Case Report

Wernicke encephalopathy associated with hyperemesis gravidarum: A case report and literature review

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ABSTRACT

Wernicke encephalopathy (WE) is a neurological pathology caused by thiamine deficiency, which usually manifests with ataxia, confusion, nystagmus, and ophthalmoparesis. The most common cause is alcohol, but other conditions such as hyperemesis gravidarum (HG) have been described. Herein, we report the case of 37-year-old Brazilian pregnant woman who presented to our department with HG complicated with WE and discuss the typical imaging findings, clinical presentation, therapeutics, and prognosis.

Key words: Hyperemesis gravidaru; pregnancy complications; Wernicke encephalopathy.

Introduction

Wernicke encephalopathy (WE) is a neurological pathology caused by thiamine deficiency which usually manifests with ataxia, confusion, nystagmus, and ophthalmoparesis.[1] The most important etiology is linked to chronic alcoholism, although other nonalcoholic etiologies, such as hyperemesis gravidarum (HG), have been described.[2] There is no specific test available to support the diagnosis. Herein, we report a case of a 37-year-old Brazilian pregnant woman who presented to our department with HG complicated with WE. Her clinical presentation, therapeutic management, image findings, and prognosis are discussed.

Case Report

A 37-year-old G1P0A0 at 15 weeks and 5 days of gestation presented to our department with nausea, vomiting, loss of consciousness, and weight loss (20 kg in 2 months). On physical examination, her blood pressure was 70/50 mmHg and blood glucose level was 149 mg/dL with normal abdominal and gynecological exams. Her hemoglobin count, platelets, leucocyte count, AST, ALT, amylase, lipase, and thyroid hormone levels were within the normal range. Table 1 shows her main electrolyte abnormalities. Suspicious of HG, electrolyte replacement was initiated. Five days after admission with continuous electrolyte replacement, vertical nystagmus [Video 1] and optic ataxia compatible with WE were noted. Magnetic resonance imaging (MRI) of the brain showed high signals in thalamus and mammillary bodies [Figure 1]. Thiamine replacement was started with 100 mg two times daily for 3 days followed by 100 mg once daily until complete resolution of symptoms was noted. Her electrolytes were continuously maintained throughout her hospital course. Her clinical symptoms progressively improved, and, subsequently, complete resolution of

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Table 1: Electrolyte values and reference values

Electrolyte/Day	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	VR
K (mmol/L)	2.5	2.4	2.4	2.6	3.0	2,4	3.1	2.9	2.8	2.8	3.0	3.0-5.0
Na (mmol/L)	130	138	138	136	138	135						135-145
Mg (mg/dL)		1.7	1.4	1.4		2.2			1.50	1.40	1,80	1.5-2.2
Ca (mg/dL)				7.6								8.5-10.2
Cl (mmol/L)			101	109	108	108						98-107

VR, Value reference, D, Day

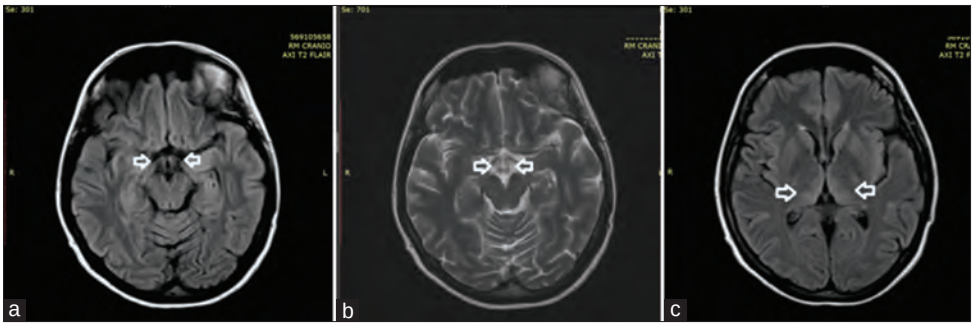

Figure 1: Magnetic resonance imaging (MRI) of the brain. Hyperintense areas in the bilateral mammillary bodies (a and b) and bilateral medial thalamus (c) are shown

her electrolyte abnormalities and clinical symptoms was achieved. She was then referred to the prenatal high-risk hospital for follow-up.

Discussion

HG is characterized by the presence of persistent and disabling vomiting during pregnancy, beginning at 4–8 weeks of gestation and, generally, persisting until weeks 14–16 of gestation, similar to the case reported.[3] The incidence HG varies from 0.3% to 3% of all pregnancies and is more prevalent in the first trimester.[4] The pathophysiology of HG has not yet been fully clarified, but it is known to have a complex multifactorial etiology, with hormonal factors, such as beta-HCG levels and estrogen, gastrointestinal disorders such as relaxation of the lower esophageal sphincter and *Helicobacter pylori* infection, changes in thyroid function, psychosocial factors such as unwanted pregnancy, and genetic factors, implicated.[3-5] In addition, a previous history of hyperemesis, current and previous molar pregnancy, pre-existing diabetes, and depression or any psychiatric illness are known to increase the risk for HG.[3]

The diagnosis of HG is usually clinical and based on the exclusion of other causes of vomiting, such as acute pancreatitis and gastrointestinal tract infections.[5] In HG, there is an increased demand for thiamine, because there is a reduction in its intake and absorption rate, leading to the depletion of its reserves in as early as 6–10 weeks after conception.[6] HG can be complicated by dehydration, weight loss, electrolyte abnormalities, nutrient deficiency, and ketonuria,[4] as well as neurological disorders such as myelinosis, WE, and Korsakoff syndrome.[7] It is also associated, due to low maternal weight, with an adverse fetal outcome such as small for gestational age fetuses and preterm birth. However, the overall rates of neonatal mortality do not appear to be different from that seen in other types of complicated pregnancies.[3]

WE is a neurological syndrome caused by the deficiency of thiamine (vitamin B1).[8] Thiamine is an important cofactor for enzymes in the pentose phosphate pathway. Because of this, its deficiency affects multiple tissues, especially those with a high turnover of thiamine, including the neural parenchyma, resulting in cellular necrosis or apoptosis.[8]

WE is generally associated with alcoholism but may occur after gastrectomies, anorexia nervosa, gastrointestinal neoplasms, liver disease, or persistent vomiting, such as in the HG that is reported in our clinical case.[9] In addition, it may also be precipitated by the administration of glucose prior to vitamin B1 replacement, which causes further consumption of thiamine during glucose metabolism.[10] It usually occurs after 2–3 weeks of vomiting during weeks 14–18 of gestation,[9] as was observed in our case.

The clinical manifestations of WE are ocular abnormalities, ataxic gait, and altered mental status, which occur together in 46.9% of patients, as also seen in our case.[3,7] Nystagmus is the most common ocular manifestation and confusion is overall the most common symptom, as was also observed in our patient.[9] More rarely, there

is a reduction of deep tendon reflexes, polyneuropathy, reduction of tonus, and dysarthria, due to axonal degeneration and demyelination.[9,10] In addition, thiamine deficiency can make the myelin sheath of central bridge neurons more sensitive to serum sodium, phosphate and potassium changes, favoring the development of myelinose pontin.[7,11]

The sensitivity and specificity are 53% and 93% for the diagnosis of WE, respectively. [9] The typical findings are hyperintense lesions in the FLAIR and T2-weighted images seen on MRI, at the level of the periaqueductal area, hypothalamic area, mammillary bodies, thalamus, and the column of fornice, as was also observed in our patient. The upper cerebellar vermis can also be affected in up to a third of cases. Abdominal, facial, vestibular, and hypoglossal cortical and nerve involvement are typical of nonalcoholic WE.[8] Serum and urine thiamine concentrations may also be helpful but are not mandatory for diagnosis.[12]

The treatment of HG should include venous hydration, avoiding the use of glycosides before vitamin B1 supplementation because of the risk of precipitating WE in the already predisposed patient. A solution with high salt concentration should be avoided because of the risk of developing myelinose pontin. In addition, it is important to correct for electrolytes and vitamins' abnormalities in addition to controlling vomiting with the use of safe antiemetics during gestation. Some recommended antiemetics include antihistamines, phenothiazines, metoclopramide, and 5HT3 antagonists.[5] In the case of suspected WE, replacement of intravenous or intramuscular thiamine should be started immediately and maintained until there is complete improvement of neurological signs and symptoms.[7] Currently, there is no consensus on the optimal dose of thiamine to be replenished, but an intravenous dose of 100–200 mg/day appears to be sufficient in nonalcoholic patients. In WE, secondary to chronic alcoholism, higher doses may be necessary.[9]

Due to the rapidity of its depletion and the beneficial effects of its supplementation, WE can be prevented with thiamine replacement in pregnant women with HG or in patients who are predisposed to vitamin C reserve depletion, such as multiparous gestation, and malnourished or patients with eating disorders.[13] Adequate nutritional support should also be provided, assessing the need for enteral or parenteral nutrition, if necessary.

The prognosis of WE depends on the stage of the disease and the prompt institution of treatment.[12] A complete resolution of nystagmus is usually observed within 1–2 weeks of thiamine replacement. However, gait disturbances may persist in up to 60% of patients.[14] If not promptly identified and treated, WE can progress to the chronic form of thiamine deficiency, represented by Korsakoff syndrome, characterized by global amnesia and constipation, usually progressing to permanent neurological disabilities, with a need to institutionalize the patient.[10] It can also progress to coma and even death, with a mortality rate varying from 20% to 30%, mainly due to pulmonary infection, sepsis and decompensated liver disease.[12]

In addition to maternal complications, thiamine deficiency may cause adverse effects on the fetus increasing its risk of spontaneous abortion, intrauterine fetal death, fetal growth restriction, and low birth weight even in the pregnancies of asymptomatic women.[13] However, fetal prognosis is usually favorable when treatment is instituted within the first 24 h of the neurological symptoms.[10]

This study has limitations. The serum and urinary thiamine concentrations were not available in our center, although thiamine concentrations may be normal and not specific to the diagnosis.[12] Other laboratory dosages, such as blood transketolase activity and thiamine pyrophosphate, may be helpful but not very reliable and were also not available.[11] Thus, the diagnosis is commonly made clinically and with MRI findings. Another MRI acquisition after resolution of the patient's symptoms would have been interesting to obtain. Despite these limitations, the reported case highlights the importance of the rapid diagnosis and prompt treatment of WE to prevent potential drastic consequences.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Consent for publication

Written consent from the patient was obtained.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Availability of data and material

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Authors' Contributions

JNFC and LABG conceived and designed the study and wrote the paper. BHLN collected the data and performed the analysis. LIM and HNF performed the analysis and reviewed the manuscript.

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