International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Moukit M et al. Int J Reprod Contracept Obstet Gynecol. 2024 Mar;13(3):695-698
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20240479

Case Series

Wernicke's encephalopathy complicating hyperemesis gravidarum: a case series

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Received: 19 January 2024
Accepted: 08 February 2024

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ABSTRACT

Wernicke's encephalopathy is an acute neuropsychiatric syndrome due to thiamine deficiency. In most cases, it is associated with alcoholism and malnutrition and rarely can be secondary to hyperemesis gravidarum and arise during the first trimester of pregnancy. The clinical signs are specific to this disorder. However, they are unknown by most clinicians, especially obstetricians, delaying treatment and leading to serious problems including maternal mortality. We report a case series of three patients diagnosed with Wernicke's encephalopathy during the first trimester based on clinical symptoms and radiological signs in two cases and only on clinical findings in case 2. A high dose of thiamine was started intravenously in all patients and the majority of symptoms resolved. Unfortunately, case 3 died, probably to a delay of diagnosis. Given this severity even with rapid treatment, prevention measures with low doses of thiamine supplementation remain at present the best treatment and should be applied in any patient presenting with hyperemesis gravidarum.

Keywords: Pregnancy, Severe vomiting, Wernicke's encephalopathy, Thiamine deficiency

INTRODUCTION

Hyperemesis gravidarum (HG) is the most frequent indication for hospitalization in the first trimester of pregnancy.[1] Generally, it resolved with symptomatic treatment including parenteral alimentation with fluids and electrolytes and antiemetics. Exceptionally, serious complications may occur, especially Wernicke's encephalopathy (WE).[2] This entity is defined as an acute neuropsychiatric syndrome characterized by the classic triad of ataxia, eye movement disorders, and mental status change secondary to Thiamine deficiency. The majority of patients that develop WE have a history of chronic alcoholism and only a few cases were described as secondary to HG loading due to inadequate diagnosis and delay of management with maternal morbidity and mortality.[2,3] We reported a series of three cases of WE managed in our department, also we review its clinical characteristics, radiological finding, and standard treatment to raise the clinician's index of suspicion about this rare neuropsychiatric entity.

CASE SERIES

Case 1

A 25-year-old woman, gravida 4 para 3, presented in our department at 9 weeks of gestation with HG. All prior pregnancies were complicated by hyperemesis gravidarum requiring hospitalization. She was hospitalized and received glucose and saline serum, antiemetic therapy, and parenteral nutrition. She was discharged ten days later on an oral diet. One week later, she presented with continued vomiting, altered mental status, and diplopia. Vital signs were normal. Neurological examination revealed normal consciousness, tachycardia, horizontal multidirectional

nystagmus and diplopia. Laboratory studies objectified elevated aspartate and alanine aminotransferase levels (180 IU/l and 250 IU/l respectively). A computed tomography scan of the brain does not reveal any sign of tumors or venous thrombosis. However, Brain magnetic resonance imaging (MRI) found an abnormal T2-weighted signal in the central pons and medial thalami suggesting WE secondary to HG (Figure 1). Plasmatic thiamine level was below the limits of detection and obstetrical Ultrasound was normal. Intravenous thiamine therapy was started immediately (500 mg×3 /day) in association with metoclopramide and omerprazol. Most of the disorders gradually subsided over days or weeks, but nystagmus persisted. She gave birth at 38 weeks to a healthy boy weighing 3160 g.

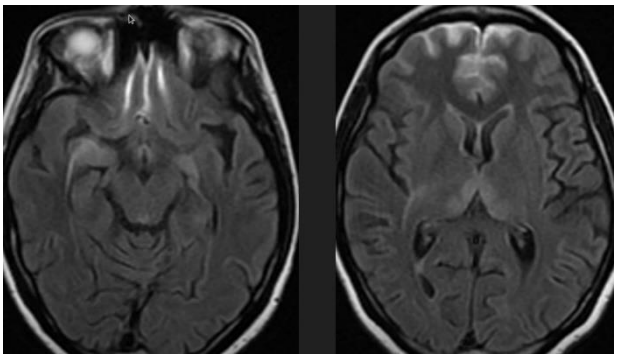

Figure 1: Abnormal T2- weighted signal in central pons and medial thalami.

Case 2

A 30-year-old woman, gravida 3 para 2, presented in the emergency department at 13 weeks gestation with persistent lethargy and blurred vision. She had been diagnosed with hyperemesis gravidarum at 10 weeks of gestation in a private clinic and treated intravenously using: saline and glucose serum with electrolytes, antiemetic therapy and omerprazol and was discharged at home with good evolution. One week before admission, she noted the apparition of severe lethargy with blurred vision. In admission, neurologic examination showed bilateral nystagmus and slowing of finger-to-nose testing in bilateral upper extremities with mild right-side ataxia. She was unable to stand upright and she could ambulate only with personal assistance. Initial laboratory analysis and brain magnetic resonance imaging were all normal. Given the history of HG and the clinical finding, our first diagnosis was WE and urgent intravenous thiamine was started in addition to other supplementations (vitamin B6 and B12) and metoclopramide with rehydratation. Thiamine levels performed outside our hospital returned, five days later, with low value and validated retrospectively our initial diagnosis. The patient was treated initially with high-dose thiamine intravenously (500 mg every 8 hours) for 3 days and transitioned to half dose (250 mg×3 /day) for 10 days. After 3 days of supplementation, her visual symptoms resolved completely. However, she still using a rolling walker for ambulation. With the resolution of her nausea and vomiting, a low dose of oral thiamine supplementation was prescribed for two weeks in association with physical therapy. Neurological and obstetrical follow-up was uneventful during pregnancy, and she gave birth at 40 weeks gestation for a healthy boy.

Case 3

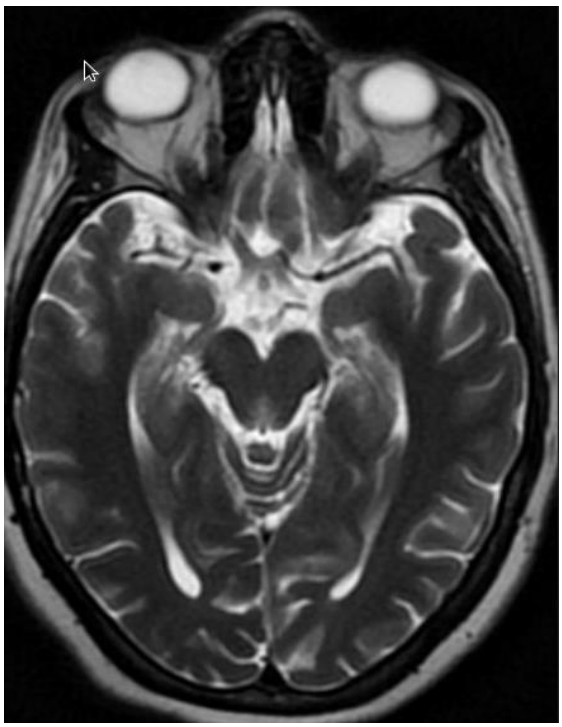

Figure 2: Abnormal T2- weighted signal in periaqueductal area.

A 21-year-old woman, primigravida, with an unremarkable medical history, presented initially at the 7th week of gestation with nausea, vomiting, and general weakness for which she was hospitalized in our department and treated with intravenous antiemetics and fluids without vitamin supplementation. Evolution was marked by vomiting persistence and diplopia. The blood pressure was 150/90 mmHg, pulse was 91 /min, and respiratory rate was 17 /minute. A neurological examination was requested and revealed loss of equilibrium with ataxia and multidirectional nystagmus. Laboratory analysis showed normal kidney and liver function tests, and the serum potassium level was 2.9 mEq/l. Cerebral magnetic resonance imaging revealed bilateral symmetrical hyperintensities in the medial and posterior thalamic and in the periaqueductal area (Figure 2). Given clinical signs and also specific cerebral images, the diagnosis of WE was made. As a serum thiamine level was not available immediately in our hospital, parenteral thiamine injection was started intravenously (500 mg every 8 hours) with potassium supplementation. Fetal ultrasound was normal and due to the fast deterioration of consciousness with quadriplegia the patient was transferred immediately in intensive care unit, intubated

and artificially ventilated. Unfortunately, after 4 days, she died secondary of a cardiac arrest. Thiamine serum level was recuperated one week after and confirmed retrospectively the diagnosis of WE.

DISCUSSION

WE is a rare central neurological disorder resulting from thiamine deficiency and is associated with significant morbidity and mortality.[4] It is mostly seen in alcoholic patient but can also occur in the non-alcoholic situation including neoplastic diseases, gastrointestinal surgery, and exceptionally hyperemesis gravidarum. In fact, during pregnancy, thiamine deficiency resulting from a combination of poor dietary intake, frequent vomiting, and the increased metabolic demands of this nutriment. WE complicate approximately 0.1 to 0.5 % of all pregnancies.[5] In our report, the mean age of patients was 25 years, as was reported in other articles, especially the systemic review of Oudman et al.[6] Our patients developed WE after a median of 4 weeks of vomiting, suggesting that thiamine depletion due to excessive vomiting leading to WE was shorter in HG than in other conditions leading to WE.[7] Clinical features are non-specific but include the classic triad of ocular abnormalities, confusion and ataxia. In all our cases, the ocular signs were described by the patients themselves. In a systemic review of 177 WE secondary to HG, the most frequently observed characteristic of the classical WE triad was eye movement disorders in 86.4% of cases, ataxia in 83.1%, nystagmus in 76.8%, and opthalmoplegia in 34.5%.[6] The full triad was present in 62.1% of patients.[6] Other clinical signs such as delirium, confusion, and problems in alertness or cognition were present in 83.6% of cases.[6] Magnetic resonance imaging is particularly important for initial diagnosis and for eliminating other diagnoses, especially vascular lesions and thrombophlebitis. Specific MRI lesions of WE are bilateral and symmetric, and involve the mamillary bodies, hypothalamic nuclei, periaqueductal gray matter, and superior cerebellar vermis.[8] However, the sensitivity of imaging is only 53% in WE following chronic alcoholism; consequently, a normal brain MRI does not exclude the diagnosis of WE, as was in case 2.[2] Serum vitamin B1 assay does not precisely reflect total vitamin B1 status and is not routinely performed. The gold standard diagnostic test is the response to high-dose vitamin B1 administration. Unfortunately, this plasmatic test is not available in our hospital and the sample is sent to another laboratory for analysis, which takes an average of 10 days for results. Major complications can arise in pregnant woman with WE as in their fetuses. On the maternal side, WE can lead to permanent neurologic lesions including the Korsakoff syndrome, which is fatal in 10 to 20% of cases.[9] In the literature, maternal death occurring during WE is estimated to 5%.[6] On the fetal side, this rare complication of severe HG can lead to miscarriage, preterm birth and intrauterine growth retardation.[10] In our study, we consider that the immediate unavailability of thiamine in our hospital was the main cause of the persistence of sequelae in all patients. According to the European Federation of Neurological Societies and the Royal College of Physicians, parenteral high dose of thiamine must be instaured immediately as soon as the diagnosis of WE is suspected clinically (500 mg 3 times daily) until symptoms resolution.[6,11] Suboptimal treatment, with relatively low doses of parenteral thiamine (<500 mg/day), was used by same authors reflecting a lack of consensus on this topic.[6,12] However, this strategy leads to long time symptoms resolution and more neurological sequels. Prevention remains the best treatment option for WE. Prophylactic parenteral thiamine supplementation (100 to 250 mg per day) in combination with vitamin B6 and B12 should be systematic in any pregnant woman presenting with severe hyperemesis gravidarum. In a systemic review, none of the cases presented with WE (177 patients) had prophylactic thiamine treatment during HG, as was in our study.[6,13]

CONCLUSION

WE during pregnancy are a rare entity that must be suspected in any pregnant woman with severe hyperemesis gravidarum associated with neurologic symptoms. Imaging diagnostics and plasmatic thiamine level should not delay rapid treatment. High doses of thiamine are still a life-saving measure, immediately ameliorating the symptoms of WE and reducing the risk of maternal and fetal complications. Prevention measures with low dose thiamine supplementation remains at present the best treatment and should be applied in situations at risk.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Moukit M, Belaabas S, Rahmoune M, Allilou I, Babahabib A. Wernicke's encephalopathy complicating hyperemesis gravidarum: a case series. Int J Reprod Contracept Obstet Gynecol 2024;13:695-8.