Wernicke's Encephalopathy Due to Hyperemesis Gravidarum Masquerading as Major Depressive Disorder:

A Reminder to Assess for At-Risk Thiamine Deficiency States

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Wernicke's encephalopathy (WE) is an acute neurologic syndrome resulting from a deficiency in thiamine. Thiamine stores can be depleted rapidly in patients with severe hyperemesis, such as in hyperemesis gravidarum (HG).[1] Early symptoms of WE are often nonspecific and can be misdiagnosed.[1] We present the case of a patient, who after being diagnosed with HG and 2 weeks post–elective abortion, was admitted to the psychiatry department of our hospital and misdiagnosed with "severe depression."

Case Report

An 18-year-old female patient with no prior psychiatric history presented to our emergency department due to behavioral changes for 2 weeks following an elective abortion at 10 weeks gestation. At presentation, the patient was inattentive and not aware of her surroundings. She was unable to provide a detailed history, but endorsed feeling "depressed and numb," with her parents providing the remainder of the history.

Her vital signs were unremarkable, with the exception of blood pressure of 96/58 mm Hg and pulse of 104 beats/minute. There were no signs suggestive of catatonia. The complete blood count was normal except for hemoglobin/hematocrit of 9.6 g/dL/32.6%. Otherwise, complete metabolic profile, vitamin B_{12}, folate, thyroid function tests, urinalysis, and chest x-ray were all within normal limits. Computed tomography (head) was unremarkable for acute abnormalities.

Following admission to the inpatient psychiatry department, our patient appeared drowsy with fluctuating mental status and confusion. She refused medications and meals, and staff observed episodes of emesis. At this point, despite initial impression of a severe major depressive episode, the patient was administered the Confusion Assessment Method (CAM)[2] for delirium with a positive result.

On hospital day 4, she became tachycardic at 160 beats/minute, and her blood pressure decreased to 90/54 mm Hg with new leukocytosis. The physical examination was notable for lower extremity weakness with distal paresthesia and ataxia. She was transferred to the internal medicine service for further evaluation and treatment. See Table 1 for magnetic resonance imaging (MRI) head and treatment. The electroencephalogram demonstrated diffuse mild-moderate slow waves. After 5 days of treatment with thiamine, WE had markedly improved, and the CAM result was negative. Our patient was discharged on oral thiamine.

Discussion

Importantly, for a comparison and review of WE due to alcoholic, nonalcoholic, HG (WE/HG), and in our patient, see Table 1.[3–11] The third most common cause of non–alcohol-induced WE is HG.[3] As in our patient, recurrent vomiting during HG likely results in thiamine deficiency, more relevant during pregnancy, when thiamine requirements increase.[1,10] Nonetheless, our patient is not the first reported case of WE misdiagnosed as major depressive disorder.[9] Importantly, nausea, vomiting, and loss of appetite are common, nonspecific presenting symptoms of thiamine deficiency, fully overlapping with HG, with loss of appetite being common to HG/thiamine deficiency and major depressive disorder.[10] Furthermore, according to a review, the spectrum of mental status changes that can occur in WE, including mental sluggishness (~20%), apathy (~10%), impaired awareness of the immediate situation, and inability to concentrate (~63%), can also be misinterpreted as major depressive disorder.[7,12]

Similar to our patient, the classic triad of WE (see Table 1) has been reported to occur in between 50% and 60% of WE/HG patients,[7,12] with 91% demonstrating MRI alterations in the thalamic region of the brain.[7] Thus, despite its non–alcohol-induced etiology, WE/HG often presents similar to alcohol-induced WE. We do caution that since a blood thiamine level was not collected prior to repletion, a deficiency was not objectively quantified. However, given MRI findings and clinical response to thiamine therapy, our patient was given a diagnosis of WE.[13]

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Table 1. Review of Wernicke's Encephalopathy (WE): Alcoholic, Nonalcoholic, Due to Hyperemesis Gravidarum (HG), and in Our Patient

WE	Alcoholic	Nonalcoholic	Due to HG	Our Patient
Epidemiology[3–5]	93% of WE cohort	7% of WE cohort	9%–12% of nonalcoholic WE cohort	N = 1
Pathology,[4,5]	Thiamine deficiency caused by several mechanisms, including inadequate dietary intake	Thiamine deficiency due to poor dietary intake, increased basal metabolic rate, and ingested nutrients lost through vomiting/diarrhea	Hypermetabolic state of pregnancy, increased fetal demand, poor intake, and malabsorption due to nausea and vomiting	Observed poor oral intake due to severe nausea and vomiting; no history of alcohol or illicit substance use
Clinical	More frequently present as subclinical syndrome	Usually presents as dramatic acute syndrome	Acute-subacute onset[7]	Acute onset
Presentation[6–9]	Common signs of WE are difficult, if not impossible, to differentiate from drunkenness		Excessive vomiting as a median present for 7 weeks (range, 1–30 weeks) before onset of WE symptomatology[7] Prodrome: visual alterations, such as diplopia or blurred vision[7]	Excess vomiting: Beginning at 4 weeks of pregnancy, markedly increased at 5 weeks gestation, and ceasing < 2 days following elective TOP at 10 weeks Behavioral changes[9]: x 2 weeks: (+) apathy, social withdrawal, decreased speech, (+) confusion, and worsening memory Physical examination: (+) vertical and horizontal nystagmus; decreased DTRs in BL patellar, ankle, and biceps reflex; (+) gait ataxia, (+) TOP at 10 weeks gestation
Classical diagnostic triad[7,8]	(+) 16%–40%; more likely to present with cerebellar signs or tremor	(+) ~ 30%; more likely to present with ocular signs	(+) ~ 50%; severe alteration of consciousness ~30%, milder impairment of consciousness = 19.0, confusion = 60.3%, apathy = 12.6% Overall pregnancy loss rate, direct and indirect = 48%; 5% of mothers do not survive WE	
MRI head	Lesions in nearly two-thirds	Higher yield of lesions varying from 97% (DWI), 99% (conventional), and 100% (FLAIR)		
Location of lesions[10]	Cortico-subcortical atrophy more common (mammillary bodies cerebellar vermis) Classically, symmetrical typical locations are more common: thalami, mammillary bodies, tectal plate, and periaqueductal area	Cortico-subcortical atrophy less common Classically, atypical locations are more common: cerebellum, vermis, cranial nerve nuclei, red nuclei, dentate nuclei, caudate nuclei, splenium, and cerebral cortex	Thalamic alterations visible in mother also visible on MRI of fetus, suggesting additional chances for congenital birth defects Typical locations are more commonly observed	MRI notable for medial thalamic, periaqueductal midbrain, and dorsal pontine abnormalities consistent with WE
Treatment[11]	IV thiamine, perhaps at higher doses than nonalcoholic WE; thiamine should be given before carbohydrates	IV thiamine; thiamine should be given before carbohydrates	Prophylactically,100 mg of IV or IM thiamine (to prevent development of WE from HG)	Started on thiamine 250 mg IV, followed by 100 mg IM for 5 days with subsequent improvement in all WE symptoms

Abbreviations: BL = bilateral, DTR = deep tendon reflex, DWI = diffusion-weighted imaging, FLAIR = fluid-attenuated inversion recovery, IM = intramuscular, IV = intravenous, MRI = magnetic resonance imaging, TOP = termination of pregnancy.
Symbol: (+) = present.

WE remains a clinical diagnosis, but a nonspecific clinical presentation can lead to a delayed diagnosis. In the case of WE/HG, this delayed diagnosis can result in adverse pregnancy outcomes.[14] Clinicians should consider WE in patients with unbalanced nutrition or clinical settings at risk for thiamine deficiency.[11,15]

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