ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN – POLONIA
VOL. XXIII, N 2, 10 SECTIO DDD 2010

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Variable types of pituitary hyposecretion in patients after hypothalamic-pituitary region neurosurgery

Różnorodne formy niewydolności przysadki u chorych po zabiegach neurochirurgicznych okolicy podwzgórzowo-przysadkowej

INTRODUCTION

The pituitary gland connected to the hypothalamus by the infundibular stalk is an anatomically complex region within which several, etiologically different, pathologies and lesions can develop, e.g. neoplasm, inflammatory, infectious, developmental as well as vascular diseases. The sellar and parasellar lesions may include micro- and macro pituitary tumors, craniopharyngiomas, Rathke's cleft cysts, chordomas, chondromas as well as meningiomas, germinomas, hamartomas and other very rare disorders [1, 4, 6, 8].

Pituitary tumors are the most commonly encountered intracranial neoplasms. The prevalence of these tumors including serious ones achieves approximately 10%. Functioning tumors are classified depending of the kind of hormone overproduction (prolactinomas, somatotropinomas, Cushing disease) whereas non-functioning pituitary tumors are mainly macroadenomas. It has to be emphasized that pituitary malignant tumors are rather unusual [1]. Transcranial and transsphenoidal neurosurgery are the methods of choice in radical treatment in most cases of pituitary adenoma and non-pituitary lesions [2–6].

Hypopituitarism is related to diminished secretion (or its lack) of one or more pituitary hormones and frequently follows both surgical and radiation therapy. It is observed usually in endocrine practice and is associated with increased morbidity and mortality [5, 6, 7, 9, 11, 12]. Pituitary-hypothalamic region surgery may result in hormonal changes, including impairment of anterior pituitary hormone secretion and failure of posterior pituitary to secrete ADH. The development of signs and symptoms of hypopituitarism depend on the rate of onset, and the magnitude of hypothalamic- pituitary damage, including the experience of the surgeon [3,4,7,9,11, 12].

The aim of the study was to determine the forms and frequency of pituitary hypofunction in our patients undergoing neurosurgical treatment.

MATERIAL AND METHOD

The studied group included 68 *patients (32*M and 36F) after neurosurgery due to hypothalamo-pituitary pathology, *aged* 19–76, observed at the Department of Endocrinology in 2005–2010. *The group covered* by the research included 23 subjects (16 F and 7 M) operated for somatotropinoma, 5 female for Cushing disease, 12 (3F, 9M) for craniopharyngioma, 23 patients (9F;14M) for non-functioning pituitary adenomas, 2 (1F,1M) for prolactinoma, 2 (1F,1M) for germinoma and 1 woman for *tumor* of the *sellar* region in the course of multiple myeloma. Nine of the patients had been operated several times (even four times).

Before being admitted to our department, some of the patients had been diagnosed and operated on in a different clinic. The time that passed from the surgery until the hormonal evaluation of the pituitary ranged from six months to 10 years. The patients with pituitary adenomas were typically operated with the use of transphenoidal surgery, yet those with unusually large adenomas and craniopharyngiomas were operated using transcranial neurosurgery. The patients were operated on by different neurosurgeons.

The retrospective review of medical records was conducted. To evaluate the function of the *hypophyseal-adrenal cortical axis, ACTH serum concentration as well as* circadian rhythm of cortisol secretion and urine cortisol *daily* excretion *were analyzed.* The functional states of *hypophyseal-thyroid and hypophyseal-gonadal axes* were assessed *by measuring serum levels of* TSH, fT4, fT3 and LH, FSH, testosterone/estradiol, respectively. In addition, serum concentrations of PRL, growth hormone and IGF-1 were studied. Diabetes insipidus was diagnosed according to the standards of the Polish Endocrinology Society.

Hormone concentrations were determined with the use of routine methods applied in clinical diagnostics in our department, which are commercially available tests. FT4, TSH, ACTH, cortisol, FSH, LH, E2, T and PRL were measured with the method of the appropriate automated chemiluminescent immunoassay systems. The assessment of pituitary function in the patients previously diagnosed and operated on in our clinic was performed in most cases ca. six months after the neurosurgery. The other patients were diagnosed during their first hospitalization in our department. Not all the patients had an evaluation of pituitary function carried out before the operation, while some patients treated previously in other hospitals did not always deliver the documentation concerning that period.

Due to the lack of a possibility to implement substitute treatment with the growth hormone in adults, no stimulation tests necessary to diagnose its insufficiency were done. Therefore, the present study does not take into account the incidence of growth hormone deficiency.

RESULTS

Postoperative pituitary hypofunction did not occur in 12 (8F; 4M) [17.6%] patients. Other patients showed disturbances in at least one hormonal axis. The frequency and forms of post surgical hypopituitarism in patients with a variable type of intracranial base pathology (hypophyseal-pituitary region) were presented in Table 1. As shown in the table, postoperative hypopituitarism occurred most frequently in patients after neurosurgery due to large tumors, mainly non-active macroadenomas and craniopharyngiomas.

Table 1. Forms and frequency of hypopituitarism in patients with variable types of sellar-parasellar pathology

Diagnosis	Number of pts	Secondary hypoadrenalism	Secondary hypothyroidism	Secondary hypo-gonadism	Diabetes insipidus
Somatotropic macroadenoma	23 (16F;7M)	13	5	2	2
Cushing disease	5F	2	-	-	-
Craniopharyngioma	12 (3F;9M)	10	11	10	7
Non-functioning macroadenoma	23 (9F;14M)	19	17	13	8
Prolactinoma	2(1F;1M)	1	1	-	-
Germinoma	2(1M;1F)	2	2	1	2
Sellar plasmocytoma	1F	1	-	-	-
Number of pts	68	48	36	26	19

In 18 patients (14F;4M) [26.5%], only secondary adrenal insufficiency was observed, in 11 (8F;3M) [11.8 %] abnormalities occurred in two axes and in 12 [3F;9M] (17.6%) in all three axes, while in 11 [1F;10M] (11.8%) pts – disturbances in 3 axes and diabetes insipidus were diagnosed. The most frequently observed pituitary disturbance was hypophyseal-adrenal cortical axis hypofunction [48 pts (23F; 25M)] (70.6%). Hypophyseal-thyroid axis disturbances developed less frequently [35 pts (10F;25M)] (51.5%), whereas hypophyseal-gonadal axes were the least frequent clinical findings [26 pts (6F;20M)] (38.2%). Diabetes insipidus was diagnosed in 19 (4F; 15M) [27.9%] patients.

DISCUSSION

For tumors located in hypothalamo-pituitary region, surgery remains the treatment of choice [4, 6, 7, 8]. Nowadays transsphenoidal surgery is indicated in the majority of patients with functioning and non-functioning pituitary adenomas. This method is considered to be safer than transcranial approach, and to lead to a lower incidence of complications, also including iatrogenic hypopituitarism [4, 5, 6, 10, 12, 13].

The outcome of surgery is determined by the surgeon's experience, the size of the adenoma and the degree of its extension beyond the sella turcica [6, 8, 11, 12]. According to different authors [2, 4, 6, 9, 10-14], the incidence and forms of iatrogenic hypopitutarism depend on the type of the disease [7, 8, 9, 11], the size and expansion of the tumor [4, 7, 9, 11], type of surgery [2, 4, 7, 9, 13], as well as the time interval between the neurosurgery and the moment of evaluating pituitary function [3, 5]. The incidence of hypopititarism is higher in patients with macroadenomas, craniopharyngiomas, non-functioning adenomas in which it already occurs before the operation [4, 7, 9, 11]. It may partly disappear following the surgery [3, 5].

The results obtained in our study, in reference to the data concerning carniopharyngiomas and non-functioning adenomas, are consistent with those reported by other authors [4, 7, 8, 9, 11, 13, 14]. In general, the high incidence of multi-hormonal pituitary hypofunction observed in our patients results from its diversity, regarding both the type of the disorders found in the hypothalamic-pituitary region, their clinical picture, the size and expansion of the tumor, the type of neurosurgical procedures which were repeated in some patients due to the relapse of the disease, and also from the fact that the surgical treatment was carried out in different clinics and at different time by neurosurgeons having different experience. The group of patients analyzed in our study was not subject to any particular selection. It was a cross-section of patients an average endocrinologist meets in their daily practice. An additional factor affecting the incidence and type of the observed post-operative pituitary damage was the time interval between the surgery and the hormonal evaluation, which was different in individual cases and ranged from six months up to ten years.

CONCLUSIONS

Hypothalamic-pituitary region neurosurgery was associated with the high frequency of variable types of postoperative pituitary hypofunction; therefore, a detailed multi-hormonal evaluation of the hypophyseal functional status is required in all patients undergoing such neurosurgical treatment.

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SUMMARY

Hypothalamic-pituitary region neurosurgery may result in hormonal changes, including impairment of anterior pituitary hormone secretion and a failure of posterior pituitary to secrete ADH. To minimize postoperative morbidity, a detailed endocrine evaluation followed by adequate management are required in all patients who underwent pituitary surgery. The aim of the study was to determine the forms and frequency of pituitary hypofunction in our patients undergoing neurosurgical treatment. 68 *patients (32*M and 36F) *aged* 19–76 were observed in the Department of Endocrinology in 2005–2010. *The group covered* by the research included 23 subjects (16 F and 7 M) operated on for somatotropinoma, 5 F for Cushing disease, 12 (3F, 9M) for craniopharyngioma, 23 (9F;14M) for non-functioning pituitary adenomas, 2 (1F,1M) for prolactinoma, 2 (1F,1M) for germinoma, 1F for *tumor* of the *sellar* region in the course of multiple myeloma. A retrospective review of medical records was conducted. To evaluate the function of the *hypophyseal-adrenal cortical axis, ACTH serum concentration, as well as* circadian rhythm of cortisol secretion and cortisol *daily* excretion, *were analyzed.* The functional states of *hypophyseal-thyroid and hypophyseal-gonadal axes* were assessed *by measuring serum levels of* TSH, fT4, fT3 and LH, FSH, testosterone/estradiol, respectively. In addition, serum concentrations of PRL, growth hormone and IGF-1 were studied. Postoperative pituitary hypofunction did not occur in 12 (8F; 4M) (17.6%) patients. Other patients showed disturbances in at least one hormonal axis. In 18 (14F;4M) patients only secondary adrenal insufficiency was observed, in 11 – disturbances in two axes and in 12 pts in all three axes were noted, while in 11 pts abnormalities in 3 axes and diabetes insipidus were diagnosed. The most frequently observed pituitary disturbance was *hypophyseal-adrenal cortical axis hypofunction (70.6%). Hypophyseal-thyroid axis disturbances developed less frequently (51.5%), whereas hypophyseal-gonadal axes were the least frequent clinical findings (38.2%). Diabetes insipidus was diagnosed in 19 patients.* Hypothalamic-pituitary region neurosurgery is associated with a high frequency of variable types of postoperative pituitary hypofunction; therefore, a detailed multihormonal evaluation of the hypophyseal functional status is required in all patients undergoing such neurosurgical treatment.

Key words: neurosurgery, hypothalamic- pituitary region, hypopituitarism

STRESZCZENIE

W następstwie zabiegów neurochirurgicznych w okolicy podwzgórzowo-przysadkowej może dojść do różnorodnych zaburzeń endokrynnych, między innymi do zmniejszenia produkcji hormonów przedniego płata i upośledzenia sekrecji wazopresyny przez tylny płat przysadki. Aby zmniejszyć ryzyko niekorzystnych następstw pooperacyjnej niedoczynności przysadki, konieczna jest dokładna ocena hormonalna wszystkich pacjentów po operacji neurochirurgicznej. Celem badania była ocena częstości i postaci niedoczynności przysadki u pacjentów po przebytej operacji neurochirurgicznej okolicy podwzgórzowo-przysadkowej w materiale własnym. Materiał stanowiło 68 pacjentów *(32*M, 36K) w wieku 19–76 lat leczonych w Klinice Endokrynologii w latach 2005–2010. W badanej grupie 23 (16K, 7M) pacjentów operowano z powodu akromegalii, 5 kobiet z powodu choroby Cushinga, 12 pacjentów (3K, 9M) z powodu czaszkogardlaka, 2 osoby – germinoma, 2 – prolaktynoma oraz 23 (9K, 14M) pacjentów z powodu nieczynnego hormonalnie gruczolaka przysadki. U jednej kobiety guz okolicy siodła tureckiego okazał się szpiczakiem. Przeprowadzono retrospektywną analizę wyników badań hormonalnych pacjentów. Dla oceny osi przysadkowo-nadnerczowej określano stężenie w osoczu ACTH, rytm kortyzolemii i wydalenie kortyzolu w DZM. Wydolność osi przysadkowo--tarczycowej i gonadalnej *określono na podstawie stężeń hormonów* TSH, fT4, fT3 oraz odpowiednio LH, FSH, E2 i T. Ponadto badano stężenie PRL, GH i IGF-1. U 12 (8K, 4M) chorych (17,6%) nie stwierdzono niedoczynności przysadki. Pozostali pacjenci wykazywali niedoczynność co najmniej jednej osi. U 18 (14K; 4M) pacjentów stwierdzono jedynie wtórną niedoczynność nadnerczy, u 11 – niedoczynność 2 osi, u 12 niedoczynność 3 osi. U 11 osób niedoczynności 3 osi towarzyszyła moczówka prosta. Najczęściej rozpoznawaną formą niedoczynności przysadki była niewydolność osi przysadkowo-nadnerczowej *(*70,6%). Rzadziej diagnozowana była wtórna niedoczynność tarczycy (51,5%). Najrzadziej stwierdzano uszkodzenie osi gonadalnej (38,2%). Moczówkę rozpoznano u 19 pacjentów. Należy wnioskować, że zabieg operacyjny w okolicy podwzgórzowo-przysadkowej często wiąże się z wysokim ryzykiem wystąpienia pooperacyjnej niedoczynności przysadki o różnorodnym charakterze. Dlatego wszyscy ci pacjenci powinni być podani pełnej ocenie hormonalnej.

Słowa kluczowe: neurochirurgia, okolica podwzgórzowo-przysadkowa, niewydolność przysadki