DOI: http://doi.org/10.4038/jrcs.v27i1.124
Journal of the Ruhuna Clinical Society 2022 27 (1): 42-44

Partial Empty Sella Syndrome Presenting with Panhypopituitarism and Masked Central Diabetes Insipidus

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Abstract

Empty sella syndrome (ESS) is an uncommon cause of hypopituitarism. It is usually detected incidentally or with neurological symptoms whereas it is rare to present with symptomatic endocrine dysfunction.

A 48-year old previously healthy man presented with generalized body weakness, lethargy, fatigue and postural dizziness of one month with no headache or visual disturbance. He also had features suggestive of hypogonadism and hypothyroidism. Panhypopitutarism secondary to partial ESS was diagnosed based on pituitary hormone testing and MRI brain. After starting glucocorticoid (GC) replacement patient developed polyuria and polydipsia and was diagnosed to have partial central diabetes insipidus (DI). He was successfully treated with hydrocortisone, thyroxin, intranasal vasopressin and testosterone. ESS causes significant pituitary dysfunction in considerable proportion of patients.

Key words: Empty sella, Hypopituitarism, Diabetes insipidus

Introduction

The empty sella syndrome (ESS) accounts only for 1.2% of cases of hypopituitarism whereas most common cause of hypopituitarism is the tumors of hypothalamic pituitary region.[1] ESS is a radiological finding in which the sella is partially or completely filled with CSF and the pituitary gland is either flattened or absent.[2] It is called partial ESS when some of the pituitary gland is visible in the MRI.[3] ESS is classified as Primary or secondary based on the etiology. The only established cause for primary ESS (PES) is the congenital absence or defect in diaphragm sellae while other causes include conditions with increased intracranial pressure allowing intrasellar herniation of subarachnoid space. Secondary ESS (SES) is caused by pituitary adenomas undergoing spontaneous necrosis, autoimmune hypophysitis, infection, surgery, trauma or by radiotherapy.[4] ESS is often detected incidentally and most common clinical presentation is with neurological symptoms including headache. It is rare to present with endocrine dysfunction.[3] Only few cases of PES presented with hypopituitarism have been reported in literature. We report a case of partial ES presented with both anterior and posterior pituitary insufficiency.

Case presentation

A 48-year-old previously healthy man patient presented with generalized body weakness, excessive sleepiness, lethargy, fatigue and postural dizziness for one month duration. He did not have anorexia, loss of weight or fever. On further questioning, he also had constipation, cold intolerance, erectile dysfunction and loss of libido over the past 1 year. There was no loss of body hair or galactorrhea. He was a father of 2 children. He denied chronic headache, visual disturbance, or head trauma or radiation therapy. There was no past or contact history of tuberculosis. He has never used alcohol and no high risk sexual behaviours were elicited.

He was averagely built with normal secondary sexual characteristics. Neither had he had gynecomastia nor skin pigmentation. His blood pressure was 100/60 mmHg and pulse rate was 78 beats per minute while supine. Blood pressure was reduced to 70/40 mmHg associated with a pulse rate of 96 bpm when examined three minutes after standing. He was not pale or dehydrated. There were no features of hypothyroidism. Fundoscopy and visual field examination were normal with no evidence of peripheral neuropathy.

His Full blood count and inflammatory markers were normal. Serum sodium was 132 mEq/L and serum potassium was 3.9 mEq/L. Serum cortisol drawn at 8 am in the morning was < 13.7 nmol/L (140-690) and the plasma adrenocorticotrophic hormone (ACTH) level was 10 pg/ml (10-60) indicating secondary adrenal insufficiency. His hormone profile revealed thyroid stimulating hormone (TSH) of 0.08 mU/L (0.5-4), free thyroxine (fT4) of 0.46 ng/dL (0.8-1.8), follicle stimulating hormone (FSH) of 0.9 IU/L (1-7), Luteinizing hormone (LH) of 0.67 IU/L, prolactin 39 ng/mL (<20), Total testosterone level <7.0 ng/dL

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(241-827) and Insulin-like growth factor 1 (IGF-1) of 82 ng/ml (90-360). Panhypopituitarism was diagnosed based on these results. His liver function tests and renal function tests were normal and he was negative for antinuclear antibodies. His mantoux test was negative and CSF examination did not reveal any abnormality.

Hormone replacement therapy was started with hydrocortisone and thyroxin. There was prompt improvement of his symptoms and general wellbeing. After 5 days of starting hydrocortisone, while awaiting MRI brain patient complained of polyuria, nocturia and increased thirst. His urine output was 4-5 L/day. Serum electrolytes, serum and urine osmolality were as shown in table 1.

Water deprivation test (WDT) was performed with administration of 2 puffs of intranasal desmopressin at the end of dehydration (Table 1). Based on the

Table 1

	Baseline	After dehydration	After Desmopressin
Serum sodium	140 mmol/L	143 mmol/L	
Plasma Osmolality	293 mosm/kg	313 mosm/kg	
Urine Osmolality	304 mosm/kg	361 mosm/kg	586 mosm/kg

results of WDT, cranial diabetes insipidus (CDI) was diagnosed and he was started on intranasal 1- desamino-8-D-arginine vasopressin (DDAVP) 1 puff (10 µg) nocte. Magnetic resonance imaging revealed partially empty pituitary sella filled with cerebrospinal fluid (CSF), with a flattened and atrophied pituitary gland and no focal lesions.(Figure 1) The pituitary stalk was normally visualized traversing the CSF space, with normal contrast enhancement. Panhypopituitarism secondary to partial ESS was diagnosed. He was followed up at endocrine clinic and was started on intramuscular testosterone at a dose of 125 mg/month. Hydrocortisone, thyroxine and DDAVP continued. At 6 months follow up patient was asymptomatic with no postural dizziness or polyuria.

Discussion

Our patient had deficiency of all anterior pituitary hormones, hyperprolactinemia and cranial diabetes insipidus secondary to partial ESS. He did not have history of any head trauma, surgery or radiotherapy. His MRI pituitary did not reveal any evidence of infarction of a pituitary tumor. It has been suggested that primary ESS often occur as a consequence of lymphocytic hypophysitis .[5]

Lymphocytic hypophysitis is often an autoimmune endocrinopathy, commonly occurring in females usually during pregnancy or postpartum period. Diagnosis is best established by histological evidence of lymphocytic infiltration.[6] Our patient didn't have evidence of autoimmunity or any other direct evidence to suggest lymphocytic hypopysitis. But it remains a possibility. Possibility of central nervous system tuberculosis was excluded. Therefore, our patient can be classified as having primary empty sella syndrome (PES).

PES was more common in females than males (4:1) and often associated with significant headache and ophthalmological symptoms such as reduced visual acuity or diplopia.[5] Visual disturbances may be due to intrasellar herniation of optic chiasm. Our patient did not have headache or visual disturbance. ES compresses the pituitary and hence lead to hormone deficiencies. But reason to present to medical care was not the endocrine dysfunction most of the times. Most patients present to either neurologists or ophthalmologists. [5]

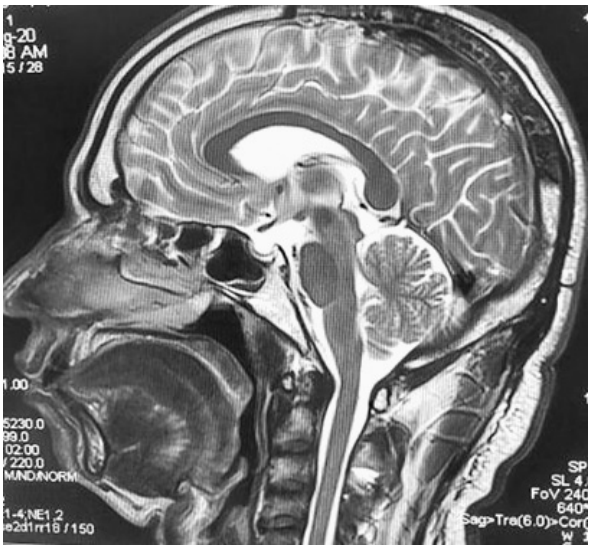

Figure 1: MRI brain – sagittal T2 weighted image showing partial empty sella (arrow)

Recent study of data from 765 patients with PES concluded that there is a gross under-evaluation of hormonal status of patients with PES. They found that hypogonadism was the most common endocrine dysfunction followed by hypothyroidism and hypocortisolism. Incidence of panhypopituitarism (defined as ≥ 3 hormonal deficiencies) was 0.6% and 0.8% in males and females respectively.[3] Another study which consisted of 213 patients with PES, re-

ported that 18% of the study population had some endocrine abnormality whereas 4.2% had panhypopituitarism.[5]

The intrasellar pathologies usually give rise to temporary diabetes insipidus (DI). However, permanent form of complete and partial cranial DI in association with empty sella syndrome have been reported.[2, 4,7]

WDT is the standard diagnostic test used to evaluate patients with polyuria. Patients with urinary osmolality <300 mosmol/kg at the end of water deprivation and > 50% increase in urine osmolality following DDAVP administration are diagnosed to have complete cranial DI. If the urine osmolality is between 300 – 800 mosmol/kg at the end of dehydration, either partial cranial DI or primary polydipsia (PP) is present.[8,9] In partial cranial DI the increase in urine osmolality after DDAVP is >9%. The increase in urine osmolality after DDAVP only <9% generally indicate PP.10 Based on these findings, our patient was diagnosed as having partial cranial DI.

Symptoms of DI may not be apparent when cranial DI coexist with hypopituitarism as polyuria is masked by hypocortisolism. Cortisol deficiency impairs renal water excretionby following mechanisms. Cortisol induces resistance to ADH at its V2 receptor in the principal cells of collecting duct. Secondly, cortisol deficiency increases ADH release via corticotrophin releasing hormone amplifies its action.[4] This phenomenon of masking of polyuria due to cranial DI by hypocortisolism is unrevealed by glucocorticoid replacement·[4,7] Time taken for unmasking polyuria ranged from immediately after to 20 days after steroid replacement.[4] Our patient developed polyuria after 5 days of steroid treatment.

In conclusion, ESS can cause significant anterior and posterior pituitary endocrine dysfunction in considerable proportion of patients even though commonly it is an incidental finding. Hence ESS should be properly evaluated for hormone deficiencies. Furthermore, GC replacement therapy for patients with hypopituitarism may unmask pre-existing central DI.

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