Symptomatic hypopituitarism revealing a primary empty sella turcica

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Summary

A 64-year-old nulliparous woman presented with clinical signs of thyroid and adrenocortical insufficiency. Subsequent hormonal investigations demonstrated a failure of all anterior pituitary functions. Pneumotomo-encephalography revealed a large arachnoid herniation, leading to the diagnosis of primary empty sella turcica syndrome with secondary panhypopituitarism. This unusual observation emphasizes the necessity of ruling out an empty sella turcica syndrome in patients with pituitary insufficiency.

Introduction

Primary empty sella turcica syndrome is a frequent cause of enlarged sella turcica (Weisberg, Zimmerman and Frantz, 1976), although in a few cases it has also been documented in sellas of normal size (Bergland, Ray and Torack, 1968). In some subjects, the syndrome remains asymptomatic for prolonged periods and the diagnosis is only made at post-mortem or following routine X-rays (Neelon, Goree and Lebovitz, 1973). When clinical signs are present, headache is the most frequent initial symptom (Berke, Buxton and Kokmen, 1975; Jordan, Kendall and Kerber, 1977). Clinical signs of endocrine disturbances are uncommon (Brisman, Hughes and Holub, 1972; Faglia *et al.*, 1973). The present article reports an unusual case of empty sella turcica, with clinical symptoms of panhypopituitarism.

Case report

A 64-year-old woman was referred to the hospital because of muscular cramps, intense asthenia, anorexia, nausea, postprandial vomiting and severe constipation. These symptoms developed one month before admission. This nulliparous patient had

normal menses until the age of 44 years. She had had a mixed parotid tumour, treated by surgery and radiotherapy 20 years before, and had suffered minor cranial trauma without loss of consciousness 5 years before. Headaches were noted subsequently but were never investigated.

Physical examination revealed an apyretic obese woman (74 kg, 164 cm). Her skin was dry and pale, her hair was brittle, sparse and coarse. Pubic and axillary hair was scarce. The relaxation phase of deep tendon reflexes was prolonged. Blood pressure was 100/60 mmHg in supine and standing positions. Heart rate was 72/min. The rest of the examination was normal.

Laboratory investigations are summarized in Table 1 and as follows: thyroxine 37.4 nmol/l; triiodothyronine 0.7 nmol/l; sodium 115 mmol/l; potassium 3.8 mmol/l; chloride 96 mmol/l; haematocrit 29%. Basal plasma concentrations of thyroid hormones and of cortisol, and urinary excretion of 17-hydroxysteroids (17-OHCS) and 17-ketosteroids (17-KS) were sub-normal. Plasma gonadotrophins were low, especially if compared with post-menopausal values. Plasma thyroid stimulating hormone (TSH) was undetectable. Hyponatraemia and normochromic microcytic anaemia were present. Fasting plasma glucose concentrations were within normal limits.

Despite a fall of the plasma glucose concentrations to 1.5 mmol/l (induced by only 0.05 u/kg body weight of insulin), no increase of plasma cortisol, growth hormone or prolactin was observed following insulin-induced hypoglycaemia. Metirapone elicited no significant steroid response. In contrast, a marked cortisol increase occurred after intravenous injection of tetracosactrin. Plasma values of thyrotrophin, gonadotrophins and prolactin remained unchanged during a combined LHRH-TRH stimulation test.

Visual fields and eye fundus were normal, standard X-rays of the skull and sellar tomography disclosed

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TABLE 1. Stimulation tests

Time (min)	- 30	0	Insulin tolerance test (0.05u./kg i.v.)			60	90	120
			15	30	45			
Glucose (mmol/l)	4.0	3.9	1.9	1.5	2.1	2.6	2.8	3.7
Cortisol (μ mol/l)	55.2	27.6	27.6	27.6	27.6	55.2	27.6	27.6
GH (mu./ml)	≤ 1	≤ 1	≤ 1	≤ 1	≤ 1	≤ 1	≤ 1	≤ 1
PRL (μ u./ml)	21	6	9	15	11	14	6	25

Metyrapone stimulation test (750 mg/4 hr for 24 hr)			
Day	- 1	0	+ 1
Urinary 17-OHCS (μ mol/24 hr)	4.9	4.2	9.0
Urinary 17-KS (μ mol/24 hr)	5.5	3.1	5.5

Tetracosactrin stimulation test (0.25 mg i.v.)					
Time (min)	0	30	60	90	180
Cortisol (μ mol/l)	82.8	331.2	276	220.8	165.6

Gonadotrophin releasing (LHRH) and thyrotrophin releasing hormone (TRH) stimulation test (200 mu. and 100 mu. i.v.)						
Time (min)	- 30	0	15	30	60	120
TSH (μ u./ml)	≤ 1.1	≤ 1.1	≤ 1.1	≤ 1.1	≤ 1.1	≤ 1.1
PRL (μ u./ml)	37	24	13	-	36	38
LH (mu./ml)	1.2	1.0	0.8	1.2	1.8	1.4
FSH (mu./ml)	2.0	3.0	2.7	2.7	3.0	4.1

TSH = thyroid stimulating hormone; PRL = prolactin; LH = luteinizing hormone; FSH = follicle stimulating hormone

moderate enlargement and ballooning of the sella turcica.

These findings were consistent with a diagnosis of panhypopituitarism secondary to a pituitary tumour. Considering the patient's clinical state, corticoid and thyroid replacement therapy was immediately started, before completing further investigations. Therefore, a pneumotomo-encephalographic examination was performed only several months later. It allowed visualization of a large arachnoid herniation, which filled up the sella turcica with air, leaving a small pituitary residue in the postero-inferior region, without any sign suggesting a pituitary tumour (Fig. 1). Thus, the final diagnosis was primary empty sella turcica syndrome with secondary panhypopituitarism. Hormonal therapy at present consists of cortisone acetate (25 mg in the morning, 12.5 mg in the evening) and of l-thyroxine (0.15 mg daily).

Discussion

The empty sella turcica syndrome accounts for about 25% of enlarged sellas (Weisberg *et al.*, 1976). Most patients are obese (75–95%), hypertensive (29–58%) females (87–91%) (Neelon *et al.*, 1973; Jordan *et al.*, 1977). The syndrome is most often

diagnosed in patients aged 40–55 years. The clinical symptoms include headache (45–80%), rhinorrhoea (0–8%) (Weisberg *et al.*, 1976; Berke *et al.*, 1975), but 38% are asymptomatic. A clinical picture of pituitary insufficiency is exceptional, although abnormal hormonal status may be revealed by laboratory studies (Weisberg *et al.*, 1976; Brisman *et al.*, 1972).

In a few cases, hormonal disturbances could be related to the association of empty sella turcica with the infarction of a hormonally active pituitary adenoma revealed at pneumoencephalography (5 cases of prolactinomas (Jordan *et al.*, 1977; Schaison and Metzger, 1969; Bar, Mazzaferri and Malarkey, 1975; Bryner and Greenblatt, 1977), 2 cases of Cushing's disease (Ganguly *et al.*, 1976; Mortara and Norrell, 1970), 2 cases of acromegaly (Neelon *et al.*, 1973; Molitch *et al.*, 1977). Diabetes insipidus associated with primary empty sella syndrome was reported in 4 cases (Schaison and Metzger, 1969; Cupps and Wolff, 1978; Marisson and Pimstone, 1973). Two cases with gonadotropic insufficiency (Neelon *et al.*, 1973; Bernasconi, Giovanelli and Papo, 1972) were also described. Five patients were found to have panhypopituitarism; 2 of them presented with clinical

FIG. 1. Sagittal tomogram of sella turcica during pneumo-encephalography.

myxoedema (Neelon *et al.*, 1973; Cupps and Woolf, 1978), one patient was admitted with generalized weakness and loss of appetite (Mortara and Norrell, 1970), and two subjects had a picture of panhypopituitarism (without further details), secondary to meningo-encephalitis and cranial trauma respectively (Schaison and Metzger, 1969).

The patient described in the present paper was, as usual, an obese female, but the clinical picture was quite unusual. Although headache was present, the clinical status was dominated by signs of thyroid and adrenocortical insufficiency. Because of the age of the patient, clinical signs of possible gonadotropic and somatotrophic insufficiency were not observable. Subsequent hormonal investigations demonstrated a failure of all anterior pituitary functions. Despite the absence of clinical, biological and radiological signs of pituitary tumour, the hypothesis of an association of empty sella turcica with infarction of a pituitary adenoma could not be absolutely ruled out.

This case emphasizes the need to rule out an empty sella turcica syndrome in all cases presenting with a pituitary insufficiency, a sellar enlargement, or both.

Acknowledgments

This work was supported in part by a grant from the Belgian Fonds de la Recherche Scientifique Médicale.

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