygonal scales over bilateral upper and lower limbs (Figure 1a and b).

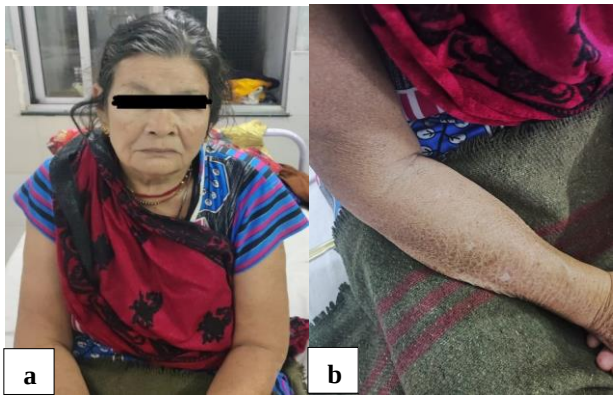

Figure 1: (a) and (b) Demonstrating the dermatological features.

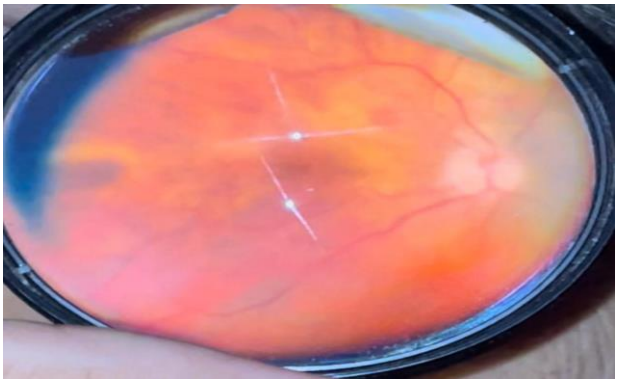

Figure 2: Fundus of the patient.

Patient was resuscitated with 25% dextrose and intravenous fluids. Emergency laboratory tests were done which revealed haemoglobin (Hb) 8.1 g/dl, white blood cell (WBC) count 8.6×10^9 g/l (granulocytes were 80% lymphocytes were 12.8%), platelet count was 219×10^9 g/l, urea was 95 mg%, creatinine was 3.3 mg%, sodium was 130 mmol/l, potassium was 4.6 mmol/l. Patient's fundus showed no changes of papilledema (Figure 3). Because of the findings of hypotension hypoglycaemia, acute kidney injury (AKI), hyponatremia we had differential diagnosis of sepsis and adrenal insufficiency. Procalcitonin was elevated value being 4.22 ng/ml, urine routine microscopy revealed 30-40 pus cells/hpf, 6-8 RBC, protein + (indicating urinary tract infection with sepsis with AKI). Patient's serum 8 am cortisol level was done which was 2.33 mcg/dl (indicating adrenal insufficiency). Morning plasma ACTH level was done 6.13 pg/ml (10-60 pg/ml), Insulin like growth factor-1 was 15 ng/ml (75-212), serum total T3-0.21 ng/ml, total T4-0.50 ng/ml, TSH-3.13 micro-IU/ml. Patients triglycerides were 195, total cholesterol 221, high density lipoprotein (HDL) cholesterol 61, low density lipoprotein (LDL) cholesterol 121, computed tomography (CT) head plain revealed lacunar infarcts in right external capsule and posterior limb of right internal capsule. Ultrasound abdomen revealed minimal inter bowel free fluid (no adrenal abnormalities). Because of the presence of alabaster like paleness (due to lack of ACTH secretion) and features of adrenal insufficiency, we suspected secondary adrenal insufficiency.

MRI brain (contrast study) showed empty sella with posterior pituitary bright spot suggesting primary empty sella syndrome (Figure 3).

2D Echo was suggestive of global left ventricular hypokinesia (anterior > inferior) with ejection fraction of 25%.

We suspected that the Insufficient pituitary hormone secretion led to adrenal cortex function failure. The urinary tract infection (UTI) and sepsis were a stressor which caused further ACTH hyposecretion which led to adrenal insufficiency and her symptoms. She experienced hyponatremia, hypoglycaemia, hypotension due to

temporary adrenal insufficiency when she experienced stress.

Table 2: Laboratory tests and results of the patient on presentation.

Laboratory test	Values (on presentation)
Haemoglobin (g/dl)	8.1
WBC count (g/dl)	8.6×10^9
Platelet count (g/l)	219×10^9
Urea (mg%)	95
Creatinine (mg%)	3.3
Sodium (mmol/l)	130
Potassium (mmol/l)	4.6
Urine	
Pus cells (pus cells/hpf)	30-40
RBC (RBC/hpf)	6-8
Protein	+
Serum 8 am cortisol levels (mcg/dl)	2.33
Morning plasma ACTH level (pg/ml)	6.13
Insulin like growth factor-1 (ng/ml)	15
TSH (microIU/ml)	3.13
TOTAL T3 (ng/ml)	0.21
TOTAL T4 (ng/ml)	0.50
Triglycerides (mg%)	195
Total cholesterol (mg%)	221
HDL cholesterol (mg%)	61
LDL cholesterol (mg%)	121

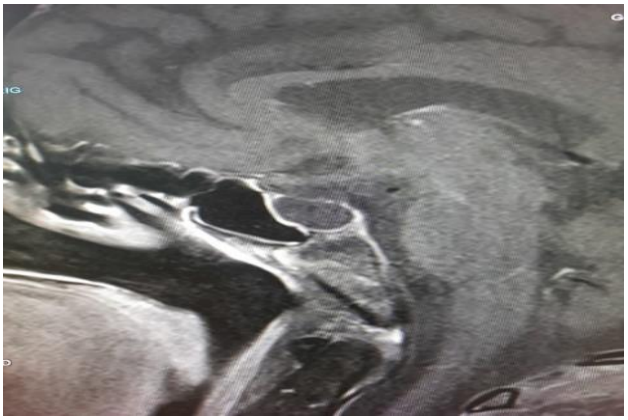

Figure 3: MRI showing empty sella.

We diagnosed the patient as having adrenal insufficiency due to inappropriate ACTH secretion caused by PES associated with decreased growth hormone and thyroid hormones. We started patient on injection hydrocortisone 100 mg QID on day 1, 50 mg QID on day 2, 50 mg TDS on day 3. Injectable antibiotics were given for UTI. Patient was then shifted to tablet hydrocortisone 10 mg (8 am), 5 mg (1 pm), 5 mg (4 pm). Eventually the patient became asymptomatic and was discharged on tab prednisolone 5 mg (8 am) and 2.5 mg (4 pm) and tab thyroxine 75 mcg before breakfast.

DISCUSSION

Empty sella is a radiological or pathological finding of an apparently empty sella turcica without any pituitary tissue. The prevalence of PES, i.e., empty sella without any discernible cause, is not precisely known; estimates range from 2% to 20%.[8] Due to the advancements in nueroimaging empty sella has become a commoner incidental finding.[8] Usually, hypopituitarism often goes unrecognised in patient with PES.

The presentation of PES ranges from global hypopituitarism to various degrees of isolated GH deficiency.[9] However, there are currently no specific guidelines, and it is unclear whether an asymptomatic adult patient in which ES was incidentally discovered should undergo hormonal testing.[8] It is commoner in females, the ratio being 4 or 5:1 over males, and it is more common in obese patients.[3] ESS is commoner in the fourth to the sixth decade of life. However, the pituitary hormonal dysfunction appears to occur at higher rates in men with empty sella.[3] In idiopathic ESS patients present with headaches and sinusitis, clear watery discharge from nose (CSF rhinorrhoea) when there is a sudden increase in CSF pressure as in coughing or sneezing. No visual abnormalities are usually present and symptoms of endocrine disorder are rare. Endocrine function is normal in about three quarters of the patients.[10] Hyperprolactinemia and GH deficiency appear to be the two most common findings in ES.[11,12] Hyperprolactinemia is present in 10-17% of cases, while GH deficiency is present in 4-60% of cases, but its clinical significance in adults is unclear.[3,12] Gonadotropin deficiency is found in 2-32% of cases, while TSH, ACTH, and antidiuretic hormone (ADH) deficiencies are less frequent, with incidences of approximately 1% each.[13] Workup for PES include: fasting cortisol, free thyroxine (FT 4), estradiol or testosterone, IGF-1, and prolactin.[8] Early-morning fasting cortisol level can be used as a screening test for ACTH deficiency, and overtly low level of cortisol (less than 3.0 µg/dl) are considered consistent with adrenal insufficiency morning cortisol levels greater than 11.0 (or, some authors suggest, 14.0) µg/dl suggest that adrenal insufficiency is highly unlikely, while morning cortisol levels of 3.1 to 11.0 (14.0) µg/dl are indeterminant and needs ACTH stimulation test. If morning cortisol levels are low, an ACTH level should be obtained and to differentiate primary from secondary/central adrenal insufficiency.[2] Owing to the advances in radiology, MRI pituitary imaging is recommended in patients who have pituitary hormone excess, hypopituitarism, or mass effect in the sella.[11,14] PES patients show increased cardiovascular risk, regardless of BMI the contributing factor being deranged lipid and glucose profile and secondary hypothyroidism (our patient had history of ischaemic heart disease).[7] Patients with empty sella are usually asymptomatic and require no treatment; however, in some cases where

isolated ACTH deficiency develops, corticosteroid treatment should be given in order to avoid fatal consequences.[15]

The presence of ESS has no effect on life expectancy, as it is generally a benign condition.[3] However, when a specific hormone deficiency or excess is present, the prognosis varies and is dependent on the specific hormone abnormality and its treatment.[2]

CONCLUSION

Adrenal insufficiency should be a differential in a patient presenting with hypotension, hypoglycaemia, hyponatremia. Further evaluation regarding whether it's a primary adrenal insufficiency or secondary adrenal insufficiency should be done. One of the cause of secondary adrenal insufficiency is ESS which can be either PES or SES (cause is identifiable).

PES is usually associated with raised ICT and is usually asymptomatic, but in our case the patient had no features of raised ICT and was symptomatic making it a rare case. The patient became asymptomatic after adequate hormonal supplementation was done. The presence of ESS doesn't affect life expectancy as it is a benign condition.

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