

# Wernicke-Korsakoff Syndrome associated with hyperemesis gravidarum and fetal death: Case report and literature review

## Síndrome de Wernicke-Korsakoff associado a hiperêmese gravídica e morte fetal: Relato de caso e revisão de literatura

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### Abstract

We describe a clinical case of a pregnant patient with hyperemesis gravidarum who progressed to abortion, Wernicke's encephalopathy, and Korsakoff's psychosis, all related to thiamine deficiency. The patient presented symptoms of disorientation, nonspecific limb movements, and fever, initially treated with metronidazole and ceftriaxone for suspected infected abortion. Subsequently, the patient was diagnosed with retained and infected abortion, and thiamine replacement therapy was initiated with an intravenous loading dose of 900 mg/day. During hospitalization, the patient presented with tetraparesis, nystagmus, decreased level of consciousness, anterograde and retrograde amnesia, confabulation, and aphasia. Magnetic resonance imaging showed lesions in the pons, typical of Wernicke's encephalopathy. The patient was empirically treated with acyclovir and ampicillin and showed clinical improvement. The text also provides a brief narrative review of the literature on the topic.

**Keywords:** wernicke encephalopathy; Korsakoff syndrome; pregnancy; hyperemesis gravidarum.

### Resumo

Descrevemos um caso clínico de uma paciente grávida com hiperêmese gravídica que evoluiu para aborto, Encefalopatia de Wernicke e Psicose de Korsakoff, ambas relacionadas à deficiência de tiamina. A paciente apresentou sintomas de desorientação, movimentos inespecíficos dos membros e febre, sendo, inicialmente, tratada com metronidazol e ceftriaxona por suspeita de aborto infectado. Posteriormente, a paciente foi diagnosticada com aborto retido e infectado e iniciou-se a reposição de tiamina com dose endovenosa de ataque de 900 mg/dia. Durante o internamento, a paciente apresentou tetraparesia, nistagmo, rebaixamento do nível de consciência, amnésia anterógrada e retrógrada, confabulação e afasia. A ressonância magnética mostrou lesões na ponte, típicas da Encefalopatia de Wernicke. A paciente foi tratada com aciclovir e ampicilina empiricamente e apresentou melhoras no quadro clínico. O texto também faz uma breve revisão narrativa da literatura sobre o tema.

**Palavras-Chave:** encefalopatia de wernicke; síndrome de Korsakoff; gravidez; hiperêmese gravídica

### INTRODUCTION

L Hyperemesis gravidarum (HG) is a severe form of nausea and vomiting associated with pregnancy, occurring in approximately 3% of pregnancies and being the leading cause of hospitalization in the first trimester of pregnancy<sup>1</sup>. Despite being common, HG often has long-term consequences and is associated with maternal and fetal morbidity and mortality. The clinical presentation of HG typically includes severe and intractable vomiting, often accompanied by >5% weight loss, ketonuria, nutritional deficiencies, and electrolyte imbalance<sup>2</sup>.

Wernicke's encephalopathy (WE) is an acute neuropsychiatric disorder caused by thiamine deficiency, characterized by the triad of mental state changes, ophthalmoplegia, and ataxia, although its presentation can vary<sup>3</sup>. Prolonged and untreated cases can progress to Korsakoff's syndrome (KS), which is characterized by impaired formation of new memories with relative preservation of other mental functions, confabulation

being a common feature. These two conditions are often described together as Wernicke-Korsakoff syndrome (WKS). The main cause of thiamine deficiency is chronic alcoholism, but it has also been described in cases of prolonged parenteral nutrition after bariatric surgery, cancer, malnutrition, Crohn's disease, and HG.

In this article, we describe a patient with hyperemesis gravidarum who experienced miscarriage, Wernicke's encephalopathy, and Korsakoff psychosis, with typical thiamine deficiency findings on neuroimaging. This is followed by a brief narrative review of the literature.

### METHODOLOGY

We reviewed the patient's medical records and analyzed laboratory and imaging tests. We obtained verbal and written

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consent from the patient to use this data in the present article. Additionally, the study was submitted to the Research Ethics Committee of Hospital Cesar Cals.

### CASE REPORT

A 32-year-old woman, at 15 weeks and five (5) days of gestation, presented with hyperemesis gravidarum associated with anemia, asthenia, and hyporexia. Two days before being admitted to the emergency service, she reported improvement in the emetic symptoms but presented with disorientation and non-specific limb movements, followed by lower limb weakness. She was taken to the hospital with symptoms of fever, purulent vaginal discharge, hypoglycemia corrected with glucose solution, and absence of fetal heartbeats. Treatment with metronidazole and ceftriaxone was initiated due to a suspected infected miscarriage, and she was referred to the obstetric referral service. At the tertiary hospital, the patient was diagnosed with confirmed retained and infected miscarriage by obstetric ultrasound and suspected uterine focus sepsis. The antibiotic therapy was modified to clindamycin and gentamicin. After clinical stabilization, the pregnancy was

terminated with misoprostol, followed by uterine curettage without complications.

The patient presented with disorientation and symptoms of hyperemesis gravidarum, raising the diagnostic suspicion of Wernicke's encephalopathy. Thiamine replacement therapy was initiated with an intravenous loading dose of 900 mg/day, followed by a maintenance dose of 300 mg/day. During hospitalization, the patient developed disproportional tetraparesis, unidirectional horizontal nystagmus, decreased level of consciousness, anterograde and retrograde amnesia, confabulation, and aphasia. Differential diagnosis tests (Table 1) and cerebrospinal fluid analysis (Table 2) were performed due to suspected herpes encephalitis, which showed elevated protein levels and pleocytosis. However, serological tests were negative for this disease as well as for Antiphospholipid Antibody Syndrome (APLS). Empirical treatment with acyclovir and ampicillin was initiated. Following thiamine replacement, the patient showed slow and progressive improvement in the clinical picture.

**Table 1.** Laboratory values in the initial evaluation of the patient.

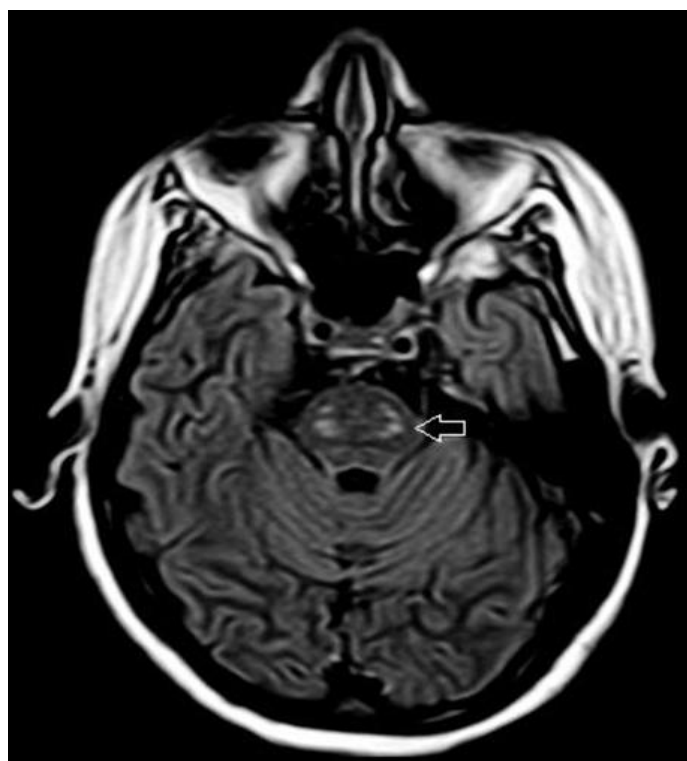
Test	Results	Reference
Hemoglobin	7,5 g	12,5 g
Leukocytes	6200 mm <sup>3</sup>	4000 a 10000 mm <sup>3</sup>
Platelets	183000 mm <sup>3</sup>	150000 -450000 mm <sup>3</sup>
CRP	5,5 mg/dL	<6,5 mg/dL
Urea	13 mg/dL	<40 mg/dL
Creatinine	0,4 mg/dL	< 1.3 mg/dL
AST	37 U/l	7-55 U/l
ALT	31 mg/dL	8-48 U/l
Magnesium	1,5 mg/dL	1,6-2,5meq/dL
Sodium	148 meq/dL	135-145 meq/dL
Potassium	2,9 meq/dL	3,5-5,5 meq/dL
Alkaline Phosphatase	23 U/l	40 - 150 U/l
GGT	38 U/l	9-36 U/l
INR	1,11 mg/dL	<1.5
APTT (r)	0,64	<1.2
Lactate dehydrogenase	193 g/dL	150-450 g/dL
Anti-Beta-2-Glycoprotein IgM and IgG	Negative	Negative
Anti-Cardiolipin IgM and IgG	Negative	Negative
Antinuclear Factor	1:80 - fine speckled nuclear pattern	Negative

**Table 2.** Analysis of Cerebrospinal Fluid (CSF)

Test	Results	Reference
Cells	12 mm <sup>3</sup>	<5 mm <sup>3</sup>
Glucose	58 mg/dL	>60 mg/dL
Protein	56,9 mg/dL	<45 mg/dL
Lactate dehydrogenase	31mg/dL	<40 mg/dL
Adenosine deaminase	0,6 mg/dL	<8 mg/dL
VDRL	Non-reactive	Non-reactive
Cryptococcus neoformans	Non-reactive	Non-reactive
EBV - IgM and IgG	Non-reactive	Non-reactive
CMV -IgM and IgG	Non-reactive	Non-reactive
Gene-Expert - Tuberculosis	Non-reactive	Non-reactive
Culture	Absence of bacterial growth	Absence of bacterial growth

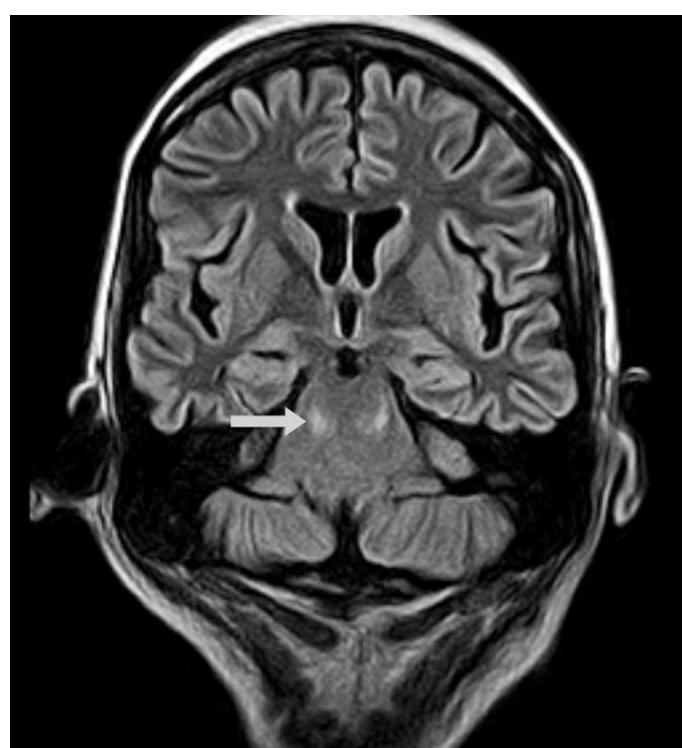
The brain MRI revealed hyperintense foci with linear signal alterations in the pontine region (Figures 1 and 2), which are

Figure 1: Axial T2 FLAIR Magnetic Resonance Imaging (MRI) image showing hyperintense lesions located in the pontine region of the brain.



typically associated with Wernicke's encephalopathy.

Figure 2: Brain Magnetic Resonance Imaging in coronal section on T2/FLAIR, showing the presence of symmetric bilateral hyperintense lesions in the pontine region.



**DISCUSSION**

Hyperemesis gravidarum (HG) is the term used to describe the severe end of the spectrum of nausea and vomiting associated with pregnancy. There are multiple pathophysiological mechanisms associated with HG, including estrogen and progesterone-induced intestinal motility and gastric emptying alterations, increased human chorionic gonadotropin (HCG)

levels, and genetic factors<sup>4</sup>. While nausea and vomiting are common during pregnancy, hyperemesis gravidarum is a debilitating condition that can lead to severe maternal complications if not properly treated, including malnutrition, anemia, hyponatremia, seizures, esophageal rupture or perforation, liver disease, jaundice, pancreatitis, deep

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vein thrombosis, pulmonary embolism, pneumothorax, rhabdomyolysis, depression, post-traumatic stress disorder, and fetal complications<sup>1</sup>. In a recent meta-analysis examining reports of HG complications<sup>3</sup>, 43 studies were found, with 11 articles describing associated neurological conditions (cases of cerebral venous thrombosis, osmotic demyelination, seizures, and Wernicke's encephalopathy).

Thiamine plays an essential role in brain carbohydrate metabolism and is critical for neurological functioning<sup>5</sup>. In cases of Wernicke's encephalopathy where alcohol is not involved, thiamine deficiency can be explained by one of four mechanisms: decreased availability, impaired utilization, accelerated utilization, and increased loss of thiamine. It is estimated that thiamine requirements increase by approximately 45% during pregnancy, and conditions such as recurrent vomiting and inadequate nutrient intake can lead to an acute state of thiamine deficiency<sup>4</sup>.

A systematic review by E. Oudman et al. identified 177 cases diagnosed with Wernicke's encephalopathy following hyperemesis gravidarum (HG) in 144 articles, yielding several interesting conclusions<sup>6</sup>:

- 1- None of the reported cases received prophylactic thiamine replacement, highlighting non-compliance with HG management protocols.
- 2 - In 91% of the cases where an MRI was performed, the procedure revealed radiological changes consistent with Wernicke's encephalopathy in the thalamic region, demonstrating high sensitivity and the importance of imaging for diagnosis.
- 3- In half of the patients with Wernicke's encephalopathy, the fetus did not survive, and in cases of fetal death, persistent maternal cognitive impairment was more frequent.
- 4- None of the reported cases received thiamine prophylaxis in cases of hyperemesis.

In 110 reported cases, treatment was administered with relatively low doses of parenteral thiamine (< 500 mg/day).

The diagnosis of Wernicke's encephalopathy is considered

challenging, with over 80% of cases diagnosed only during autopsy studies. The fact that the classic triad of symptoms (ataxia, ophthalmoplegia, and altered mental status) is present in a small portion of patients, the nonspecific nature of symptoms in early cases, and critically ill patients potentially having their clinical picture obscured by sedation and other diagnoses, such as sepsis, contribute to delayed diagnosis of this condition<sup>7</sup>. Although there are laboratory tests available for thiamine measurement, currently, there are no rapid, reliable, routine diagnostic tests.

Magnetic resonance imaging (MRI) assists in diagnosis and can identify Wernicke's encephalopathy-related lesions in two-thirds of patients. Areas of hyperintensity on T2 sequences, decreased signal on T1, and diffusion abnormality around the aqueduct and third ventricle and within the medial thalamus, dorsal medulla, tectal plate, and mammillary bodies can typically be identified<sup>7, 8</sup>.

The general recommendation from experts is that treatment for Wernicke's encephalopathy should be initiated whenever there is clinical suspicion, with a minimum of 500 mg of thiamine administered three times a day for 2-3 days<sup>9</sup>. When an effective response is observed, 250 mg of thiamine should be administered daily via intravenous or intramuscular routes<sup>10</sup>. A Cochrane review concluded that there is insufficient evidence to guide physicians on the dose, route, or duration of thiamine administration for the treatment or prophylaxis of Wernicke's encephalopathy<sup>11</sup>.

#### CONCLUSION

Although Wernicke's encephalopathy is a well-described complication in pregnant women with vomiting, it is rarely documented. The lack of awareness among healthcare professionals regarding the risk of neurological complications from acute thiamine deficiency can lead to diagnostic and therapeutic delays. We advise a low threshold for parenteral thiamine replacement in pregnant women with persistent vomiting, as severe thiamine deficiency induced by hyperemesis gravidarum can result in severe maternal neurological symptoms and fetal death.

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