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Case Report

An uncommon presentation of Wernicke-Korsakoff's syndrome in pregnancy: Case report ☆,☆☆

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ABSTRACT

Wernicke's encephalopathy is an acute neuropsychiatric syndrome resulting from severe thiamine (vitamin B1) deficiency. Symptoms occur with an acute onset and may vary according to the brain area involved. Altered consciousness is the most common clinical feature, together with ocular abnormalities and ataxia. We report the case of a pregnant women affected by pre-gestational hyperthyroidism that caused an uncommon presentation of Wernicke's encephalopathy. Symptoms differed from the classic triad and diagnosis was made possible by a thorough analysis of anamnestic factors and brain MRI. Alongside thiamine supplementation, a multidisciplinary approach which included physiokinesis and a phoniatric support was fundamental for the patient's recovery.

Introduction

Wernicke's encephalopathy (WE) is an acute neuropsychiatric syndrome resulting from severe thiamine (vitamin B1) deficiency [1]. Thiamine plays a role in many biological pathways including ATP synthesis and production of myelin and neurotransmitters such as glutamic acid and GABA. Thus, its deficiency may impair cell metabolism, leading to cell damage, which is reversible after prompt and adequate treatment [1].

Symptoms occur with an acute onset and may vary according to the brain area involved. Altered consciousness is

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Table 1 – Serum values from time of admission to delivery.

	18 weeks of GE	19 weeks of GE	21 weeks of GE	27 weeks of GE	34 weeks of GE	37 weeks of GE
Hemoglobin (g/dL)	8.7	7.9	8.7	8.1	11.2	11.1
Platelets (10^9/L)	143	129	183	177	106	105
INR	1.07		1	0.98	0.97	0.96
APTT	0.77		1	0.84	0.93	0.86
Fibrinogen (mg/dL)	615		692	518	486	471
Amilases (U/L)	247	130	66			
Lipasis (U/L)	803	485	133			
TSH (mIU/L)	<0.005	0,7	0,7	0,9		
FT3/Ft4 (normal values: 2-5/8-17 ng/L)	2.4/12.9	2.7/10.3	3.2/12	3.2/10.4		
AST (U/L)	83	67	27	13	34	
ALT (U/L)	202	40	53	21	52	31
gGT (U/L)	96		106		57	
LDH (U/L)	156		137	145		148
Bile acids (μmol/L)					15,9	34,8
25-OH-vitamin D (μg/L)		<4				
Folic acid (μg/L)		7,5				
Vitamin B12 (ng/L)		271	661			
Thiamine (nmol/L)		114				

the most common clinical feature together with ocular abnormalities and ataxia. Other less frequent clinical presentations include hearing loss, hypothermia or hyperthermia, epileptic seizures, distal polyneuropathy, absent deep-tendon reflexes, hypotension, tachycardia and respiratory symptoms [2].

About 80% of patients with WE develop Korsakoff's syndrome, which is characterized by permanent memory defects, especially of the working memory, disorientation to time and emotional changes [3].

The non-specific clinical presentation of WE often leads to an incorrect recognition of the disease. Diagnosis is clinical and may be confirmed by determining blood thiamine concentrations [4]. MRI has 54% sensitivity but is 90% specific [5].

Treatment with intravenous or intramuscular thiamine is safe and should be commenced immediately to prevent progression to Korsakoff syndrome [5].

We report the case of a pregnant women affected by pregestational hyperthyroidism that caused an uncommon presentation of WE. To our knowledge, similar cases reported in the literature are extremely limited, as the majority of cases of WE in pregnancy are related to transient gestational hyperthyroidism [6,7].

Case report

A 27-year-old 18-week pregnant woman was referred to our emergency department for persisting hyperemesis gravidarum, which had caused a 10 kg weight loss since the beginning of pregnancy together with severe alterations of liver function tests and serum pancreatic enzymes (Table 1). During the previous 4 weeks, the patient had received hospital care in another center where a diagnosis of hyperemesis gravidarum had been made. While in hospital, the woman had undergone a magnetic resonance cholangiopancreatography, which revealed the presence of a subacute inflammation of the pancreatic parenchyma, an endoscopic ultrasound, which was negative, and a thyroid ultrasound, which was also negative. Autoimmune screening was positive for ANA, c-ANCA and ASMA, while testing for viral hepatitis had resulted negative. In the suspicion of an autoimmune hepatitis, the patient had received a 6-day treatment with Deltacortene 50 mg/day, which was interrupted due to lack of clinical and laboratoristic improvement.

The patient had a 6-year history of hyperthyroidism which had been treated with propylthiouracil, and bisoprolol, both continued during pregnancy.

At time of admission to our emergency department, the patient reported dizziness, memory loss and weakness in her lower limbs. Vital parameters were normal except for mild tachycardia (125 bpm). Neurological examination revealed pluridirectional horizontal nistagmus, diffuse hyposthenia of the trunk and of the proximal lower limbs, and diffuse absent Deep Tendon Reflexes (DTR). The following day the patient developed severe dysphagia and dysphonia and was transferred to ICU where she was put on enteral nutrition. By that time the patient was no longer able to keep an upright position.

Thyroid function tests showed a suppressed thyroid-stimulating hormone and normal values of thyroid hormones (FT3 and FT4). Thyroid receptor antibodies were negative as were anti-throglobulin and anti-thyroperoxydase antibodies.

A brain MRI revealed T2/flair hypersintensity in the hypothalamus, in the area adjacent to the third ventricle floor, in the infundibular region, in the median eminence, in the mammillary bodies, in the periacqueductal area, in the inferior colliculi, in the medial geniculate bodies and in the mesial thalamic region bilaterally (Fig. 1).

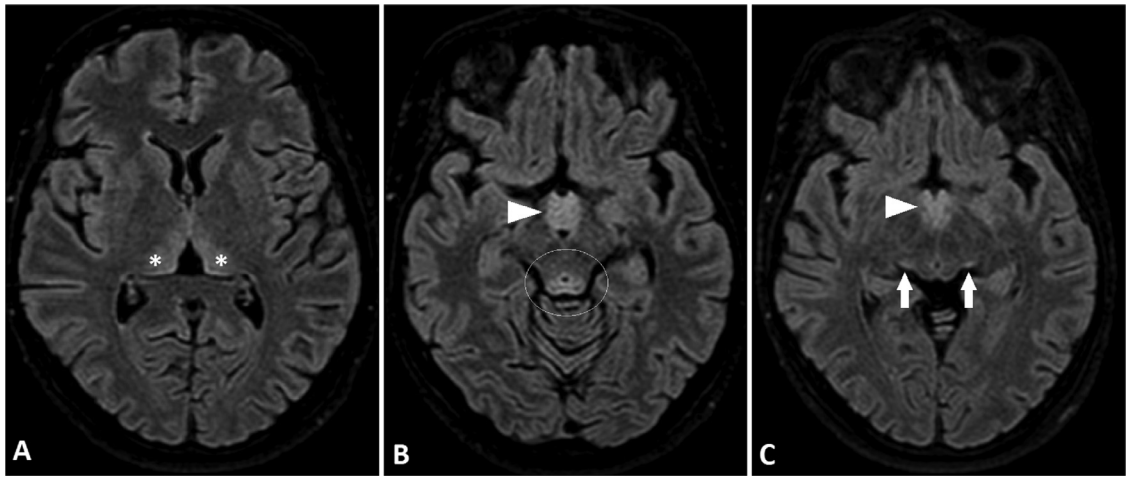

Fig. 1 – Axial T2-weighted fluid-attenuated inversion recovery (FLAIR) sequences showing the presence of (A) bilateral and symmetrical areas of hyperintensity in the dorsomedial thalami (asterisk), (B) hyperintensity of the midbrain tegmentum and periacqueductal gray matter (circle), (B, C) hyperintensity of the hypothalamus (arrowhead) and (C) geniculate bodies (arrows).

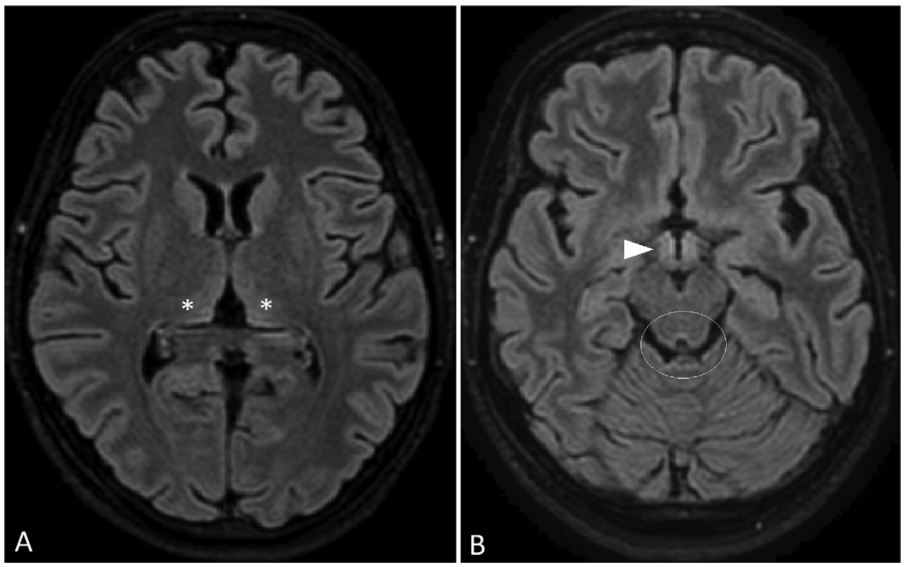

Fig. 2 – Follow-up MRI performed 10 days after admission. Axial T2-weighted FLAIR sequences showing complete signal restoration of the (A) dorsomedial thalami (asterisk), (B) periacqueductal gray matter (circle) and hypothalamus (arrowhead).

Lumbar puncture ruled out infectious diseases and both electromyography and electroneurography were negative.

In the suspicion of WE, the patient received intravenous thiamine 500 mg 3 times per day for 2 days, followed by thiamine 100 mg once a day. She also received supplementation with folic acid, iron, a vitamin B complex and was put on a daily physiokinesis program.

The patient began to show resolution of confusion and improvement of dysphonia, dysphagia and hyposthenia of the trunk and of the proximal part of the lower limbs within 14 days of starting on intravenous thiamine. However, absence of rotuleus and Achilles DTR persisted. Laboratory tests improved (Table 1).

A second brain MRI performed 10 days following the first scan revealed a nearly complete resolution of the T2 hyperintensity in all affected areas except for the medial geniculate bodies (Fig. 2). One month after admission, dysphagia had resolved although mild hypophonia and anterograde amnesia persisted. The patient was able to walk with no need of support, although extension of the knees was still non-optimal due to hyposthenia.

The patient developed intrahepatic cholestasis during the third trimester of pregnancy and was treated with ursodesoxycholic acid 300 mg 3 times a day. She continued to receive thiamine 100 mg orally and vitamin B complex for the whole duration of pregnancy.

At 36 weeks of gestation memory was considerably improved and lower limb hyposthenia was resolved although absence of rotuleus and Achilles DTR persisted bilaterally. The patient was able to walk with no need of support, although she presented a wide-base gait and mild difficulty in lifting thighs against gravity

Also, the patient developed insomnia and anxiety, which was treated with haloperidol.

She gave birth to a healthy boy at 37 + 4 weeks of gestation. Labor was induced with a cervical-ripening balloon and prostaglandins. Due to non-reassuring cardiotocography, the baby was delivered with a Kiwi vacuum. The newborn weighed 2510 kg. Apgar score at 1 and 5 minutes was 9 and 10 respectively. Post-partum was uneventful. The patient did not need particular treatment as her condition progressively improved until she obtained complete recovery.

The patient also signed an informed consent that allowed us to publish the case and patient anonymity has been preserved.

Discussion

We described the case of an uncommon presentation of WE. Symptoms differed from the classic triad and diagnosis was made possible by a thorough analysis of anamnestic factors and brain MRI. Alongside thiamine supplementation, a multidisciplinary approach which included physiokinesis and a phoniatric support was fundamental for the patient's recovery.

Thiamine is a water-soluble vitamin, which is absorbed in the duodenum and is predominantly stored in the liver [8]. The active metabolite of vitamin B1, thiamine pyrophosphate, acts as a cofactor for transketolase in the pentose phosphate pathway and as a cofactor for pyruvate dehydrogenase and alpha-ketoglutarate dehydrogenase in the tricarboxylic acid cycle [8].

The recommended dose of thiamine in adults is 1.4 mg per day or 0.5mg of thiamine per 1000 kcal consumed (the higher the carbohydrate intake, the higher the need). The body's reserves of vitamin B1 are only 30-50 mg, so any malnutrition condition lasting more than 3-4 weeks can totally deplete the vitamin's stores. This dose is higher in children, in critically ill patients and during pregnancy and lactation [9].

Thiamine deficiency may impair cell metabolism, leading to lactate production, excitotoxic damage, apoptotic cell death, mitochondrial dysfunction, cytotoxic edema and disruption of the blood-brain barrier permeability [10].

Symptoms occur with an acute onset and include altered consciousness, ocular abnormalities and ataxia. Mental alterations result from an involvement of the thalamus and of the mammillary bodies and may range from confusion, behavioral disturbances mimicking an acute psychotic disorder to apathy, coma and death [11]. Ocular disturbances, including nistagmus, occur in about 29% of patients while loss of equilibrium with incoordination of gait and trunk ataxia affects 23% of patients. Both symptoms are due to involvement of the cerebellar vermis and of the vestibular dysfunction [12]. Less frequent clinical presentations include hearing loss, due to damage of the thalami, hypothermia or hyperthermia, caused by the involvement of the posterior and anterior hypothalamic regions, epileptic seizures, caused by glutamatergic hyperactivity, distal polyneuropathy, absent deep-tendon reflexes, hypotension, tachycardia and respiratory symptoms [2].

The prevalence of Wernicke's encephalopathy in the general population has been estimated to vary between 0,4 and 2,8%, although studies have shown that as many as 80% of cases are not recognized and the diagnosis is often only made post-mortem [8,13].

Brain lesions in WE usually follow a symmetric distribution among structures that surround the third and fourth ventricles and the aqueduct. The most commonly affected structures are the mammillary bodies, involved in up to 80% of cases [5]. Lesions in the dorsomedial thalamus have been associated with memory loss. Atypical lesions, usually in non-alcohol related WE, can be located in the cerebellum, vermis, cranial nerve nuclei, red nuclei, dentate nuclei, caudate nuclei, splenium and cerebral cortex [5].

While WE has been classically associated with alcoholism, it has increasingly been reported in other disorders causing malnutrition and malabsorption [7].

Thiamine deficiency may occur in pregnancy even with a standard thiamine supplementation, and, if inadequately treated, may lead to WE, central pontine myelinosis and death [14].

WE is rare in hyperemesis gravidarum (HG), with a prevalence that ranges between 0.04% and 0.13% [6].

Hyperthyroidism causes an increase in the demand for ATP and upregulates the Krebs cycle, for which thiamine is an important coenzyme. This, combined to the decreased absorption of vitamin B1 in hyperemesis and to the increased demand of thiamine in pregnancy, predisposes to WE [7].

Diagnosis is clinical and may be confirmed by determining blood thiamine concentrations [4]. Cerebrospinal fluid may be characterized by raised protein concentrations while electroencephalography may show non-specific slowing of the dominant rhythm, especially in a later stage [1]. MRI shows typical (thalami, mammillary bodies, tectal plate and periacqueductal area) and atypical (cerebellum, cranial nerve nuclei, cerebral cortex) signal intensity alterations. Disruption of the brain-blood barrier may be also seen in these regions [15].

The recommended treatment is a parenteral dosage of at least 500mg of thiamine hydrochloride dissolved in 100ml of normal saline, given by infusion over a period of 30 minutes, 3 times per day for 2-3 days. According to others, the correct dosage is 200 mg, 3 times daily. In case of no response, supplementation may be discontinued after 2-3 days. If an effective response is observed, 250 mg of thiamine may be administered intravenously daily for further 3-5 days or until clinical improvement. Initial improvements can be observed within the first week but usually takes 1-3 months to resolve [1]. High-dose parenteral administration facilitates passive diffusion of thiamine across the blood-brain barrier. Because magnesium serves as a cofactor for thiamine activity, its level should also be checked and supplemented via oral or parenteral administration in cases of hypomagnesemia [5]. Under-treatment of WE leads to irreversible complications, known as Korsakoff's syndrome, characterized by thalamic and mammillary body degeneration and frontal lobe atrophy, which determine perma-

nent memory defects, disorientation to time and emotional changes [7].

Patient consent

Informed written consent was obtained from the patient for publication of this case report.

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