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DEVELOPMENT OF CENTRAL DIABETES INSIPIDUS IN A FEMALE PATIENT AFTER SURGICAL TREATMENT OF PITUITARY ADENOMA

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ABSTRACT — The purpose of the article is to provide some insight into the current medical literature and relevant works on the issue of diabetes insipidus and clinically analyze the medical record of a female patient of the Endocrinology Department of Tver Regional Clinical Hospital who was operated for prolactin-secreting pituitary macroadenoma, with diabetes insipidus developed in the postoperative period.
There was a clear cause-effect relationship between the previous neurosurgical intervention in the hypothalamic-pituitary area and a developed clinical picture of diabetes insipidus. The diagnosis of diabetes insipidus was confirmed by laboratory and instrumental studies. Treatment with desmopressin has proved to be effective. The variety of causes and possible severe complications of diabetes insipidus require its accurate differential diagnosis in order to distinguish between its various forms and other causes of polyuria in the postoperative period, while ensuring the administration of a pathogenetically targeted and safe treatment. We assume that analyzing this clinical case will improve the awareness of doctors about this disorder for its identification and timely treatment.

KEYWORDS — diabetes insipidus, antidiuretic hormone, polyuria, polydipsia, transnasal adenomectomy.

INTRODUCTION

Diabetes insipidus (DI) is a group of diseases that are based on a defect in the synthesis, secretion or action of the antidiuretic hormone (ADH), which leads to the failure of the kidneys to reabsorb water and concentrate urine, and is manifested by excessive thirst and excretion of a large amount of diluted urine [1].

According to its etiology, DI is classified into central, nephrogenic, dipsogenic, and gestagenic [2]. Central diabetes insipidus (CDI) is the most common form, detected with a frequency of 1:25,000. Its prevalence varies from 0.004% to 0.01%. The disease can be detected at any age, but most often develops between 20 and 40 years [2, 3]. According to some researchers, the disease can be equally common in both men and women, whereas others argue that women predominate with the ratio of 2.2:1 [3].

There has recently been a trend towards an increase in CDI due to a growing number of brain surgeries [1]. Acute CDI occurs in 13–30% of patients in the postoperative period after transsphenoid surgeries [2, 3]. For the manifestation of CDI, the secretory capacity of the neurohypophysis has to reduce by 85% [3, 4].

There are various options for the course of postoperative CDI such as a transient form, when acutely manifesting DI resolves on its own within 3–5 days [4], a permanent form associated with an acute onset, but does not go away within six months [5], a form with three-phase development, which occurs only in 3–5% of patients and can lead to either persistent permanent polyuria or recovery if there is a sufficient number of functioning neurons to adequately respond to changes in blood osmolality [2, 4, 5].

Prognostic factors for the development of CDI after removal of large formations in the hypothalamic-pituitary area include the size and nature of its growth, type of surgical access, age and gender of the patient [6]. The risk of permanent CDI is higher in young adults, men with a large weight of intracellular tumor, with intraoperative cerebrospinal fluid leaks, in individuals with preoperative DI, with repeated surgeries on the hypothalamic-pituitary area, as well as with a large resection of the contents of the Turkish saddle or with damage to suprasellar structures during surgery [4, 5, 7].

If the decrease in the total water content in the body with DI develops faster than the adaptive mechanisms of the brain can react, it gets dehydrated, shrinks, separates from the dura mater with vascular rupture and intracranial hemorrhages, increased intracranial pressure with compression injuries of the brain stem [10].

In the postoperative period, polyuria may be associated with hyperglycemia and glucosuria, with normal excretion of fluids administered in the perioperative period [11]. Given the variety of causes that lead to DI or just to polyuria in the postoperative period, it is important to clarify the etiology of the disease and correctly conduct a differential diagnosis, which allows administering pathogenetically correct and safe treatment.

Aim

to present a clinical analysis of a patient in the Endocrinology Department of Tver Regional Clinical Hospital with postoperative CDI.

Case Description

A 59-year-old female patient S. who lives in Tver was admitted to the Endocronology Department of Tver Regional Clinical Hospital on July 4th, 2019 with complaints of severe dry mouth, thirst, especially at night, weakness, drowsiness, frequent urination up to 5–6 times during the night; increased blood pressure (BP) to 180/110 mm Hg accompanied by tremor, frequent urination.

According to the patient's history, from the age of 20, she had complained of heart palpitations, clubbed fingers, narrowed field of vision, *flies before the eyes*. In July of that year, she had a brain CT which revealed a 15×17×22 mm formation in the cavity of the Turkish saddle (pituitary adenoma with intra-suprasellar growth). The patient was referred to a neurosurgeon who administered more tests which revealed an increased blood prolactin level of 51.17 ng/ml (normally 4.79–29.9), while the levels of insulin-like growth factor 1, somatotropic and adenocorticotropic hormones were within the normal ranges. During the ophthalmological examination, angiopathy of the retina of both eyes was diagnosed. In the same month, the patient was hospitalized to the Endocrinology Department for further examination, more detailed assessment and treatment planning. Taking into account the presence of prolactin-secreting pituitary macroadenoma, absence of clinically significant changes in perimetry data, and high risk of surgical treatment, conservative treatment was administered.

The patient was re-admitted to the hospital in July 2017 with the diagnosis of hyperprolactinemia, prolactin-secreting pituitary macroadenoma with intra- and suprasellar growth. The new brain CT scan showed pituitary adenoma of the previous size (15×19×17 mm), and chiasmal compression was detected. Ophthalmological examination revealed edema of the optic disc in both eyes. The patient refused the proposed surgical treatment of adenoma. She was observed by an endocrinologist on an outpatient basis. The woman received treatment with cabergoline (an agonist of dopamine receptors with a prolonged action) – 0.25 mg 2 times a week.

The disease progressed and a transnasal transsphenoid adenomectomy was performed in May 2019. In the early postoperative period, there was an improvement in vision, an increase in the volume of vision fields, but there was frequent urination and an episode of polyuria; and increased oral dryness was observed. Those symptoms were regarded as the development of diabetes insipidus. The patient was administered 60 micrograms of desmopressin daily, but refused to take the drug. The above-mentioned symptoms of the disease worsened, and the patient was readmitted to the Endocrinology Department in order to clarify and confirm the diagnosis of postoperative hypopituitarism and select therapy.

On admission, the patient's condition was estimated as satisfactory. Normal constitution, height — 165 cm, weight — 144 kg. BMI — 52.9 kg/m^2 corresponding to Grade 3 obesity. Skin of normal color, normal moisture, dry on the elbows. Narrow whitish striae on the skin of the abdomen. Visible mucous membranes — pink. Thyroid enlargement (Degree 1), dense, heterogeneous, painless. Parathyroid glands — not palpable. Symptoms of thyrotoxicosis and tetany — negative. On lung auscultation: breath sounds — harsh, no rales revealed. Pulse —76 BPM, rhythmic. BP — 135/90 mm Hg. Heart tones — muted, rhythmic, accent of tone II on the aorta. Tongue — moist with a white coating. Abdomen — soft and painless. Liver, spleen, and kidneys — not palpable. Costovertebral angle tenderness test — negative on both sides. Pulsation of the dorsal arteries of the foot — weakened on the right side. Skin of the feet — dry, peeling. Swelling of the shins and feet. Regular stools, smooth and soft. Diuresis — approximately 5.0 liters.

Blood biochemistry revealed hypercholesterolemia, hypertriglyceridemia (total cholesterol — 6.98 mmol/L, triglycerides — 3.90 mmol/L); bilirubin, transaminases, thymol turbidity test, total blood protein were within the normal ranges, urea — 5.0 mmol/L, creatinine – 90.6 mmol/L,GFR CKD-EPI — 60 ml/min/1.73 m^2, potassium — 4.4 mmol/L, calcium — 2.5 mmol/L, sodium — 123 mmol/L. Fasting and postprandial blood glucose levels did not exceed the normal ranges. Prolactin, somatotropic, thyroid-stimulating and free T4 levels and the diurnal rhythm of cortisol secretion were normal.

The patient's urinalysis showed low specific gravity, urinary sediment without pathology, and no glucose. To assess the kidney concentration capacity, the Zimnitsky urine test (renal osmoregulation function study) was done. According to its findings, the total diuresis was 6,500 ml, which was regarded as polyuria. Day diuresis was equal to night diuresis and amounted to 3,250 ml, there was nocturia. Fluctuations in specific gravity were from 1,003 g/L to 1,004 g/L, which was regarded as decreased kidney concentration capacity of hypostenuria type.

The complete blood count revealed an increased ESR to 55 mm/h, it later decreased to 20 mm/h.

Based on the data obtained, the patient was diagnosed with central diabetes insipidus, the state after transnasal transsphenoidal adenomectomy on prolactinomas of the pituitary gland.

In accordance with the diagnosis, desmopressin was administered: 0.1 mg at 8 a.m. and 0.2 mg at 10 p.m. The treatment resulted in a positive dynamics in the patient's condition: the frequency and volume of urination decreased, and during the night the frequency of urination decreased to 1–2 times.

Upon discharge, a repeated renal osmoregulation function study (Zimnitsky test) was performed. The total diuresis was 1,980 ml, the day diuresis was 810 ml, and the night diuresis was 1,170 ml. Fluctuations in the urine specific gravity ranged from 1,006 to 1,014. Consequently, the treatment was effective, polyuria was stopped, and the concentration capacity of the kidneys improved.

The patient was discharged with recommendations to continue the treatment started on an outpatient basis. Since our patient is still at a high risk of remission of postoperative CDI, which usually occurs 3–6 months after surgery, it is recommended to instruct the patient about the symptoms of water intoxication and measures for its prevention and treatment.

DISCUSSION

In this clinical case, there is a clear cause-effect relationship between the previous neurosurgical intervention in the hypothalamic-pituitary area for prolactin-secreting pituitary macroadenoma, when the manifestations of diabetes insipidus developed immediately after the operation (dry mouth, polyuria), and the effectiveness of administered therapy with a synthetic analog of vasopressin. These facts combined with laboratory and instrumental findings confirm the central type of diabetes insipidus.

It can be assumed that the analysis of this clinical case will improve the awareness of doctors about this pathology and will allow them to recognize and start treatment of CDI in a timely manner.

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