May 5th, 12:00 AM

Wernicke's Encephalopathy Secondary to Hyperemesis Gravidarum

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Introduction:

Wernicke's encephalopathy (WE) is a neurological disorder secondary to thiamine deficiency that is precipitated by administration of glucose-containing fluids prior to thiamine supplementation. Though WE is typically diagnosed among alcoholics (12.5%), the prevalence among nonalcoholics can vary from 0.04-0.13% [1]. Around 30-40% of patients with underlying thiamine deficiency will only experience one of the symptoms from the typical triad, with the complete triad (encephalopathy, oculomotor dysfunction/nystagmus, and ataxia) only evident among 5-16% of the population [2,3]. Among the non-alcoholic patient population presenting with WE, a history of vomiting is more frequent [4]. While nausea affects around 80% of pregnant women, an extreme form of the same affects only 0.5 to 3%, however can lead to severe nutritional deficiency [5]. Pregnant women have an increased demand for thiamine and among patients with underlying hyperemesis gravidarum, thiamine (vitamin B1) rapidly depletes. Thiamine is an essential cofactor with regard to carbohydrate metabolism and in cells with high metabolic requirements and inadequate stores, neuronal damage can occur [6]. WE remains a clinical diagnosis and thus difficult to observe in patient presenting with a low index of suspicion.

Case Presentation:

We present the case of a 22-year-old female, G1P0 at 16-weeks gestation with prior history of hyperemesis gravidarum on an ondansetron pump, who presented to our community emergency department for the evaluation of confusion, worsening vomiting and an elevated blood pressure. Her obstetrician referred her to the emergency department for worsening drowsiness and confusion, where she presented somnolent with a limited history. She had prior trials of metoclopramide, promethazine, and doxylamine-pyridoxine that were unsuccessful in alleviating her symptoms. She was prescribed prenatal vitamins, though it was uncertain if she had been compliant secondary to the hyperemesis. Family was unable to be reached during evaluation in the emergency department.

On physical exam, the patient was found to be ill-appearing however nontoxic. Her initial vital signs were blood pressure 164/108, tachycardic at 153 beats per minute, 98.4°F temporally, respirations of 18 breaths per minute, and oxygenating 99% on ambient air. Neurologically, she was very somnolent but arousable to loud verbal stimuli and oriented to person, place, and time although confused intermittently. She was tachycardic, without significant murmurs auscultated. A Zofran pump was noted to be attached in her flank. The remainder of the physical exam was benign. Laboratory studies were significant for a transaminitis (AST 84 U/L, ALT 171 U/L), an alkaline phosphatase of 134 U/L, and a lactic acidosis of 2.8 mmol/L. Serum alcohol was normal. Quantitative hCG was 83,712 mIU/mL. The remainder of laboratory studies were within normal ranges. An electrocardiogram noted sinus tachycardia at 146 beats per minute. An abdominal ultrasound noted a viable intrauterine pregnancy with the estimated gestational age of 16 weeks and 2 days. MRI of the brain without contrast was significant for restricted diffusion in bilateral paracentral thalami, concerning for a recent infarction in the distribution of the artery of Percheron (Figures 1 through 3); subsequent MRA and MRV were negative. During the course of her hospitalization, she exhibited waxing and waning levels of consciousness and developed memory loss and confabulations. Further history revealed that she recently quit alcohol use upon learning of her pregnancy. Symptoms and MRI findings were consistent with Wernicke's encephalopathy, thus she was initiated on IV thiamine infusions after a thiamine level was obtained (27 nmol/L; reference range: 70-180), with eventual improvement of her mentation. She was discharged in improved condition and referred to high-risk maternal fetal medicine as well as neurology for close outpatient follow-up.

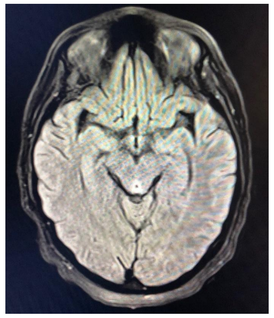

Figure 1: axial slices, unenhanced magnetic resonance imaging of the brain at the level of the mammillary bodies and aqueduct, T2/FLAIR sequence.

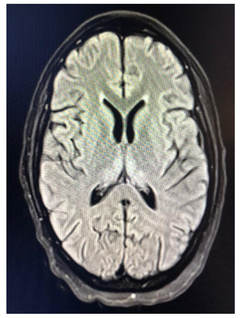

Figure 2: axial slices, unenhanced magnetic resonance imaging of the brain at the level of the thalamus, T2/FLAIR sequence.

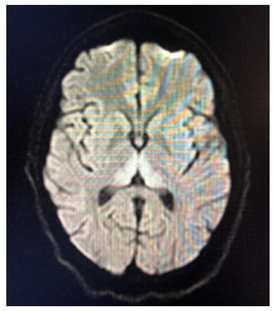

Figure 3: axial slices, unenhanced magnetic resonance imaging of the brain at the level of the thalamus, trace diffusion weighted images.

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Discussion:

Wernicke's encephalopathy is an underdiagnosed condition that can be missed during evaluation in the emergency department, particularly when presented with confounding risk factors. A patient that remains untreated can be fatal as this condition progresses to coma and death if left untreated. IV administration of thiamine has been shown to be safe, with one recommended regimen as 500mg IV infused over a duration of 30 minutes TID for 2 consecutive days and 250mg IM or IV once daily for an additional 5 more days [7]. A systematic review revealed that an estimated 63.6% of patients are treated with subtherapeutic dosing [8]. Chronic cognitive disorders resulted among 65.4% of the population, pregnancy loss in half of cases and maternal death in 5%. Another study reviewed 49 cases with an overall pregnancy loss rate and planned abortion among 47.9% [9]. These studies highlight the importance of thiamine supplementation to women with prolonged vomiting even before initiating parenteral nutrition [10]. Nutritional deficit among high risk populations can also be observed among children with persistent vomiting and prolonged parenteral nutrition [11].

A retrospective review of six women developing neurologic symptoms following hyperemesis revealed complete neurologic recovery after thiamine administration on follow-up examinations [12]. Thus, when the diagnosis is suspected, parenteral thiamine should be initiated. The sensitivity of imaging via MRI in revealing WE is 53%, with a specificity of 93%. MRI, rather than CT, is therefore useful in confirming the diagnosis, however, absence of abnormalities on MR imaging does not exclude the diagnosis [13]. If left untreated, a majority will develop Korsakoff psychosis, characterized by memory impairment and confabulation. An approach to overdiagnosis with subsequent treatment to prevent prolonged neurocognitive impairment may be preferred, given that it is quite safe to administer thiamine [14].

We emphasize this case as an important consideration for emergency physicians to maintain a high clinical suspicion of Wernicke's encephalopathy in the broad context of a patient that presents with an altered mental status, and more specifically among the pregnant population that may be high risk for malnutrition and electrolyte imbalances in the context of hyperemesis gravidarum. Our case was complicated by the patient's history of concurrent alcoholism. Both undoubtedly played a pivotal role in her development of severe thiamine deficiency.

Conclusions:

Wernicke's encephalopathy (WE) is a neurological disorder secondary to thiamine deficiency precipitated by administration of glucose-containing fluids prior to thiamine supplementation. It is typically associated with alcoholism, however, also high risk malnutrition states, one of which includes hyperemesis gravidarum. The emergency physician should be conscious of the complications regarding patients presenting with hyperemesis gravidarum, as Wernicke encephalopathy should be considered in the differential with populations at risk for underlying thiamine deficiency [15].