



Diagnostic dilemmas in a patient with anaemia. Empty sella syndrome — a case report

Dylematy diagnostyczne u chorego z niedokrwistością.
Zespół pustego siodła — opis przypadku

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Abstract

Empty sella syndrome is defined as a group of clinical symptoms developing as a result of herniation of the subarachnoid space within the sella, which is often associated with some degree of flattening of the pituitary gland. It is usually recognized incidentally during brain imaging studies performed for different indications, and in most cases this condition is asymptomatic. However, it may result in impairment of various endocrine glands, for which the pituitary gland produces its crinins. Despite the high incidence of empty sella syndrome (up to about 5% of the population) it is commonly ignored as the cause of various symptoms. We present a case of 55-year-old patient admitted to the department of internal medicine due to anaemia and progressive weakness, with recognized hypothyroidism and adrenal gland insufficiency in the course of empty sella syndrome. (*Pol J Endocrinol* 2010; 61 (4): 400–403)

Key words: anaemia, hypothyreosis, adrenal gland insufficiency, empty sella syndrome

Streszczenie

Zespół pustego siodła definiuje się jako grupę objawów klinicznych rozwijających się w wyniku wpuklenia się przestrzeni podpajęczynówkowej do siodła tureckiego, co często powoduje ucisk przysadki. Zespół ten zwykle rozpoznaje się przypadkowo podczas badań obrazowych mózgu przeprowadzonych z różnych wskazań i w większości przypadków nie powoduje on żadnych objawów. Czasami jednak skutkuje on zaburzeniami czynności różnych gruczołów wydzielania wewnętrznego, spowodowanymi upośledzeniem produkcji przez przysadkę hormonów tropowych dla tych gruczołów. Mimo stosunkowo częstego występowania zespołu pustego siodła (u ok. 5% populacji), zwykle nie bierze się go pod uwagę jako możliwej przyczyny różnych symptomów. W niniejszej pracy przedstawiono przypadek 55-letniego pacjenta, przyjętego na oddział chorób wewnętrznych z powodu niedokrwistości i postępującego osłabienia, u którego rozpoznano niedoczynność tarczycy i niewydolność kory nadnerczy w przebiegu zespołu pustego siodła.

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Słowa kluczowe: niedokrwistość, niedoczynność tarczycy, niewydolność kory nadnerczy, zespół pustego siodła

Introduction

Empty sella syndrome, documented for the first time in 1951 by Busch et al., is defined as a group of clinical symptoms developing as a result of herniation of the subarachnoid space within the sella, which is often associated with some degree of flattening of the pituitary gland [1–3]. There are two classical types of empty sella syndrome: primary and secondary. The aetiology of the primary empty sella (PES) is associated with congenital incomplete formation of the sellar diaphragm, which is associated with increased intracranial pressure that can be stable or intermittent. In the case of secondary empty sella syndrome, it may be caused by various pathological conditions such as: pituitary adenomas under-

going spontaneous (ischaemia, haemorrhage) or induced (pharmacotherapy) necrosis or by radiotherapy, neurosurgery, or infections [4]. PES is more common in women with arterial hypertension and is usually found incidentally during CT/MRI examination performed for the other indications. In autopsies, PES occurrence rates amount to 6–20% [5]. In most cases, the clinical course is asymptomatic. In 20–50% of cases, patients present with endocrine abnormalities: partial hypopituitarism (5%), total hypopituitarism (25%), or hyperprolactinaemia (10%) [4–7]. Slow development of hypopituitarism constitutes the most common feature of described clinically-overt cases. The insidious onset significantly delays the diagnosis and makes it difficult and complicated.



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A case report

A 55-year-old man was admitted to hospital in March 2009 because of anaemia, progressive weakness, weight loss, dizziness, and musculoskeletal pain with progressing intensity for several months. The patient's history included: peptic ulcer disease, haemorrhage of the upper GI tract, chronic pancreatitis (the patient had formerly been hospitalized in the Surgery Department several times), and diabetes mellitus type 2 (diagnosed two years earlier). In 1996 (at the age of 42) the patient had myocardial infarction, which appeared to be the first symptom of coronary artery disease. In 2002 he underwent percutaneous coronary angioplasty of the circumflex branch of the left coronary artery and the marginal branch of the right coronary artery, along with a stent implantation into the anterior descending artery. Four months before admittance to the hospital the patient discontinued treatment with bisoprolol and nitrates because of low blood pressure. It is worth noting that the patient's mother had a history of lung cancer. Despite this fact, the patient smoked 30–40 cigarettes daily. His laboratory findings (performed ambulatory) included anaemia (haemoglobin level of 10.5 g/dL) and positive occult blood test. The patient's clinical and family history along with the results of the laboratory findings suggested that his complaints may have resulted from cancer.

In the physical examination there were no significant abnormalities except attenuation of tendon reflexes in the lower extremities and disturbances of superficial sensibility of the left upper extremity, corresponding to radial nerve damage.

In routine laboratory findings (Table IA and IB) we found anaemia, low iron level, normal total cholesterol, LDL cholesterol, and triglyceride levels. The occult blood test was negative. We did not reveal the presence of parasites in the stool. The level of antinuclear antibodies was within the normal range. Radiological examinations (chest x-ray, ultrasound of: abdominal cavity, pelvic cavity, and thyroid gland, and CT of abdominal cavity) and oesophagoscopy of the upper GI tract showed no significant abnormalities except many calcifications in the pancreas (probably as a result of chronic pancreatitis) and hiatal hernia. Since laboratory and radiological examinations did not explain the source of the patient's complaints, we considered hormonal disturbances in differential diagnosis. Laboratory tests of the pituitary — thyroid axis (Table II) suggested secondary hypothyroidism. An additional test of the pituitary — adrenal axis, pituitary - gonadal axis, and prolactin level showed diminished endocrine function of the pituitary gland (Table II). MRI imaging of

Table IA. Results of laboratory findings

Tabela IA. Wyniki badań laboratoryjnych

Blood cell count	Results
Leucocytes ($\times 10^3/L$)	7.2
Erythrocytes ($\times 10^6/L$)	3.8
Haemoglobin level [g/dL]	11
Hematocrit (%)	32.4
Blood smear	
Neutrophiles (%)	64.2
Basophiles (%)	3.1
Eosinophiles (%)	9.2
Lymphocytes (%)	6.4
Monocytes (%)	3.6
Serum level of	
Phosphorus [mg/dL]	4.2
Total calcium [mg/dL]	9.7
Sodium [mmol/L]	139
Potassium [mmol/L]	4.3
Iron [μ g/dL]	49
Total protein [g/L]	6.1
Bilirubin [mg/dL]	0.4
Creatinine [mg/dL]	0.83
Glucose [mg/dL]	67
HbA _{1c} (%)	6.1

Table IB. Results of laboratory findings

Tabela IB. Wyniki badań laboratoryjnych

Serum activity of	Results
ALT [U/L]	11
SGOT [U/L]	23
GGTP [U/L]	16
AP [U/L]	72
sAlpha-amylase [U/L]	61
CPK [U/L]	94
Serum level of	
Antibody ds DNA [IU/mL]	14.1
ANA [RU/mL]	3.8
antigen Ca 19.9 [u/mL]	<3
Vitamin B ₁₂ [pg/mL]	280
Folic acid [ng/mL]	4.8
Total cholesterol [mg/dL]	164
HDL [mg/dL]	46
LDL [mg/dL]	103
TGL [mg/dL]	74

Table II. Results of hormonal assay

Tabela II. Wyniki badań hormonalnych

Hormone	Serum level	Range
TSH [uIU/mL]	0.28	(0.35–5.0)
fT ₃ [pmol/L]	2.9	(4–8.3)
fT ₄ [pmol/L]	3.8	(9–20)
ACTH [pg/mL]	28.1	(10–60)
LH [IU/L]	0.84	(1.5–10)
Prolactin [mIU/L]	560	(78–461)
DHEAs [ug/dL]	93.8	(130–410)
Testosterone [nmol/L]	0.2	(8.2–34)
Cortisol (8.00) [ug/mL]	1.4	(6–28)
Cortisol (18.00) [ug/mL]	0.5	(4–15)

the pituitary gland suggested the occurrence of a subarachnoid pouch in the sellar and suprasellar region. The anterior lobe of the pituitary gland was significantly thinned, hypothalamic infundibulum was displaced by a subarachnoid pouch in the right side, and compression of the optic chiasm was observed. The patient was provided with levothyroxine (50 ug/24 h) and hydrocortisone (20 mg/24h). After seven days of hormonal supplementation, significant improvement in the patient's clinical condition was observed. The patient was seen by physicians from the Neurosurgery Department, who decided to continue with noninvasive treatment. Then patient was systematically seen and evaluated at an Outpatient Ambulatory Clinic. Two months later the patient complained of blurred vision (mainly on the right side) and vertigo, which were absolute indications for surgical intervention. The patient was operated with the use of endoscopic technology without any complications. Five months after surgical treatment the patient feels well and does not report any complaints. The results of laboratory findings are within the normal range (Table III).

Discussion

As was already stated, PES may be clinically asymptomatic and discovered as an „incidental” finding. On the other hand, it may produce symptoms associated with diminished endocrine function of the pituitary gland (ranking from mild insufficiency to severe hypometabolic crisis) or with severe intracranial hypertension and rhinorrhea [8]. In the case of the asymptomatic course, patients are unlikely to develop progression of endocrine or neurologic abnormalities in a follow up, and results of radiological examination tend to remain unchanged. It is reasonable to re-evaluate patients every

Table III. Results of laboratory findings 5 months after surgical procedure and during thyroid and adrenal gland hormone supplementation

Table III. Wyniki badań laboratoryjnych wykonanych 5 miesięcy po zabiegu chirurgicznym, w trakcie substytucyjnego leczenia niedoczynności tarczycy i kory nadnerczy

Laboratory finding	Result	Range
TSH [uIU/mL]	0.5	(0.35–5.0)
fT ₄ [pmol/L]	16	(9–20)
Cortisol (8.00) [ug/mL]	14	(6–28)
Erythrocytes ($\times 10^6/L$)	4.5	(3.5–5.3)
Hemoglobin level [g/dL]	13.5	(11–18)

24–26 months [4]. There are many clinical conditions that could promote the onset of secondary empty sella, such as: obesity (coexistence of hypercapnia increases the intracranial pressure), pregnancy (coexistence of hypoplastic sellar diaphragm and higher pituitary volume of up to 2–3 times, particularly in the case of multiple pregnancy), diabetes mellitus type 2, arterial hypertension, or the use of some drugs [9–11]. Weakness (with coexistence of anaemia) was the primary complaint of our patient. His clinical and family history strongly suggested neoplastic disease. With this suspected diagnosis, the patient was admitted to the Department of Internal Medicine. However, anaemia is also a frequent finding in hypopituitarism, and treatment with levothyroxine and hydrocortisone leads to a rapid improvement in haemoglobin levels [12]. The second most common laboratory alteration in patients with PES is slight hyperprolactinaemia with the association of secondary hypogonadism (observed in our patient) [4]. The third common alteration (not seen in our patient) is hyponatraemia to varying degrees. Hypopituitarism is a frequently overlooked cause of severe hyponatraemia [13]. According to Diederich et al., unrecognized hypopituitarism is the cause of about 20% of cases of that alteration [14]. The presented case is a good example of the diagnostic dilemmas of both anaemia and empty sella syndrome. Differential diagnosis of anaemia had lasted for at least several months before admittance to our department. It appeared that the key point in the diagnostic process was the exclusion of neoplastic disease, even though the occult test was positive, and so was the test for endocrine abnormalities — laboratory findings that suggested dysfunction of the pituitary gland and determined the diagnostic and therapeutic management.

Despite the high prevalence of PES (about 5% of the population) [15], this condition is frequently overlooked

as the cause of various clinical symptoms. It should be emphasized that this disease is a multifaceted condition. On one hand it may be clinically silent, but on the other it may lead to endocrine deficiency of varying degrees. In the case of our patient, we faced the problem of hypothyroidism and adrenal insufficiency, which were direct causes of anaemia.

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