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Hypopituitarism - Not such an obvious symptom

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Abstract

The pituitary gland is the central endocrine gland that controls the entire human endocrine system.

Materials and methods

To write this article, data bases such as PubMed and Google Scholar were searched using the following terms: hypopituarism, cerebral lymphoma, hypogonadism, hypothyroidism.

Despite its small size, it dominates over the other endocrine glands. The pituitary gland is located inside the skull, in the so-called Turkish saddle. It secretes a number of hormones: growth hormone (GH), prolactin (PRL), adrenocorticotropic hormone (ACTH), thyrotropic hormone (TSH), folliculotropic hormone (FSH), luteinizing hormone (LH), melanotropin (MSH), oxytocin, vasopressin.

This paper presents the case of a diagnostic and therapeutic challenge of a young 33-year-old man from Poland, who initially reported few symptoms and eventually turned out to be an interesting endocrine case.

Keywords

Hypopituarism, cerebral lymphoma, uremia, tertiary hypothyroidism, hypogonadism

The case presented

A young man, 33 years old, with no history of chronic diseases or medications, presented to his primary care physician because of persistent dry mouth. The dry mouth was so bothersome that the patient drank very large amounts of water to reduce his symptoms. In the outpatient setting, a rheumatology and ENT diagnosis was made, to rule out Sjorgen syndrome. Due to the large amount of fluid intake and increased diuresis (5-6l/day), the patient was referred to the nephrology clinic. Attention was drawn to the general urine examination, which determined a urine specific gravity of <1.005 (norm 1.012-1.026) and hypernatremia in peripheral blood plasma of 149 mmol/l (norm 136-145 mmol/l). The patient was referred to the endocrinology outpatient clinic with suspicion of a hormonal cause of the reported symptoms and then to the hospital for further diagnosis. On admission to the hospital, the endocrine function of the pituitary gland and other endocrine glands was determined (Table 1).

Table 1. Hormonal results of the patient during the first hospitalization compared with current norms.

	Findings	**Laboratory standards**
Specific gravity of urine	<1,005	1,012-1,026
Serum osmolality	299 mosm/kgH2O	285-300
ACTH	15,75 pg/ml	7,20-63,6
Cortisol	16,89 ug/dl	5,27-22,45
FSH	4,17 mlU/ml	1,40-18,10
LH	3,42 mlU/ml	1,5-9,3
Prolactin	3,2 ng/ml	2,1-17,7
Growth hormone	0,22 ng/ml	0,0300-2,470
TSH	1,7 miU/L	0,55-4,78
Estradiol	26,47 pg/ml	0,00-39,80
Testosterone	341,65 ng/dl	165-753

Based on the tests performed, the suspicion of simple uremia was raised. During hospitalization, the diagnosis of uremia was carried out. A dehydration test was performed between 08:00 and 14:00, but the test was discontinued due to very severe drying of the mucous membranes reported by the patient. During the test, the patient did not feel the need to micturate, and a weight loss of 0.6 kg was observed. There was an increase in serum osmolality from 304 to 311

mosm/kgH2O, serum sodium from 146 to 149 mmol/L and urine specific gravity to 1.015. Due to the inconclusive results, the test was repeated. To reduce the patient's reported discomfort, the test was performed at night. During the test, an analogous increase in sodium concentration, plasma osmolality and a decrease in body weight of more than 3% were observed. After the test, desmopressin was administered, which resulted in a decrease in the feeling of thirst, the amount of urine passed, a decrease in serum sodium concentration and an increase in urine specific gravity. Based on the tests performed, a diagnosis of central simple uremia was made. Treatment included desmopressin 60ug 1 tabl. in the morning, half tabl. in the evening. The patient was referred for an MRI study of the pituitary gland. The examination did not describe focal changes in the pituitary gland and pituitary stalk. Attention was drawn to a well-demarcated, heterogeneous oval lesion with calcifications located within the pineal gland, which does not have the character of a typical cyst and requires further diagnosis. After about 7 months, an MRI scan of the head was repeated. The examination noted an enlargement in the size of the lesion, which convexed toward ventricle III (Figure 1). A suspicion of a lesion of the nature of a pineal gland- pinealoma (Figure 2).

Another contact with the patient was obtained only after six months. The patient reported to the endocrinologist's office with symptoms such as weight loss (about 10 kg), chronic fatigue, loss of appetite, lack of libido, low blood pressure values in home measurements, muscle tremors, cold attacks and problems with concentration and memory. Adrenal insufficiency was suspected, and the patient was referred to the hospital for urgent diagnosis. During hospitalization, pituitary and peripheral hormone tests were again performed (Table 2).

Table 2. Hormone test results of a patient after referral to the hospital with suspected adrenal insufficiency.

	Findings	**Laboratory standards**
ACTH	10,20 pg/ml	7,20-63,6
Cortisol	1,4 ug/dl	5,27-22,45
FSH	<0,30 mIU/ml	1,50-12,40
LH	<0,30 mlU/ml	1,7-8,6

	Findings	Laboratory standards
Prolactin	870 mIU/l	86-324
IGF-1	59,9 ng/ml	114-247
TSH	1,2 mIU/l	0,27-4,20
fT3	0,92 pg/ml	2,02-4,43
fT4	0,31 ng/dl	2,02-4,43
Testosterone	<0,20 ng/ml	2,8-8

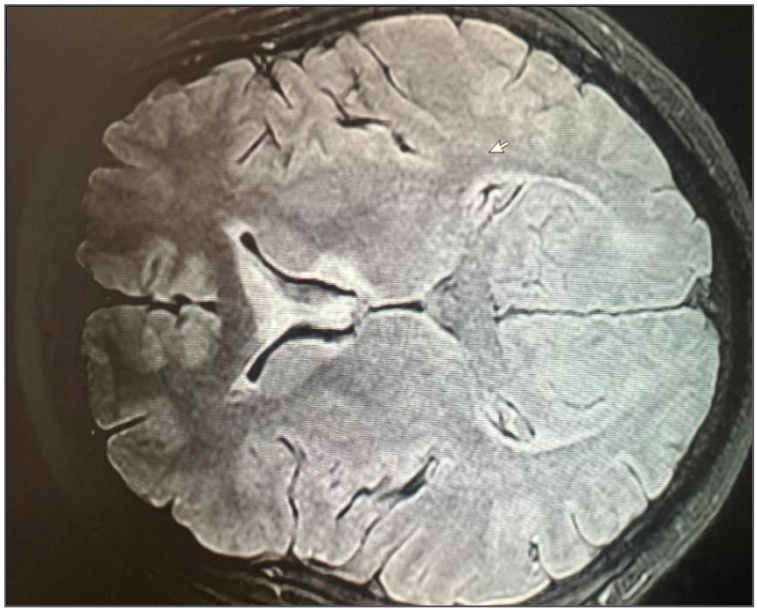

Figure 1. MRI scan of the head (cross-section of the brain) with well-demarcated areas of ventricle III.

Source: Own study. Department of Radiology, Lublin Regional Specialized Hospital 2023.

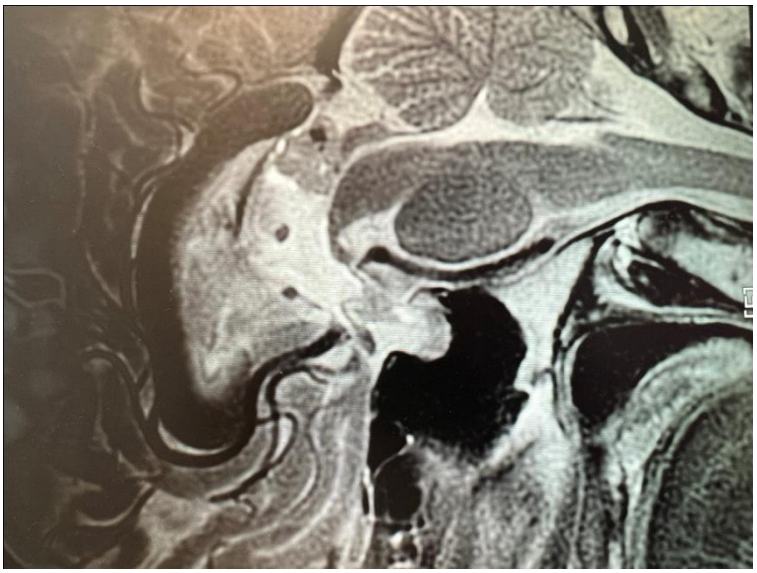

Figure 2. MRI scan of the head (sagittal section of the brain) pineal gland – pinealoma.

Source: Own study. Department of Radiology, Lublin Regional Specialized Hospital 2023.

On the basis of the tests performed, the diagnosis was made of hypopituitarism with deficiency of sex hormones, insulin-like growth factor, secondary adrenal insufficiency and tertiary hypothyroidism. MRI of the head and pituitary gland was performed again, in which areas of pathological enhancement with diffusion restriction were described periventricularly, in the corpus callosum, in the pituitary funiculus, and in the pineal gland. The lesions also spread to the lining of the lateral ventricles. In the funnel they model the optic nerve junction. Progression of lesions compared to previous studies. Lesions within the pituitary itself are not described. The image suggests lymphoma. The diagnosis was expanded to include a CT scan of the chest and abdomen - with no palpable abnormalities. The patient was referred to the Department of Neurosurgery, where a biopsy of the tumor was performed. The patient was diagnosed with brain lymphoma. From the hospital the patient was discharged with the recommendation to take hydrocortisone, levothyroxine, testosterone gel. The patient was referred to the Clinic of Tumors of the Nervous System in Warsaw for treatment.

Discussion

Hypopituitarism is a set of symptoms associated with a deficiency of one or more pituitary hormones. Complete pituitary hypopituitarism is said to occur when all hormones are deficient. Hypopituitarism occurs with a frequency of 350-455 per million, the annual incidence is estimated at 42.1 per million. The most common growth hormone deficiency observed in hypopituitarism is found in 1 in 3-4 thousand people. [1,2,3,26] Hypopituitarism has been associated with increased mortality, particularly due to cardiovascular and cerebrovascular diseases. [19,20,27]

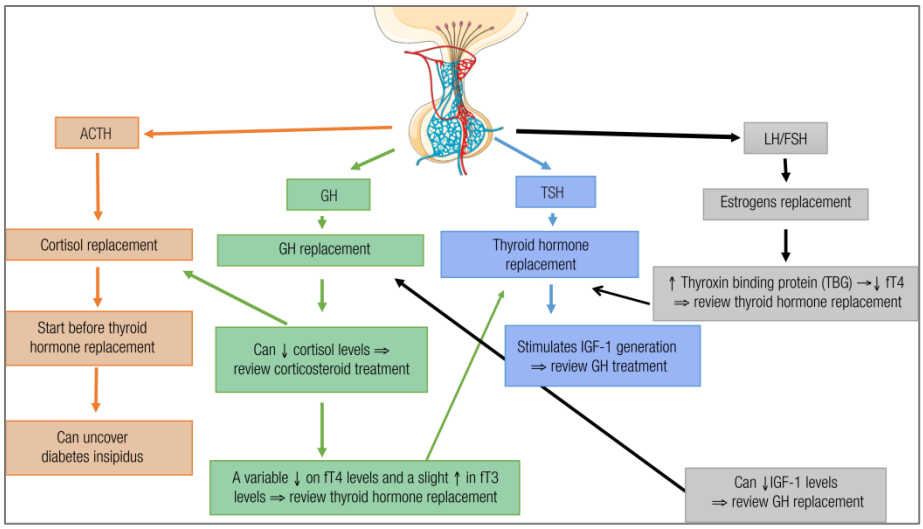

Figure 3. Pituitary hormone replacement and interactions.

Source:Management of hypopituitarism: a perspective from the Brazilian Society of Endocrinology and Metabolism, Scielo Brasil Arch. Endocrinol. Metab. 65 (2) Mar-Apr 2021

There are many causes of hypopituitarism, the most common include tumors of the hypothalamic-pituitary region, inflammatory lesions of the brain, traumatic brain injury, iatrogenic effects, pituitary ischemia, vascular disorders, congenital disorders, and isolated hormone deficiencies.[4,13] Symptoms of hypopituitarism can be varied. Symptoms are influenced by the site of pituitary damage, the age at which the damage occurred, gender and the duration of deficiencies of specific hormones. The most common symptoms include menstrual disorders with infertility, lack of lactation after childbirth, impotence, pubic and axillary hair loss, weakness, lethargy, low blood pressure, orthostatic hypotension, hypoglycemia, dry and pale skin, easy freezing, weight loss, delayed growth in children. In the case of hypopituitarism, which regulates the other endocrine glands, the functioning of each

hormonal line should be checked. [5,7,16,17] To evaluate beyond the level of a particular hormone itself, a number of additional specific tests are used. In the case of our patient, only simple uremia was initially suspected, which was differentiated from central uremia, renal uremia and psychogenic uremia. Thanks to a dehydration test and then with desmopressin, the central cause of the uremia could be confirmed. With the cooperation of specialists such as a rheumatologist, laryngologist specialist and nephrologist, the search was narrowed to the pituitary gland.[4,6,8,9]

Somatoropin hypopituitarism in adults is less pronounced than in children. In adults, a decrease in muscle mass, fat gain, and a higher risk of fractures through decreased bone mineral density are noteworthy. Symptomatic hypoglycemia, lipid disorders may occur. [6,18] In the diagnosis of growth hormone deficiency, low levels of the hormone (GH) that do not increase after intravenous administration of short-acting insulin or after administration of GHRH are considered in the evaluation. Insulin-like growth factor (IGF1) levels are also used in the determination of pituitary somatotropin function.[10,11,24,25] In deficient or abnormal adrenocorticotropin (ACTH) secretion, cortisol levels may initially be normal. Insufficient secretion of ACTH is experienced in stressful situations (stress, illness, fever, physical exertion). A helpful way to diagnose secondary adrenal insufficiency is to determine morning serum cortisol (between 8:00 and 9:00 am) and ACTH levels. A stimulation test with CRH is also used, after administration of which cortisol levels should increase.[12,13,14,15] In tertiary hypothyroidism, reduced TSH and fT4 levels are observed. It results from the absence or insufficient levels of thyroliverine (TRH). It should be differentiated from secondary hypothyroidism. Symptoms are less marked than in primary hypothyroidism.[21,22,23] Hypogonadotropic hypogonadism (HH), also referred to as central or secondary hypogonadism, can be congenital or, more commonly, acquired. Acquired hypogonadism is very common in patients with hypopituitarism due to pituitary adenomas, their surgical treatment or radiotherapy, usually accompanied by other pituitary hormone deficiencies. In adults, clinical features of hypogonadism in men include reduced libido, erectile dysfunction and infertility, and in women oligomenorrhea or absence of menstruation, reduced libido, dyspareunia and infertility, which may be exacerbated by coexisting hyperprolactinaemia and adrenal/ovarian androgen deficiency. Long-term estrogen deficiency can cause regression of secondary sexual characteristics, urinary symptoms, decreased muscle mass and bone density, and dyslipidaemia. Similarly, long-term testosterone deficiency is associated with an increased risk of metabolic

disorders.[19,28,29,30] The main treatment, if possible, is to remove the cause of hypothyroidism. The second and most important treatment, is hormone replacement, compensating for existing hormonal deficiencies. Appropriate peripheral hormones are used: oral corticosteroids (e.g. Hydrocortison) for secondary adrenal insufficiency, oral preparations of l-thyroxine for thyroid hormone deficiency, preparations of testosterone (for men) and estrogen with gestagens (in premenopausal women) for secondary gonadal insufficiency, recombinant human growth hormone in children with adhesion deficiency. Substitution treatment usually requires chronic treatment, in the situation of permanent pituitary damage is carried out for life, and treatment with a growth hormone preparation - until the completion of the growth process. It is very important to remember and inform patients that in certain situations (infections, stress) it is necessary to increase the doses of glucocorticosteroids taken. Discontinuation of compensatory treatment without consulting a doctor is a threat to health and life.[18]

Summary

This paper presents a case of diagnostic and therapeutic challenge to a young 33-year-old man from Poland, who initially reported few symptoms, but eventually turned out to be an interesting endocrine case. The case demonstrates that initial symptoms can be non-specific and that specialists in various fields of medicine must work together to make a definitive diagnosis and successfully treat the patient.

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