PITUITARY FUNCTION IN PATIENTS WITH PRIMARY EMPTY SELLA SYNDROME

Tomris Erbaş, M.D., Sema Akalın, M.D., Miyase Bayraktar, M.D., Olcay Gedik, M.D., Aydan Usman, M.D., Nezaket Adalar, M.D., Tunçalp Özgen, M.D., Muzaffer Eryılmaz, M.D., Ferzan Telatar, M.D.

Departments of Endocrinology (T.E., S.A., M.B., O.G., A.U.,N.A.,F.T.), Neurosurgery (T.Ö.) and Radiology (M.E.) Faculty of Medicine, Hacettepe University, Ankara, TÜRKİYE

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SUMMARY :

Sixteen patients with the primary empty sella syndrome were analyzed in regard to clinical findings, x-ray features and dynamic endocrine testing. One patient had no endocrine disturbance, three had a panhypopituitarism and one had diabetes insipidus. Hyperprolactinaemia, the most common endocrine disturbance detected was found in six patients. Other patients had some degree of partial pituitary insufficiency.

KEY WORDS :

Empty Sella Syndrome, Dynamic Endocrine Testing, Pituitary Function.

INTRODUCTION

The empty sella syndrome is defined as intrasellar herniation of the suprasellar cistern (11,17). Empty sella occurring in patients who have not undergone pituitary surgery or radiation treatment is called the primary empty sella syndrome. Increased intracranial pressure and congenital anomaly of the sellar diaphragm may be important factors in development of cisternal herniation (2,3,12). Intrasellar cisternal herniation may compress the pituitary gland and affect the function of the hypophysis. A high incidence of pituitary dysfunction was documented in patients with the primary empty sella syndrome. These consisted of panhypopituitarism, secondary hypogonadism, hyperprolactinaemia, isolated ACTH insufficiency and diabetes insipidus (4).

In the present study we have evaluated the results of dynamic endocrine testing of pituitary function in sixteen patients with the primary empty sella syndrome.

PATIENTS AND METHODS

Sixteen patients with the primary empty sella syndrome were referred to the Section of Endocrinology, Dept. of Medicine, Hacettepe University from 1989 to 1991. The diagnosis was made if cerebrospinal fluid density was detected within the sella on thin collimation CT reconstructions. Plain skull x-rays were also taken. In none of the patients was there any evidence of a coexisting pituitary microadenoma. Visual fields were evaluated by perimetry.

Endocrinological studies:

TRH and LHRH stimulation tests were performed on the same day. Samples for TSH, LH and FSH were drawn before and 30,60,90 min. after the iv. injection of 200 μg TRH (Protirelin, Ferring GmbH, FRG) and 100 μg LHRH (Gonadorelin, Ferring GmbH, FRG). An increase of at least 2.7 μU/ml in TSH and 2 ng/ml in LH levels was regarded as normal (6).

An insulin tolerance test was performed on consecutive days between 08.30-10.30 A.M. Samples for glucose, cortisol and growth hormone (GH) were drawn prior to and 30,60 and 90 min. following the injection of insulin iv. at a dose of 0.1 u/kg. A blood glucose level below 40 mg/dl was considered an adaquate stimulus for GH and cortisol secretion. Increment of 7 ng/ml or more in growth hormone levels and 12 μg/dl or more cortisol levels were considered to exclude GH and cortisol deficiencies (6).

Plasma glucose levels were determined by the glucose oxidase method. All pituitary hormones and cortisol levels were determined by commercially available radioimmunoassay kits. The intra- and interassay coefficients of variation were less than 10% for all hormones.

RESULTS

The clinical features of 16 patients are shown in Table 1. Nine of the patients were women (56.2%). Their mean age was 38.3±12.6 years (range 19-69 years). Nine patients were overweight (56.2%) and the whole group had a mean body mass index (BMI) of 27.6±6.1 (range 18.5-43.9).

None of the patients had a previous history of pituitary radiation or pituitary surgery. Seven of the women were multiparous and one was primiparous. The number of pregnancies ranged from one to seven. Hypertension was recorded in three patients(18.7%).

Table 1 : Clinical features of 16 patients with primary empty sella syndrome.

Age	Sex	BMI (kg/m²)	Hypertension	Pregnancies	Galactorrhoea	Amenorrhoea	Clinical status	Dynamic test results*
46	F	32.9	+	7			Diabetes İnsipidus	↓ ADH
41	F	23.2		2		+	Panhypopituitarism	Panhypopituitarism
48	F	31.7		4	+	+		↑ PRL ↓TSH
36	F	25.3		2				Normal
25	F	28.4			+	+		↑ PRL ↓Cortisol and GH
40	F	24.1		4	+	+		↓ Cortisol ↑PRL
34	F	19.2		1		+	Panhypopituitarism	Panhypopituitarism
40	F	31.1		3	+			↓ TSH PRL
40	F	43.9	+	4		+		↓ GH
19	M	24.8						↓ Cortisol and GH
46	M	27.9						↑ PRL
69	M	24.5	+					↑ PRL
20	M	18.5						↓ Cortisol, GH and LH
25	M	33.3						↓ GH and LH
35	M	29.0						↓ Cortisol
49	M	24.7					Panhypopituitarism	Panhypopituitarism

* ↑denotes increases and ↓denotes decreases in hormone levels.

Twelve patients had chronic headaches as presenting symptoms (75%). In one patient there was evidence of posterior pituitary dysfunction resulting in clinical diabetes insipidus. Other presenting complaints included galactorrhea-amenorrhoea (three patients), galactorrhoea (one patient) and amenorrhoea (three patients). All women of fertile age had amenorrhoea and galactorrhoea. One male patient had enuresis nocturna and bilateral optic atrophy. None of the patients had cerebrospinal fluid rhinorrhoea, diabetes mellitus or hydrocephalus. Neuro-ophthalmological examination did not disclose visual defects in any of the patients.

Nine patients had symmetrical enlargement of the sella with preservation of the closed configuration on plain skull x-rays. Two patients had a double contour in the sellar floor and one patient had a deep sella. The skull x-ray was normal in four patients.

During endocrine testing, one patients showed no evidence of endocrine dysfunction (6.2%). Three were found to have panhypopituitarism (18.7%). In these cases, the GH, ACTH, TSH, LH and FSH secretions in response to stimulation were insufficient. One patient had diabetes insipidus with a history of marked polyuria and polydypsia. However in that patient, anterior pituitary function was intact. Hyperprolactinaemia was the most common finding. Serum prolactin levels were elevated in four women and two men (37.5%). In these two men no additional hormonal disturbances were found.

The growth hormone increases were inadequate in eight patients (50.0%) and peak cortisol levels were inadequate in eight (50.0%), three of which presented with panhypopituitarism. Isolated ACTH insufficiency was documented in one patient (6.2%) while isolated LH-FSH insufficiency was not seen. Secondary hypogonadism was documented in two men. These patients also had other pituitary insufficiencies besides. The TSH response to TRH was blunted in two patients. Of these one also demonstrated hyperprolactinaemia.

DISCUSSION

The primary empty sella syndrome is generally found in middle-aged women who are obese and hypertensive (16,22). In our patients, nine (56.2%) were female, most were obese and three (18.7%) were hypertensive. Headaches were a common symptom. Rhinorrhoea has been reported in the literature but occured in none of our cases (1,18,20). An increase in cerebrospinal fluid pressure could be responsible for this. Although, visual field abnormalities have been reported in the literature previously, none were observed in our patients (2,9,16,20).

The primary empty sella syndrome is frequently confused with an intrasellar adenoma when lateral skull x-rays reveal an enlarged sella. Radiologically the empty sella is best evaluated by CT scans and magnetic resonance imaging. These procedures have almost entirely replaced invasive cisternography(14,15).

In our series the clinical diagnosis of empty sella syndrome was confirmed by CT scans.

Although the majority of studies report normal pituitary function in the primary empty sella syndrome (2,7,16,22,23), Ekblom et al. have documented some degree of hypothalamic-pituitary dysfunction in up to 80% of their patients(10). In another series, the most frequently encountered impairments were panhypopituitarism (10%), isolated secondary hypogonadism(10%), hyperprolactinaemia(8%) and isolated ACTH insufficiency (2%)(4). On the other hand, Buchfelder et al. found hyperprolactinaemia in 32%, panhypopituitarism in 57% and partial anterior pituitary insufficiency in 17.3% of their patients(6).

Our findings are in agreement with studies that show abnormal pituitary function in most patients with primary empty sella syndrome. In previous reports, the common abnormality was deficient GH secretion which was noted in eight of our patients, three of whom were obese. This deficiency could be attributed to obesity or advanced age in some patients (2,8,10,13,21,22). Measurement of PRL concentration is also very important in the evaluation of a patient with an enlarged sella. Our patients, slightly increased serum prolactin concentrations resemble non-tumorous hyperprolactinaemia and incidence of hyperprolactinaemia in our series is consistent with the reports in the literature (5,6,23).

Posterior pituitary function is altered in only a few cases of empty sella syndrome. Compression of the stalk or hypothalamus may lead to antidiuretic hormone deficiency (4,19,24). Diabetes insipidus was also rare in our series.

There is no correlation between pituitary dysfunction and type of intrasellar herniation or size and shape of the sella turcia(24).

The primary empty sella is a benign condition that is being diagnosed with increasing frequency since the advent of non invasive radiological techniques. Because the incidence of pituitary dysfunction is high, the patients with primary empty sella syndome should be evaluated periodically with pituitary function testing.

Correspondence : Tomris Erbaş M.D.,
Hacettepe University, Faculty of Medicine,
Department of Endocrinology,
Sıhhıye-Ankara-TÜRKİYE

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