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Wernicke-Korsakoff syndrome in the course of thyrotoxicosis — a case report

Zespół Wernickego-Korsakowa w przebiegu nadczynności tarczycy — opis przypadku

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Abstract

Wernicke-Korsakoff syndrome (also called Wernicke's encephalopathy) is a potentially fatal, neuropsychiatric syndrome caused most frequently by thiamine deficiency. The three classic symptoms found together are confusion, ataxia and eyeball manifestations. Memory disturbances can also be symptoms. Wernicke's encephalopathy mainly results from alcohol abuse, but also from malnutrition, cancer, chronic dialysis, thyrotoxicosis and, in well-founded cases, encephalopathy associated with autoimmune thyroid disease (EAATD). The coexistence of many factors makes a proper diagnosis difficult, delays appropriate treatment and consequently reduces the chance of complete recovery.

We present the case of a 53 year-old female with Wernicke's encephalopathy caused by chronic malnutrition, surgical operation, as well as thyrotoxicosis. She received treatment with intravenous thiamine administration and also anti-thyroid treatment which caused satisfactory regression of her neurological symptoms. **(Pol J Endocrinol 2011; 62 (2): 178–180)**

Key words: *Wernicke-Korsakoff syndrome, thiamine deficiency, thyrotoxicosis*

Streszczenie

Zespół Wernickego-Korsakowa (nazywany także encefalopatią Wernickego) jest potencjalnie śmiertelnym zespołem neurologicznym, spowodowanym najczęściej niedoborem tiaminy. W skład klasycznej triady objawów wchodzą: ataksja, splątanie oraz zaburzenia gałkoruchowe. Obserwuje się również zaburzenia pamięci świeżej, będące objawami zespołu Korsakowa. Encefalopatia Wernickego jest wynikiem przede wszystkim nadużywania alkoholu, ale również niedożywienia, chorób nowotworowych, przewlekłej dializoterapii czy tyreotoksykozy. Współistnienie wielu czynników utrudnia postawienie właściwej diagnozy, opóźnia podjęcie stosownego leczenia, a w konsekwencji redukuje szanse całkowitego wyzdrowienia. Analizując przyczyny encefalopatii, w uzasadnionych przypadkach należy również rozważyć możliwość istnienia encefalopatii związanej z chorobami autoimmunologicznymi. Przedstawiamy opis 53-letniej kobiety, u której encefalopatia Wernickego została spowodowana przewlekłym niedożywieniem, pogłębionym dodatkowo rozległym zabiegiem chirurgicznym i nierozpoznaną wcześniej nadczynnością tarczycy. Parenteralna suplementacja tiaminy oraz leczenie przeciwtarczycowe pozwoliły uzyskać satysfakcjonujące ustąpienie objawów neurologicznych. **(Endokrynol Pol 2011; 62 (2): 178–180)**

Słowa kluczowe: *zespól Wernickego-Korsakowa, niedobór tiaminy, nadczynność tarczycy*

Introduction

Wernicke-Korsakoff syndrome constitutes a group of neurological and psychiatric symptoms resulting from thiamine (vitamin B1) deficiency. Some authors distinguish a neurological part (called Wernicke's encephalopathy) from a psychiatric one, known as Korsakoff or amnestic syndrome. In clinical practice, these syndromes might occur separately, but more than 80% of patients with Wernicke's encephalopathy also develop Korsakoff syndrome, therefore both of them are often referred to as the joint Wernicke-Korsakoff syndrome. Partial or complete dysmnesia is most characteristic for amnestic syndrome. To diagnose the illness, two out of the following four symptoms must be present: malnutrition, eye symptoms, cerebellar symptoms and mild dysmnesia. The classic triad of confusion, ataxia and nystagmus was first described by Wer-

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nicke in the 19th century. Thiamine deficiency is caused most frequently by chronic alcohol abuse, and more rarely by gastrointestinal tract diseases, chronic haemodialysis, prolonged intravenous feeding, neoplastic diseases, AIDS, hyperemesis gravidarum or thyrotoxicosis.

The mortality rate in this syndrome remains 10–20% mostly due to under-diagnosis and cardio-pulmonary complications [1,2].

A case report

A 51-year old woman was urgently admitted to hospital because of worsening, sharp abdominal pain, vomiting and fever reaching 39 o C. The patient's history was unremarkable, she had not abused alcohol and had not received any long-term treatment. The last menstruation had been normal. On admission, malnutrition (BMI — 19 kg/m^2), corresponding probably to low economic status and peritoneal symptoms, was revealed during the physical examination. Laboratory evaluation revealed microcytic anaemia Hgb — 9 g/dL, RBC — 4.49 T/L, MCV — 65.7 fl, iron deficiency Fe — 2.2 umol/L (N: 5.5–28.6 umol/L), elevated markers of inflammation WBC — 29.4 G/L, CRP — 268.5 mg/L (N: < 5 mg/L) and low concentration of proteins: total protein 4.9 g/L (N: 6.0–8.0 g/L), albumin 37.55% (N: 53–66%).

During the urgently conducted exploratory laparotomy, a fragment of necrotic caecum was removed; in the histopathological examination, no neoplastic cells were found. The patient was re-operated after three days, owing to the lack of tightness of enteroanastomosis. Due to increasing anaemia, 5 units of erythrocytes mass was transfused. Additionally, the patient received albumin (total dose 100 g) and a high-protein diet. After 19 days of hospitalisation, the woman's clinical condition improved enough for her to be discharged and continue her convalescence at home.

After five days, the patient was re-admitted to the surgical ward owing to fever and profuse wound suppuration. The patient was given ciprofloxacin (400 mg/ /24 h *i.v.*) according to the result of bacteriological culture. Gradually, regression of fever, healing of the wound and decrease of inflammatory parameters were observed. Although her general state was improved, she developed apathy, loss of appetite and reluctance to engage in physical rehabilitation. The neurology and psychiatry services were consulted, who found normal consciousness, bradypsychia, hypokinesia, succinct answer and indifference.

Moreover, she displayed difficulties with retracing a sequence of events, memorising, mental blanks and narrowed interest. The neurological examination revealed disorientation with respect to time and place, pupilloplegia, exophthalmic ophthalmoplegia, and four-extremity ataxia with a predominance of lower limb immobilising the patient. Computer tomography (50 ml of ultravist was administered) of her brain was normal. Suspecting Wernicke-Korsakoff syndrome, the patient was moved to a neurological ward and after measuring the level of vitamin B1 (0.9 ug/dL; N: 1.6––4.0 ug/dL), intravenous supplementation of thiamine (3 × 200 mg) was applied. Additional examinations revealed tachycardia (130/min) and progressive cachexia (BMI — 17 kg/m^2), even though the level of inflammatory parameters and haemoglobin were within normal ranges. Apart from Wernicke-Korsakoff syndrome, her clinical condition suggested thyrotoxicosis, which was confirmed by laboratory findings: TSH — 0.05 mLU/L (N: 0.5–5.5 mlU/L, fT_4 — 29.8 pmol/L (N: 9–24 pmol/L), anti-TPO — 69.68 IU/mL (N: < 34 IU/mL), anti-TSHR — 2.6 IU/L (N: < 2.0 IU/L).

Thyroid ultrasound examination revealed diffused and marked hypoechogenicity. Diagnostic process was extended to cerebrospinal fluid analysis, vitamin B_{12} and folic acid evaluation, which remained normal. Angio-MRI with venous phase evaluation of the brain was also performed to exclude venous stroke, but only a small aneurysm of the anterior communicating artery was found. On account of persistent dysmnesia, confabulation and disorientation, psychological tests (Benton, Bender) were conducted, which indicated an organic background to the disorder. Apart from the aforementioned thiamine, thiamazole (60 mg/24 h) and propranolol (30 mg/24 h) were introduced into therapy. After eight weeks of hospitalisation, the patient was discharged without significant eyeball symptoms, or walking assistance, as little imbalance still remained. Disorientation and dysmnesia constituted the main problems.

Discussion

Thiamine is a water-soluble vitamin. Its active metabolite produced in the liver is thiamine pyrophosphate, an important coenzyme for carbohydrate metabolism and generating cellular energy. Usually, thiamine deficiency is associated with chronic alcohol abuse interfering with the active gastrointestinal transport of thiamine. In other cases, due to chronic liver diseases, activation of thiamine pyrophosphate from thiamine is decreased. Ogershok et al., in analysing a series of cases of Wernicke's encephalopathy, demonstrated that as many as half of patients had no history of alcohol abuse [3].

In 1968 Enoch and Williams first described the case of a 61-year old woman with Wernicke's encephalopathy, anorexia and thyrotoxicosis. The authors suggested that thyrotoxicosis might significantly increase demand for vitamin B1 [4]. Interestingly enough, enceph-

alopathy develops only when thyrotoxicosis overlaps with previous malnourishment, triggered for exampl, by hyperemesis gravidarum.

Neither malnutrition nor thyrotoxicosis alone should cause Wernicke-Korsakoff syndrome; however, their coexistence augments the depletion of thiamine, as happened in our case. Anaemia, iron deficiency, low capacity of proteins and albumin reflected chronic undernourishment of the patient in question. Additionally, two operations on the gastrointestinal tract, which necessitated an abstemious diet, and post-operative complications, intensified catabolism and further deficiency of vitamin B1. Due to her increasing state of confusion, computer tomography of the brain with administration of iodine contrast medium was performed. This examination might have exacerbated undetected former hyperthyroidism. The coexistence of adverse conditions caused finally Wernicke-Korsakoff syndrome.

Thyrotoxicosis considerably increases the demand for thiamine. Iossa et al. proved in an animal model that thyroid hormones have a direct influence on mitochondrial mass inside cells, all the same carbohydrate metabolism in the Krebs cycle, which is the main source of energy [9]. Thiamine is an important coenzyme in pyruvic acid transformation into acetyl CoA — a cycle Krebs' substrate. It is also responsible for decarboxylation of α-ketoglutarate acid required in the Krebs cycle. Therefore, it seems that an extra supply of vitamin B1 must be provided in the case of an increased tissue metabolism.

Thiamine influences the process of wound healing. The lack of tightness of enteroanastomosis, which was the reason for re-operation on our patient, delayed and hindered wound healing, and was probably the result of thiamine deficiency.

It has been suggested that vitamin B1 plays a crucial role in several biochemical pathways in the brain. Ba et al. proved in their research that thiamine deficiency deteriorates cellular metabolism, leading to apoptosis or serious neuron cell dysfunction and structural abnormalities of the cell membrane [10].

Imaging has a vital role to play in diagnosing Wernicke-Korsakoff syndrome. However, classic computer tomography rarely reveals pathology. MRI is the modality of choice, since having better contrast resolution might indicate the presence of discrete haemorrhagic focus in mammillary bodies. To exclude ischemic focuses, tumours of the brain and venous stroke, classic computer tomography and angio-MRI were used in our patient.

Encephalopathy associated with autoimmune thyroid diseases (EAATD) is also worth noting. Described in the course of Hashimoto's and Graves' diseases, it is characterised by loss of consciousness, behavioural changes, tremor, myoclonus, involuntary movements, stroke-like focal signs, psychiatric symptoms and responsiveness to treatment with corticosteroids. Interestingly, EAATD often occurs in patients with normal thyroid hormone profile and seems not to correlate with thyroid function [11–13], but more with autoimmune vasculitis of the brain or accumulation of immune complexes. A diagnosis of EAATD is still mostly based on exclusion criteria [14, 15]. In our case, EAATD was taken into consideration, but the classic triad of Wernicke-Korsakoff syndrome, the low concentration of vitamin B1, and the clinical improvement after its administration (without steroids), allowed us to make a correct diagnosis.

Conclusions

Wernicke-Korsakoff syndrome should be considered in a diagnostic process not only in patients who abuse alcohol. Any delay in correct diagnosis is burdened with a high mortality rate. Adequate supplementation of thiamine must be taken into consideration while planning nutritional and pharmacological treatment in malnourished patients with chronic diseases.

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