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Diabetes insipidus in the diagnosis of polyuria

Abstract

Diabetes insipidus is a rare condition, whereas polyuria may be a symptom of numerous other ailments. Polyuria intensifies thirst (polydipsia), which appears to be a natural reaction to an excessive loss of water in the organism. Before diagnosing rare conditions, hypoglycaemia and kidney failure must be excluded. Borderline cases must consult with an endocrinology specialist.

Key words: polyuria, polydipsia, diabetes insipidus

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Introduction

Diabetes insipidus (DI) is a rare illness caused either by vasopressin deficiency (central diabetes insipidus, also known as neurohormonal) or by a lack of renal canal sensitivity to vasopressin (nephrogenic diabetes insipidus) [1].

The prevalence of diabetes insipidus is one case per 25,000 population, with no sex difference. Central diabetes insipidus is the result of damage to the supraoptic nuclei in the hypothalamus, where vasopressin is secreted. In such a case, the damage leads to permanent DI. In rare cases, for example when a patient suffers either post-operative infundibulum hypothalamus damage or rear hypothalamus lobe damage (the area which transports and stores the neurohormone), the disorder may be a passing matter. Neurohormonal diabetes insipidus is caused in most cases by:

- hypothalamus tumours (craniopharyngiomas, invasive pituitary macroadenomas);
- hypothalamic-pituitary area inflammation;
- injury;

- post-operative condition or post-radiotherapy condition (RTH);
- ectopic secretion by other malignant tumours;
- empty sella syndrome [1, 2].

Moreover, neurohormonal diabetes insipidus may be idiopathic, either genetically or immunologically based.

Nephrogenic diabetes insipidus is caused by a genetic defect in the vasopressin receptors in the kidneys and occurs only in males. It may also occur in either acquired neuropathies, such as hypercalcaemia (e.g. hyperactive parathyroid glands) or hyperkalaemia (e.g. primary aldosteronism).

The clinical picture of diabetes insipidus is influenced by the following symptoms:

- excessive thirst (polydipsia);
- polyuria (passing > 4 litres of urine a day);
- low specific gravity of the urine (< 1,005; so-called diluted urine);
- frequent nightly urination and quenching of thirst;
- additionally, symptoms of hypothalamic-pituitary tumour may occur [1].

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Diagnosis of the disorder is determined by a two-stage dehydration test and a vasopressin test. First of all, this allows the exclusion of psychogenic-based polydipsia (psychogenic diabetes insipidus, thirst neurosis), when polyuria is caused by habitual excessive fluid intake. Furthermore, the test enables us to determine whether we are dealing with neurohormonal diabetes insipidus or nephrogenic diabetes insipidus (Table 1). The test is carried out in hospital, prior to excluding polyuria in diabetes.

The dehydration test is a urine concentration test which consists of the complete restriction of fluid intake. The test begins in the morning and the patient is weighed every 30 minutes. Simultaneously, the specific gravity (or osmolarity) of successive samples is calculated, as well as the plasma osmolarity. The test continues as long as the body mass reduces by 3% of the initial weight proportion or the concentration of sodium in the blood serum exceeds the upper limit of normal. The test usually takes a few hours and enables the calculation of the vasopressin in the blood serum. In central diabetes insipidus the vasopressin concentration is very low, whereas nephrogenic diabetes insipidus causes high vasopressin concentration. In central DI neither a urine specific gravity nor urine osmolarity increase is reported (osmolarity < 250 mOsm/kg) with a plasma osmolarity increase (norm: 275–190 mOsm/kg). On the other hand, in psychogenic polydipsia, once vasopressin is stimulated, urine specific gravity increases.

The vasopressin test appears in the second phase of the diagnostic process. It differentiates central diabetes insipidus from nephrogenic diabetes insipidus. In the dehydration test, as soon as successive urine samples do not reveal significant differences in osmolarity (< 10%), a vasopressin analog is admin-

istered, either orally (0.2 mg) or intranasally (20 µg). Only then can the specific gravity, osmolarity and volume of the successive portions of urine be calculated. If the urine concentration increases by at least 50% after desmopressin is administered, this indicates that we are dealing with central diabetes insipidus. However, a persistent decrease in urine specific gravity and its osmolarity suggests nephrogenic diabetes insipidus. In a case where a magnetic resonance imaging (MRI) of the head has not been performed on a patient before the test, such a procedure must absolutely be conducted [1].

The treatment of diabetes insipidus depends upon its cause. In the case that central diabetes insipidus is a symptom of a large hormonally inactive pituitary adenoma, what appears to treat the cause is a neurosurgical procedure through the transsphenoidal route. On the other hand, in the symptomatic treatment of diabetes insipidus we employ a substitution which involves an individually calculated dose of a long-acting vasopressin analog (desmopressin). The substance is administered via the intranasal or oral route. The effectiveness of the treatment can be evaluated easily: as soon as the clinical symptoms disappear, plasma osmolarity returns to normal and the sodium in the serum normalizes. If diabetes insipidus results from acquired kidney damage, care of the underlying illness and symptomatic treatment seem to be essential (with appropriate hydration and fluid deficiency correction). Any symptoms of diabetes insipidus caused by electrolyte disturbances disappear as soon as the disturbances are equalized. In diabetes insipidus resulting from genetic defects in the vasopressin receptors, what appears to be a basis for treatment is an appropriate diet with sodium restriction and a thiazide diuretic. If there is a partial sen-

Table 1. Differential diagnosis of psychogenic diabetes, central diabetes insipidus and nephrogenic diabetes insipidus based on the results of dehydration and vasopressin tests

	Thirst neurosis	Central diabetes insipidus (neurohormonal)	Nephrogenic diabetes insipidus
Dehydration test (urine concentration test)			
Urine specific gravity [g/ml]	Gradually increases	< 1,005	< 1,005
Urine osmolarity	Gradually increases to meet the norm	< 250 mOsm/kg	< 250 mOsm/kg
Vasopressin concentration in the plasma	Initially low, increases	Low	High
Vasopressin test (desmopressin 0.2 mg PO)			
Urine specific gravity	There is no indication for the test*	Increases by ≥ 50% (200–400%)	Low, does not increase

*due to satisfactory results of the dehydration test

sitivity to vasopressin, large doses of hormone seem appropriate [1]. Prognosis depends upon the cause of the disorder but is usually auspicious. Even untreated diabetes insipidus does not pose any threat to a patient's life, providing the patient drinks plenty of fluids. In cases of unconscious patients (such as those with an injury or after brain area surgery) and patients with a thirst disorder, fluid balance should be a particular focus. Substitution treatment allows patients to perform normal life activities without troublesome symptoms of the illness.

Case report

On 2 November 2010, a 65-year-old woman patient with tumours of both kidneys (potentially malignant) was admitted after an incident of gastrointestinal bleeding to the ward of the day hospice in Bydgoszcz with symptomatic treatment continuation and further care in mind. Moreover, the patient suffered depressive disorders, bipolar disorder, secondary anaemia and diabetes mellitus Type 2 treated with insulin. Lesions in both kidneys had been detected two years before and since then the patient had been closely monitored by urologists at the Oncology Centre. She did not qualify for an operation. While she was monitored, the doctors observed normal creatinine values. On 25 October 2010, when in the surgical unit of a City Hospital, she underwent a CAT scan on her head, which demonstrated cerebral oedema features, and pituitary gland extension to 13 mm (suspicion of a pituitary gland tumour).

When the patient was admitted to the unit, her condition was very serious. She was barely conscious and illogical. Additionally, she experienced severe renal failure (creatinine 4.9 mg/dl) in the polyuria phase with diuresis of 3–5 l/day and erratic BMs. The patient reported dyspnoea and pain in her abdominal cavity. A clinical examination revealed low sensitivity of the abdominal membranes and moderate rest dyspnoea, without features of stasis over the lung fields. Owing to the malady and the medical condition of the patient, we administered the following procedures: subcutaneous hydration in accordance with fluid balance, diuresis forced by furosemide (40 mg/day IV), and 2.5 mg of hypodermically injected morphine in the case of either acute pain or dyspnoea. Omeprazole (20 mg) continued to be administered and the steroidotherapy (dexamethasone administered intravenously, 8 mg/day) intensified due to the cerebral oedema displayed in the CAT scan images. Soon, her medical condition improved and this facilitated conscious contact with the patient. A creatinine

concentration decrease was reported and the volume touched the norm (4.9 → 1.1 mg/dl) without ionic disturbances. However, polyuria and excessive thirst persisted (up to 5 l/d) and this provided the basis for maintaining a Foley catheter in the urinary bladder. Owing to obstinate astriction, manual removal of an impacted stool was necessary but as soon as intensified pharmacological treatment was implemented, bowel evacuation normalized. Badly-managed glycaemia and intense hunger were causes of a dexamethasone dose reduction (to 2–2–0 mg PO). The patient's medical condition was stabilized. However, sluggishness and malaise appeared and venlafaxine was administered with a morning dosage of 150 mg. Additionally, the thyroid hormone level was tested and the results revealed the following: TSH 0.79 μ IU/ml (N: 0.27–4.20), FT3 1.1 pmol/l (N: 3.1–6.8), FT4 0.7 pmol/l (N: 12–22). Secondary hypothyreosis was identified and L-thyroxine was administered with an initial dosage of 25 μ g/day. Since pituitary adenoma was diagnosed, the patient was assessed by an endocrinologist, who confirmed secondary hypothyreosis and increased the L-thyroxine dosage to 50 μ g/day. The specialist found neither Cushing's syndrome symptoms nor acromegaly. To determine and differentiate the causes of the intense thirst and polyuria, he decided to conduct a further investigation to calculate urine specific gravity. When this turned out to be low (1,003 g/ml), 0.1 mg of desmopressin was implemented, which led to diuresis reduction (to 1.75 l within one day) and the urine specific gravity increased. Such treatment facilitated catheter removal from the urinary bladder, which significantly improved the quality of the patient's everyday life. Moreover, we applied rehabilitation, during which the patient performed both active and passive activities and maintained a sitting position. We also attempted a change from a lying to a standing position. She then tried to walk with assecuration. The patient was discharged in good condition.

Discussion

One of the main problems in the aforementioned case was excessive urinating. Polyuria occurs if a patient passes more than 2,500 ml of urine a day and it may be a symptom of numerous illnesses. In such a case, renal status must be checked, since diuresis may result either from uraemia or the polyuria phase of acute renal failure. Moreover, hyperglycaemia should also be excluded because glycosuria leads to osmotic diuresis. Polyuria also accompanies hypercalcaemia and psychogenic polydipsia. Finally, polyuria may

result from central diabetes insipidus or nephrogenic diabetes insipidus (discussed above) [3].

The patient experienced many ailments which could have contributed to the polyuria, and what follows to polydipsia. Before the patient was admitted to the hospice, she had gastrointestinal bleeding which brought about acute renal failure. The descending course of such a dysfunction is polyuria. Furthermore, the steroid therapy, administered owing to suspicion of brain metastasis, together with insulin-treated diabetes, led to poorly-managed blood sugar which could also have been a cause of the polyuria and intense thirst. In addition, the CAT scan of her head demonstrated pituitary extension and implied a tumour which contributed to central diabetes insipidus. The reported case does not allow us to elaborate on features of the tumour. However, we are inclined to believe that there was metastasis either from the site of disease progression (lack of histopathology examination results) or from the hormonally inactive adenoma. Metastases to the pituitary gland are not frequent (less than 1% of patients with neurosurgical recommendations and approximately 5% of autopsied patients diagnosed with cancer) and usually manifest disseminated cancer [4]. Tumours which most often give rise to metastases for the organ include breast cancer and lung cancer [4, 5]. Metastases are usually located in the rear lobe of the pituitary gland or in both frontal and rear lobes (84.6% of 201 cases of metastases); however, frontal metastases comprise 15.4% of all cases [6]. Such locations of metastases make us think that their symptoms cause diabetes insipidus [4, 6].

A diabetes insipidus diagnosis should be preceded by a dehydration test. In the reported case, the patient was admitted to the hospice in a very bad condition. She experienced dehydration symptoms, renal failure and unlevelled diabetes and a dehydration test could have worsened her condition. A urine specific gravity calculation seemed a much easier and more available test. Since there was a diabetes insipidus suspicion, the test was administered. The virtually immediate and good reaction to vasopressin analog treatment confirmed the initial diagnosis. Desmopressin in the treatment also gave a visible effect, since the diuresis and thirst diminished after a few hours. Undeniably, this improved the patient's comfort and made medical assistance easier.

A pituitary gland tumour diagnosed with medical imaging facilitates a full evaluation of the hormonal functions of the organ. In the reported case, the patient's condition restricted examinations to a TSH

concentration test and a thyroid hormones test. Since there were no manifestations of either acromegaly or Cushing's disease, it was decided to abandon tests which would calculate the concentration of growth hormone, ACTH and cortisol. Moreover, the patient took dexamethasone, which impedes a proper interpretation of pituitary-adrenal axis hormone concentration test results. The nature of the tumour and the spread of the disease are not confirmed (the good clinical status of the patient and the lack of progression speak against spread); it may be an accidentally detected regular pituitary adenoma, which would require further diagnostics and perhaps even neurosurgical treatment. Full evaluation of the hormonal function of the pituitary gland and hypothalamic-pituitary area imaging by means of a scanning procedure may be considered, providing the patient's condition normalizes, and depends upon further progression of the underlying disease. At times, numerous symptoms and treatment are reflected in the life span of patients under palliative care. The kind of acute renal failure treatment the patient was given was neither expensive nor troublesome and once her clinical condition normalized and a low-cost test had been recommended, her condition improved considerably. Since then, she has reached nearly full capacity after home rehabilitation, which has enabled her to function normally. After a few months, due to the severity of polyuria, a hospice doctor increased the dose of desmopressin which led to urine output reduction to 1.5 l a day. Full diagnostics of the pituitary hormone are planned to be conducted at the Endocrinology Outpatient Clinic at the Oncology Centre in Bydgoszcz.

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