SEVERE ANTERIOR HYPOPITUITARISM – RARE PRESENTATION OF PRIMARY EMPTY SELLA SYNDROME

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INTRODUCTION

The term "primary empty sella" (PES) refers to a neuroradiological entity characterized by a cerebrospinal fluid (CSF) filled sella, with a small pituitary gland compressed to the rim of the fossa. While its aetiology is not completely clear, it is currently being viewed as related to the mechanical transmission of the CSF pressure through an incomplete sellar diaphragm [1, 2]. PES has been reported in 6-20 % of unselected autopsies [1]. PES is also a frequent incidental finding due to widespread use of computerized tomography (CT) and magnetic resonance imaging (MRI) techniques. More rarely, PES patients present with CSF rhinorrhoea, visual field defects or papilloedema [3]. Global hypopituitarism is thought to be rare in PES [5, 6]. Hyperprolactinaemia due to distortion of pituitary stalk is present in about 10% of cases [7]. GH is the most frequently affected hormone and few recent studies have demonstrated a decreased pituitary GH reserve in 35-60% of adult PES subjects [5, 8].

CASE REPORT

A 42 years old woman presented in emergency with a few weeks history of recurrent swelling of lower limbs, mild generalized puffiness and gradually increasing generalized weakness. She was almost bed bound for the previous one week due to severe generalized weakness, dizziness and drowsiness. When asked in detail about the previous health, her husband told that she had been feeling lethargic, fatigued, weak and depressed always for about two to three years. She would go to some practitioners for her non-specific complaints, get symptomatic management but never felt any significant improvement. Routine laboratory tests were carried out on some occasions that did not show anything except mild anaemia for which she was often prescribed haematinics and multivitamin preparations. She had amenorrhea for about three years, which was attributed to early menopause but never investigated. She was not a known case of hypertension or diabetes. There was no history of any significant known illness in her past. She is a mother of three children aged 21, 19 and 17 years respectively, all born through normal vaginal deliveries and course of all pregnancies was uneventful. She was a non-smoker and non-alcoholic. On examination, she was a sick looking woman with a medium built, drowsy and confused. She had a pulse rate of 58 beats per minute and blood pressure 100/60 mm of Hg. She had a puffy face with a dry, thick, pale skin and almost absent eyebrows, mild ankle and sacral oedema was present. On neurological examination, she was semiconscious and confused, with a sluggish verbal response to loud commands, pupils were normal and equal on both sides, with a normal direct and consensual light reflex and fundoscopy revealed normal optic discs on both sides. There were no signs of meningeal irritation and no focal deficit. Abdomen was slightly protuberant and soft, but no viscera were palpable and flanks were not dull. Chest and heart were normal on auscultation. Haemoglobin was 9.2 g/dl with a normochromic and normocytic picture, total leukocyte count 7.0 x 109/l and platelets 219 x 109/l. Serum urea was 4.9 mmol/l, creatinine: 78 umol/l; sodium: 117.8 mmol/l; potassium:

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3.7 mmol/l; chloride: 83 mmol/l; calcium: 2.3 mmol/l; bilirubin 22 umol/l; ALT: 52 u/l and alkaline phosphatase 326 u/l. ECG revealed sinus rhythm. Ultrasonography of abdomen and chest x-ray also revealed a normal study. Considering secondary hypocortisolism due to hypopituitarism as the likely cause of this hyponatraemia, serum cortisol sample was drawn and patient was administered intravenous hydrocortisone 100 mg 6 hourly, thyroxine 100 ug orally daily was added later in the day when serum T3, T4 and TSH were confirmed to be very low compared to their reference ranges also. Serum T3 was < 0.3 nmol/l (reference range: 1.3-3.1), Free T4 was 0.45 ug/dl (reference range: 5.1-14.1) and TSH 0.6 u/l (reference range: 0.4-4.0). Serum cholesterol (fasting) was 6.8 mmol/l and triglycerides 1.6 mmol/l. serum cortisol: 4.6 ug/dl; FSH: 2.99 mIU/ml; LH: 0.10 mIU/ml, Estradiol 9.68 pg/ml and Prolactin 03 ng/ml. Serum electrolytes levels came within reference range alongwith gradually normalized as well as her general condition and consciousness level. After four days, her estimated serum sodium level has gone was 134 mmol/l, potassium: 4.2 mmol/l. She was prescribed to take oral Tab hydrocortisone 40 mg in the morning and 20 mg tablet at 6 pm. After four more days she was prescribed to a physiological maintenance dose of oral Tab hydrocortisone 20 mg in the morning and 10 mg at 6 pm. MRI of the brain and pituitary area revealed that Sella was filled with CSF signal intensity and pituitary gland appeared compressed against the floor (Figure-1 & 2). There was no evidence of erosion or destruction of the sella. Rest of the brain, brain stem and posterior fossa appeared normal. These findings were consistent with the diagnosis of Empty Sella syndrome. DEXA scan suggested decreased bone mineral density, with a T-score of – 1.6 at left hip and – 1.4 at lumbar spine. She has shown great improvement in general health after five months on

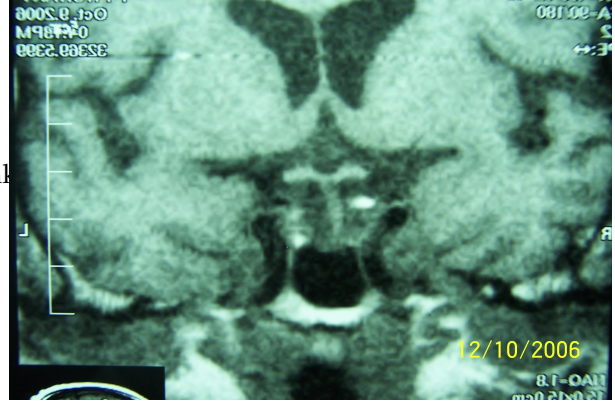

Figure-1: MRI Pituitary showing A T1 Weighted Image of Pituitary Fossa in Which Sella is Filled with CSF Signal Intensity and Pituitary Gland Appears Compressed Against the Floor. Pituitary Stalk is Visible, Extending from Optic Chiasma to the Base of Pituitary Fossa

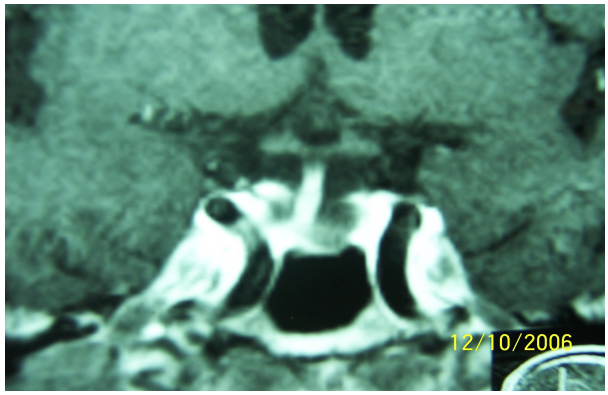

Figure-2: A T1 Weighted Image of Pituitary Area Obtained after Contrast Enhancement, shows A CSF Filled Sella with A Small Pituitary Gland, Compressed against the floor

replacement therapy with hydrocortisone, thyroxine, low dose oestrogen pill and alfacalcidol. Her haemoglobin is 11.4 g/dl now, 24 hour urinary cortisol excretion is 241.92 ug/24hr (reference range: 32.0 - 243.0) and free T4 is 10.09 ug/dl.

DISCUSSION

PES may be associated with a variable clinical conditions ranging from the occasional discovery of a clinically asymptomatic arachnoid pouch within sella turcica to severe intracranial hypertension [4,5]. Endocrine dysfunction may present as mild hyperprolactinaemia to varying degrees of pituitary hormone. Our case of severe anterior hypopituitarism due to PES is an example of the fact that the development of hypopituitarism often goes unrecognized in patients of PES, resulting in delayed diagnosis. A few recent studies have revealed that hypopituitarism, including secondary adrenal insufficiency, is a frequently

overlooked cause of severe hyponatraemia [9]. In our patient, secondary hypothyroidism also contributed to neurological alteration, generalized weakness and anaemia, as reported by other authors [2].

Anaemia is a frequent finding in hypopituitarism; hydrocortisone and thyroxine treatment elevates haemoglobin level in most patients [10]. In our patient haemoglobin improved from 9.2 g/dl to 11.4 g/dl in a few months with hydrocortisone, thyroxine and sex hormone replacement.

We could not carry out serum IGF-1 level in our patient because of non-availability of the facility locally. We expect serum IGF-1 and GH reserve to be low in this patient, because growth hormone (GH) is the most vulnerable pituitary hormone and its secretion is disturbed very early in the case of damage to the pituitary gland; this is in agreement with the fact that somatotrophe cells account for up to 50 % of the normal pituitary gland volume [8]. GH replacement in adults improves their quality of life [8]. We could not check GH reserve of the pituitary by a provocation test and considered GH replacement yet, because of excellent symptomatic improvement with hydrocortisone, thyroxine and oestrogen replacement, satisfactory bone mineral density and potential cost of therapy.

Headache and visual field alterations are the two main reasons for neurological study that leads to the diagnosis of PES. Other neurological features reported in patients with PES are dizziness, syncope, cranial nerve disturbances and convulsions [11,12].

Slight hyperprolactinaemia is the second most common hormonal alteration found in these patients after GH deficiency, followed by hypogonadotrophic hypogonadism [2,13]

In conclusion, patients with PES should always be submitted to endocrine, neurological, and ophthalmological evaluation at presentation because of the very high incidence of these abnormalities. Endocrine screening should be followed by specific endocrine testing when hormonal abnormalities are suspected. This procedure is able to detect all the affected patients with a very low number of unconfirmed diagnoses.

All endocrine deficits should be treated with appropriate medical substitution. Hyperprolactinaemia always improves after dopamine agonist treatment. In those patients where PES is accompanied by signs and symptoms of intracranial hypertension, severe headache, visual alterations, and rhinorrhoea, surgery is indicated.

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