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Recognizing Wernicke's Encephalopathy in Pregnancy: Early Signs and the Importance of Thiamine - Case Reports

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Abstract

Wernicke encephalopathy (WE) is a less frequently occurring but severe neurological disorder resulting from thiamine deficiency. Chronic alcoholism is the most common and serious risk factor for Wernicke encephalopathy. However, nonalcoholic causes like hyperemesis gravidarum also induce WE. Besides, the clinical presentations and early diagnosis of the disease are often challenging but essential to avoid severe maternal and fetal complications. In our investigation, we report two cases of pregnant women with persistent vomiting and neurological symptoms, including abnormal eye movements and gait disturbances. Both patients were diagnosed with WE based on clinical findings and MRI evidence of characteristic periaqueductal lesions. Prompt administration of high-dose intravenous thiamine resulted in significant clinical improvement, with symptom resolution and successful transition to oral thiamine therapy. These cases highlight the importance of considering Wernicke encephalopathy in pregnant women with prolonged vomiting. Early recognition and treatment with thiamine can prevent severe neurological complications and improve maternal and fetal outcomes.

Keywords: *Early Diagnosis, Hyperemesis Gravidarum, Neurological Complications, Pregnancy, Thiamine Deficiency, Wernicke's Encephalopathy.*

Introduction

While thiamine deficiency is most commonly associated with chronic alcoholism, it can also occur due to hyperemesis gravidarum. This deficiency can lead to a rare neurological complication known as Wernicke encephalopathy [1]. While the classic triad of WE, confusion, ataxia, and ocular abnormalities (nystagmus, ophthalmoplegia) - results from thiamine deficiency, it is only present in 16-33% of patients initially [1, 2]. This underscores the importance of considering WE even in cases with atypical presentations.

Hyperemesis gravidarum is an obstetrical disorder denoting aggressive vomiting and consequential loss of weight, with dehydration as another consequence. It can cause ketonemia, where ketones are found in blood and urine. Since a single set of criteria has not yet been universally agreed upon, hyperemesis gravidarum is regarded as the worst manifestation of nausea and vomiting in pregnancy [3]. Between 0.3% and 3% of pregnant women may be affected by this condition, mainly reported among Western populations. It occurs in a small number of

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pregnancies, with rare exceptions being acute pancreatitis or some other underlying medical cause [4]. The association between hyperemesis gravidarum and Wernicke encephalopathy highlights the critical need for prompt diagnosis and intervention. Early action can prevent severe neurological consequences not only for the mother but potentially for the developing fetus as well.

While alcoholism is the primary condition historically associated with Wernicke encephalopathy, it only accounts for about 50% of cases. Nonalcoholic individuals can also develop Wernicke encephalopathy and often exhibit different symptoms and radiological findings compared to alcoholic patients, making the diagnosis of Wernicke encephalopathy more challenging [5]. In this paper, we present two case reports that illustrate the challenges in diagnosing Wernicke's encephalopathy in pregnant women due to its diverse clinical presentations. These cases emphasize the importance of recognizing early signs such as confusion, ocular abnormalities, and gait issues to ensure prompt treatment.

Case Report-1

A 29-year-old pregnant woman (gravida 2, para 1) presented at Saveetha Medical College hospital at 18 weeks of gestation. She reported a history of a previous uncomplicated vaginal delivery but no significant past medical or surgical history. Her presenting concern was a 15-day history of persistent vomiting and abnormal eye movements. With the ultrasound revealing a viable intrauterine pregnancy and no evident fetal abnormalities, the decision to carry out an MRI of the brain stem was prompted by the patient's ongoing vomiting and neurological signs of concern. With the MRI revealing lesions in the periaqueductal area, these findings become highly suggestive of Wernicke encephalopathy, as shown in Figure 1. Clinically, Wernicke's encephalopathy due to thiamine deficiency was diagnosed based on the presentation and MRI findings. Thiamine replacement (IV, 100mg thrice daily) was started without delay, and a marked improvement in her symptoms was recognized soon after. The persistent vomiting subsided, and she was transitioned to oral thiamine supplementation and discharged home with close clinical follow-up.

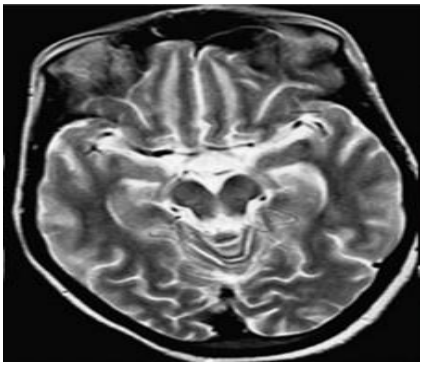

Figure 1. Wernicke Encephalopathy with Hyperemesis Gravidarum

Case Report-2

A 30-year-old pregnant woman (gravida 3, para 1, abortus 1) presented at Saveetha Medical College hospital at 25 weeks of gestation. She reported a 14-day history of severe vomiting, slurred speech, and rotatory eye movements. It's important to note that despite receiving antiemetics and intravenous fluids, her symptoms persisted. Fetal ultrasound confirmed the baby's growth was on track for gestational age based on her last menstrual period. A neurological examination and subsequent MRI scan of the brain were performed due to the combination of persistent vomiting and neurological symptoms. Both the neurological exam and the MRI findings

confirmed the diagnosis of Wernicke encephalopathy (WE) with hyperintensified lesions in the periaqueductal region, shown in Figure 2. Following the diagnosis, the patient was started on high-dose thiamine supplementation under the close supervision of a neurologist. Following the initiation of thiamine supplementation, the patient experienced a gradual improvement in her symptoms.

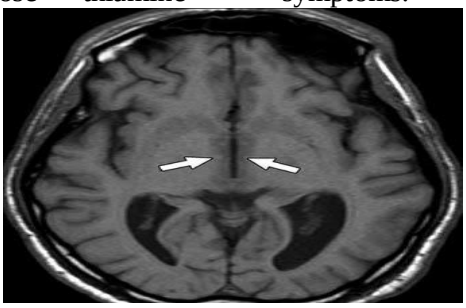

Figure 2. Wernicke Encephalopathy with Hyperintensified Lesions

Discussion

Severe health issues-including Wernicke syndrome (WS), Korsakoff syndrome (KS), Marchiafava-Bignami (MB) disease, and wet and dry beri-beri (BB)-are associated with thiamine (vitamin B1) deficiency [6]. Deficiencies in thiamine are often suspected in people at risk of malnutrition due to various factors, including chronic alcohol consumption, prolonged fasting, hunger strikes, surgical procedures on stomach or intestines, malabsorption, hyperemesis gravidarum, neoplastic diseases, HIV infection, chronic kidney disease, severe infections, burns, or extended application of parenteral nutrition [6, 7]. During pregnancy and lactation and in conditions such as hyperthyroidism, the body has increased requirements for thiamine [8].

Thiamine, a water-soluble essential vitamin, plays a critical role in numerous physiological processes. The human body maintains a limited reservoir of thiamine, with total body stores estimated to be around 25-30mg. These stores are depleted over approximately 18 days in the absence of dietary intake. The recommended daily allowance (RDA) for thiamine is established at 0.4mg per 1000 kcal, a level readily achievable through a balanced adult diet [9]. Pregnant women exhibit an increased daily thiamine requirement, reaching up to 1.5 mg. Wernicke's encephalopathy (WE) remains a well-established consequence of thiamine deficiency, though the precise underlying biochemical mechanisms require further elucidation [10].

Thiamine pyrophosphate (TPP) is a critical cofactor in the central nervous system for pentose phosphate pathway enzymes [11, 12]. Any alterations in thiamine status will disturb energy homeostasis in the affected cells, especially those tissues characterized by high thiamine turnover, such as the nervous parenchyma. This will paradoxically result in the death of neurons, either through the pathway of necrosis or that of apoptosis [12, 13]. Pregnancy Wernicke's encephalopathy has many of its causes linked to insufficient thiamine in the diet, increased demand for the vitamin during pregnancy, and depletion of the stores of the vitamin from other causes. Hyperemesis gravidarum worsens the pathogenesis of Wernicke's encephalopathy, which now poses a challenge to thiamine status [10]. Wernicke's encephalopathy (WE) shows significant advancement at about 14-16 weeks of gestation after prolonged vomiting for more than three weeks due to hyperemesis gravidarum [11]. Nutritional deficiencies are attributed to derangement of liver function tests in over 50 percent of Wernicke's encephalopathy (WE) patients following hyperemesis gravidarum. Current liver dysfunctions accompanying hyperemesis

gravidarum, however, would further enhance individual risk to develop WE [14]. According to its definition, the classic triad of Wernicke's encephalopathy (WE) includes encephalopathy, ataxia, and ocular motor abnormalities, specifically, nystagmus and gaze palsies. However, this typical presentation is not always observed [15]. Encephalopathy in WE typically present as confusion, lethargy, and, occasionally, an agitated demeanor. The vestibular deficits appear almost concurrently. Most adults with WE display peripheral neuropathy, characterized by absent deep tendon reflexes, hypotonia to some degree, and weakness in the lower limb muscles [14].

The classic triad of Wernicke encephalopathy was not readily apparent in either of the presented cases.

Case 1: This patient presented with persistent vomiting and abnormal eye movements, suggestive of oculomotor dysfunction but lacking the other two classic features. While the abnormal eye movements could be nystagmus, a definitive diagnosis based solely on this symptom is challenging.

Case 2: This case presented with severe vomiting, slurred speech, and rotatory eye movements. Slurred speech can be a sign of encephalopathy, but without confirmation of cognitive impairment, the classic triad remains incomplete. The rotatory eye movements could be nystagmus, but further evaluation is needed.

These cases highlight the importance of considering WE as a potential diagnosis in pregnant women with even atypical presentations. Diagnosing WE following hyperemesis gravidarum necessitates a high degree of clinical suspicion. The diagnostic approach typically relies on clinical features, response to thiamine supplementation, and neuroimaging findings. While blood pyruvate and lactate levels can explain thiamine deficiency, transketolase activity measurement, a complex and often unavailable assay, is not routinely employed [12]. Given the absence of significant side effects associated with thiamine administration and the potential for irreversible neurological damage, if left untreated, treatment with thiamine should not be delayed for confirmatory assay results. In such cases, empirical therapy with thiamine, often through multivitamin administration, is the standard approach [10].

While magnetic resonance imaging (MRI) findings can be a valuable tool in diagnosing Wernicke's encephalopathy (WE), mainly when used in conjunction with clinical signs, its sensitivity is reported to be around 53%, with a high specificity of 93% according to Antunez et al. This suggests that MRI may be more helpful in ruling out WE than definitively confirming it [10, 16]. Wernicke's encephalopathy (WE) manifests characteristic hyperintensities on T2-weighted MRI sequences. These lesions are predominantly localized in brain regions highly susceptible to thiamine deficiency due to their dependence on oxidative phosphorylation for energy production. The most common locations include the medial thalami, peri-aqueductal gray matter, and areas surrounding the third and fourth ventricles. Less frequently, lesions may involve the caudate nucleus, medulla, hypothalamus, or solely the mammillary bodies [10,17]. Follow-up MRI in WE patients typically demonstrates a reduction or even complete resolution of lesions, as observed in one of our cases. Studies investigating hyperemesis gravidarum patients support this finding, reporting a decrease in lesion size and intensity within six to eighteen weeks of treatment. In some cases, MRI scans normalized as early as four weeks postpartum [11, 18].

The Royal College of Obstetricians and Gynaecologists (RCOG) recognizes the importance of preventing thiamine deficiency and subsequent Wernicke encephalopathy (WE) in pregnant women experiencing hyperemesis gravidarum (HG) (RCOG, 2023). Their Green-top Guideline No. 69 outlines a multifaceted approach to HG management, including supportive care, antiemetic

medications for nausea and vomiting control, and in severe cases, hospitalization for intravenous fluids and nutritional support. However, the guideline emphasizes thiamine supplementation as a critical component of this strategy. To address this risk, RCOG recommends routine thiamine administration (100mg, oral or parenteral) for all women with prolonged vomiting due to HG (RCOG, 2023). This supplementation is particularly important before administering glucose-containing fluids, as glucose can exacerbate thiamine deficiency (RCOG, 2023). Treatment for Wernicke encephalopathy (WE) involves immediate thiamine replacement therapy. One approach involves administering a high dose of thiamine parenterally (through injection or intravenous infusion). A typical regimen is 500mg administered three times a day (TID) until symptoms improve [19]. The European Federation of Neurological Societies (EFNS) recommends a slightly different approach. They suggest starting with 200mg of thiamine administered intravenously three times a day (TID) prior to giving any glucose-containing fluids. This initial treatment continues until signs and symptoms of WE begin to improve. Early detection and intervention with thiamine supplementation are crucial for a favorable prognosis in WE associated with hyperemesis gravidarum. Clinical improvement can often be observed within six weeks of initiating appropriate therapy [10].

Conclusion

A timely diagnosis and treatment of Wernicke's encephalopathy during pregnancy would save the mother from ensuing secondary neurological injuries and fetal complications. Hence, intervention must occur as early as possible while engaging all other parties, such as obstetricians, neurologists, and nutritionists, in the process.

Although rare, Wernicke's is one serious neurological manifestation of pregnancy, especially complication with hyperemesis gravidarum for which thiamine deficiency may set in. Clinical suspicion, timely neuroimaging, and rapid commencement of parenteral thiamine treatment would redound to the benefit of the mother and baby. Further studies must, therefore, be conducted to foster the creation of relevant diagnostic tools and expanding preventive measures so that we can help moderate the burden on life from this potentially disastrous condition.

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