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Addison's Disease, Idiopathic Intracranial Hypertension and Empty Sella - In a 40-Year-Old Woman

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Summary:

A 40-year-old woman having normal menstrual history got admitted into Bangabandhu Sheikh Mujib Medical University (BSMMU) because of vomiting for previous two months, with a background history of irregular steroid intake for her bodyache for about six years. She was gaining weight and gradually losing vision in her right eye and noticed increased body pigmentation. Physical examination revealed BMI 29 kg/m^2, generalized pigmentation more marked in palmar crease and oral mucosa, secondary optic atrophy in right eye and papilloedema in left eye. After biochemical and radiological investigation she was diagnosed as a case of Addison's disease with idiopathic intracranial hypertension (IIH) with empty sella.

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Introduction:

Idiopathic intracranial hypertension (IIH) can rarely be associated with an underlying endocrine disorder such as Addison's disease[1], Cushing's syndrome, hyperthyroidism, hypoparathyroidism or with administration of thyroxin or growth hormone. Though cases of IIH associated with Addison's disease have been in reported in children, there are very few documented case reports of this association in adults[2, 3]. We describe a case of an adrenal insufficiency associated with IIH leading to empty sella in a 40-year-old female.

Case Presentation

A 40-year-old woman with a normal menstrual history was admitted to BSMMU because of vomiting for previous two months. She was taking tablet predisolone 5mg irregularly about 6 years for her bodyache. She was gaining weight and at the same time noticed increased body pigmentation. She was also gradually losing vision in right eye. She had no history of postpartum hemorrhage. On examination she was conscious, obese (BMI 29 kg/m^2), afebrile and her blood pressure was 100/70 mmHg with no postural drop. She had generalized pigmentation including pigmentation of her palmer crease (Fig 1) and oral mucosa. Opthalmoscopy revealed secondary optic atrophy in right eye and papillodema in left eye. No focal sign was found on neurological examination. All her secondary sex characteristics were normal. Initial biochemical analysis revealed serum sodium 130mmol/L, serum potassium 4.1mmol/L, serum creatinine 1.2 mg/dl, plasma random glucose 5.9 mmol/L, normal complete blood count with normal PBF, ESR 40mm in first hour. MRI of brain demonstrated empty sella (Fig 2). Lumbar puncture performed in lateral decubitus position revealed CSF pressure of 200mm of water. CSF analysis showed WBCs 4/mm^3, RBC nil, organism nil, protein 0.3g/L and glucose 3.5mmol/L. MT was 5mm, x-ray chest normal, and abdominal ultrasound including adrenal glands revealed no abnormality. Her baseline endocrine test is seen in Table 1.

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Table-I

Baseline endocrine test reports

Test	Result	Comment
ACTH	207.0 pg/ml	high
Serum Cortisol	25.5 nmol/L	low
LH	39.02 IU/L	normal
FSH	19.43 IU/L	normal
Prolactin	14.90 ng/ml	normal
TSH	1.49 mIU/L	normal
FT4	11.20 pmol/L	normal

Initially she was put on oral hydrocortisone 30mg, ondensetrone 24mg and acetazolmide 500mg daily in divided doses. At the same time CSF drainage was done. As vomiting continued, with consultation of endocrinologist and neurologist fundal photgraph (Fig 3) and perimetry were done and she was switched to intravenous dexamethasone 15mg, ondensetrone 24mg daily in divided doses. In addition lumbar drainage was done. Vomiting subsided and vision also improved significantly as evidenced by follow up fundal photograph (Fig 4) and perimetry after three weeks. She was then switched to oral dexamethasone followed by oral prednisolone. Her follow-up electrolyte showed persistent hyponatraemia which was corrected by addition of fludrocortisone 0.1mg with prednisolone 7.5mg per day.

Discussion:

According to her background history of steroid intake, obesity and opthalmoscopic findings, initially we labeled her as a case of iatrogenic Cushing syndrome with raised intracranial pressure (ICP). Her vomiting can be attributable to raised ICP. However, presence of pigmentation was the clinical clue that led us to think an alternative possibility. After biochemical analysis she was found to be a case of Addison's disease and her raised ICP could be attributed to Addison's disease. As very low serum cortisol and very high ACTH were strongly suggestive of diagnosis of Addison's disease, so we did not go for synecthine test. Her long history of irregular low dose steroid intake was responsible for chronicity of illness but was not sufficient for replacement. There are a few reports about the development of raised ICP in Addison's disease[2,3]. Increased serum and CSF arginine vasopressin peptide (AVP) in a glucocorticoid deficient state is the likely cause of raised ICP in Addison's disease[4]. The mechanism of empty sella in this case is probably due to raised ICP or an autoimmunity which is associated with autoimmune adrenal failure[5]. Our main concern was cortisol replacement and to halt the progression of visual loss. During management with the physiological replacement dose of corticosteroid her hyponatraemia was persistent, which was corrected by addition of fludrocortisone. As her vision was improved by acetazolamide and lumbar drainage we did not go for our initial plan of lumbo peritoneal shunt.

IIH is defined as the clinical syndrome of raised intracranial pressure in the absence of the space occupying lesion or vascular lesion, without the enlargement of cerebral ventricles for which no causative factor can be identified[6]. Historically IIH was referred to as pseudotumor cerebri as it mimics an intracranial tumor. More recently it has been referred to as benign intracranial hypertension (BIH). This term has also been abandoned because a small but significant number of patients develop visual impairment or visual loss, as in our case. However, even the current term IIH is inaccurate because this condition frequently associated with obesity or with the use of medication including various antibiotics (tetracyclines, nitrofurantoin and nalidexic acid), amiodarone, cyclosporin, both systemic steroids use and withdrawal[1] and oral contraceptive pill. Moreover various endocrine disorders have also rarely been reported in association with IIH, including Cushing syndrome[7] hyperthyroidism[8] as well as administration of thyroxin or growth hormone[9]. There are very few reported cases of IIH associated with Addison's disease in adult[1, 2]. Our case is an addition to the world literature of such a rare association.

Although the pathophysiology of IIH is uncertain the mechanisms that have been proposed for its development include increased production of CSF, reduced CSF absorption or increase cerebral venous pressure causing a secondary increase in CSF pressure. Analysis of the CSF arginine vasopresssin peptide (AVP) in the patient with IIH demonstrate it to be elevated compared to healthy controls[4] This reveals that patient with glucocorticoid deficiency have increased

plasma level of AVP and a sustained hypersecretion of AVP despite plasma dilution[10]. Thus it is possible that increased serum and possibly CSF AVP may mediate IIH in Addison's disease.

It is to be mentioned here that we were unable to measure serum or CSF AVP to provide the mechanistic link amongst Addison's disease, ICP and AVP. We also failed to rule out the role of autoimmunity in Addison's disease and empty sella. Finally, we could not establish raised ICP purely due to Addison's disease or steroid or combination of both.

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