A Case Report of Nonalcoholic Gayet-Wernicke Encephalopathy: Don't Miss Thiamine

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Gayet-Wernicke encephalopathy (WE) is an acute neurological disorder resulting from deficiency of thiamine, commonly related to chronic abuse of alcohol, but frequently missed or overlooked as a diagnosis when a nonalcoholic patient presents with atypical signs and symptoms of the disease. The diagnosis of the disease is clinical, and confirmation is done by magnetic resonance imaging. We aim to highlight a case of WE in a nonalcoholic postoperative surgical patient receiving total parental nutrition where high-dose intravenous administration of thiamine in time mitigated the symptoms of disease and prevented permanent neurological sequelae. We spotlight the significance of adequate thiamine for postoperative malnourished surgical patients. (A&A Practice. 2020;14:e01230.)

GLOSSARY

ASA = American Society of Anesthesiologists; **BMI** = body mass index; **CPR** = cardiopulmonary resuscitation; **FLAIR** = fluid-attenuated inversion recovery; **GCS** = Glasgow Coma Scale; **ICU** = intensive care unit; **MRI** = magnetic resonance imaging; **MV** = minute ventilation; **MVI** = multivitamin infusion; **Pco₂** = partial pressure of carbon dioxide; **PEEP** = positive end-expiratory pressure; **Po₂** = partial pressure of oxygen; **Spo₂** = oxygen saturation; **TPN** = total parental nutrition; **WE** = Gayet-Wernicke encephalopathy

Gayet-Wernicke encephalopathy (WE) is an acute but serious neurological pathology due to thiamine deficiency. Thiamine is an important water-soluble vitamin, essential for maintaining the cellular osmotic gradient. It also acts as a coenzyme in metabolism of glucose and is needed for normal activity of neurons. Thiamine deficiency in brain tissue can hamper the normal signal of neurons leading to clinical signs and symptoms of WE.¹⁻³

WE is commonly seen in alcoholics, with a prevalence of 12.5% as alcohol inhibits utilization of thiamine.⁴ However, it has also been reported in nonalcoholic patients, with an incidence of 0.8%–2.8% in autopsy reports and only 0.04%–0.13% in clinically reported cases.⁵ In nonalcoholic patients, it is often undiagnosed or underdiagnosed due to a low level of suspicion. Here, we report a case of WE in a nonalcoholic postoperative patient receiving total parental nutrition (TPN) with multivitamin infusion (MVI). The aim of this report is to alert anesthesiologists and clinicians about this rare complication, as this can be easily confused with other neurological problems, particularly in nonalcoholic patients in an intensive care unit (ICU). A written patient

consent was obtained to use or disclose protected health information.

CASE REPORT

A 22-year-old Indian man with body mass index (BMI) of 18.2 kg/m² and American Society of Anesthesiologists (ASA) physical status IE was transferred to our anesthesia ICU for ventilator support after emergency exploratory laparotomy. He had a chief complaint of sudden progressive abdominal pain associated with vomiting without stool or flatus passage for 2 days and was diagnosed with intestinal perforation and peritonitis. He had a placement of gastrostomy tube and retrograde duodenostomy with duodenal decompression for duodenal perforation with placement of a feeding jejunostomy. He received 1 cycle of successful cardiopulmonary resuscitation (CPR) intraoperatively for sudden asystole. Severe hypotension was the probable cause. He had no history of alcohol or other drug abuse. On arrival to the ICU, his heart rate was 120 beats per minute and blood pressure was 102/64 mm Hg on norepinephrine (0.15 µg/kg/min) and dopamine (10 µg/kg/min) infusions. His initial laboratory findings were unremarkable. His arterial blood gas showed metabolic acidosis: pH, 7.28; partial pressure of carbon dioxide (Pco₂), 34 mm Hg; partial pressure of oxygen (Po₂), 101 mm Hg; bicarbonate, 19.5 mmol/L; oxygen saturation (Spo₂), 95.5%, and base excess, -4.5.

On postoperative day 2, the inotropic support was tapered slowly and by postoperative day 4, the patient was weaned from the inotropes. On postoperative day 5, the patient suddenly developed a tense and rigid abdomen, so jejunostomy feedings were not initiated. The patient was dependent on TPN with intravenous MVI (containing 6 mg of thiamine) once daily. Synchronized intermittent mandatory ventilation (tidal volume [V_T] = 350–400 mL,

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respiratory rate = 10–12/min, positive end-expiratory pressure [PEEP] = 5–8 cm H₂O, minute ventilation [MV] = 4.2–4.8 L/min, plateau pressure [P_{plat}] = 14–16 cm H₂O, peak pressure [P_{peak}] = 23–25 cm H₂O) was continued because of poorly compliant lungs (0.04–0.05 L/cm H₂O) and failed weaning trials. A tracheostomy was performed on postoperative day 8 due to altered sensorium and a worsened general condition. His condition gradually improved over the next 2 weeks. He became fully conscious and started to obey verbal commands with a Glasgow Coma Scale (GCS) score of 11. He responded well to spontaneous breathing trials with minimal ventilatory support. TPN had to be continued due to failure of intermittent enteral feeding trials.

On postoperative day 33, the patient suddenly developed intermittent bilateral horizontal nystagmus. It gradually increased and was associated with a change in mental status. Electroencephalography and ophthalmic and otorhinologic examinations did not identify other abnormalities. Despite supportive treatment, his general condition and neurological status further deteriorated (GCS = 5), with persistent bilateral horizontal nystagmus, confusion, disorientation, reduced deep tendon reflexes, and facial twitching. He had 2 episodes of generalized tonic clonic seizures and became unresponsive. Mechanical ventilation with full ventilatory support was restarted. Computed tomography scan of his brain revealed tiny ischemic and hemorrhagic spots in the thalami and basal ganglia (Figure 1). Supportive treatment, including intravenous antiepileptics, was continued, but no improvement was seen. Lower extremity dopplers, nerve conduction velocity, electromyography, cerebrospinal fluid analysis, and serum biochemistry were also inconclusive. The patient was negative for human immunodeficiency virus and dengue serology. The gastrostomy and duodenostomy tube were removed by the surgeon, as the drainage through them were minimal.

On further evaluation, magnetic resonance imaging (MRI) of the brain with T2-weighted fluid-attenuated inversion

recovery (FLAIR) sequences revealed bilateral symmetrical abnormal hyperintensities in the frontal lobes, thalami, basal ganglia, periaqueductal gray matter, mammillary bodies, and superior cerebellar peduncles (Figures 2–5A). Hypoxic injury to the brain secondary to CPR was provisionally diagnosed. However, hypoxic injury was ruled out, as the patient initially had neurological improvement following surgery that then deteriorated a few weeks later. As the patient had some clinical features consistent with WE, he was treated with high-dose parenteral thiamine with an intravenous dose of 500 mg, followed by 200 mg 3 times a day. There was a significant improvement in mental status and muscle strength within 5 days. Jejunostomy tube was removed by the surgeon, and it could not be used for the feeding. Intravenous thiamine 250 mg once a day was continued for the next 5 days. Magnesium, potassium, vitamin C, and phosphate were also supplemented simultaneously. The patient became conscious, alert, and started to maintain adequate oxygenations on room air (tracheostomy tube in situ). As the patient started to improve, he also started to tolerate enteral feeding through a nasogastric tube. He was transferred to the stepdown unit on oral thiamine (through a nasogastric tube) 100 mg 3 times a day for 3 weeks for further management.

MRI scan was repeated after 1 month of thiamine treatment. It revealed significant interval change with near-complete resolution of the cortical and brainstem lesions and partial resolution of bilateral medial thalamic hyperintensity (Figures 2–5B). Oral thiamine, 100 mg, once a day was continued. The following month, the patient's trachea was decannulated successfully and discharged home.

The patient was followed for 6 months. His symptoms resolved completely with no amnesia, and the patient is completely independent with no neurological deficit or sequelae.

DISCUSSION

Nonalcoholic WE, though rare, has been reported in malnourished patients,^{2,5} hyperemesis gravidarum,^{2,5} and sepsis.⁵ It has also been reported in postoperative patients who underwent bariatric^{2,5,6} or gastrointestinal resection surgeries^{2,5–7} and those on prolonged TPN.^{6–8} However, diagnosis of nonalcoholic WE is often difficult, with 75%–80% patients misdiagnosed.^{1,3,5} In 11% of patients, WE has no symptoms. The clinical triad of ophthalmoplegia, ataxia, and mental disturbances is only reported in 10%–20% patients. In the majority of cases (82%), confusion or other mental changes are the only symptoms. Other symptoms include ataxia, polyneuropathy, oculomotor dysfunctions, and irritability.⁶

WE is caused by severe thiamine deficiency. Thiamine is a water-soluble vitamin absorbed in the duodenum or jejunum either by active transport or a passive mucosal process depending on thiamine levels. Daily requirement of thiamine is 5 mg, with a half-life of 9–18 days. Total reserve of thiamine in the body can be up to 30 mg.² Thiamine is converted to thiamine pyrophosphate by the enzyme thiamine pyrophosphokinase in the presence of magnesium.⁵ Thiamine pyrophosphate is an important coenzyme for enzyme metabolism, degradation of glucose, and cerebral energy use. Therefore, its deficiency limits brain metabolism, and by the 14th day, brain lesions occur

Figure 1. Computed tomography of brain: tiny ischemic and hemorrhagic spots in thalami and basal ganglia.

Figure 2. Sagittal MRI. A, Sagittal views of MRI of brain showing involvement of frontal lobes, thalami, basal ganglia, mammillary body, and midbrain. B, After thiamine treatment, improvement is seen in MRI scan with near resolution of frontal lesions and thalami. MRI indicates magnetic resonance imaging.

if left untreated.² However, critical illness, malnutrition, and chronically depleted conditions increase the body's requirement of thiamine.^{5,9,10}

In our case, the patient developed bilateral horizontal nystagmus on postoperative day 33, which progressed to confusion, disorientation, seizures, and unconsciousness. These symptoms can be attributed to thiamine deficiency,

as thiamine reserves were depleted. Zuccoli and Pipitone¹¹ stated that it takes around 3–4 weeks to utilize the body's reserves of thiamine. In our case, underlying malnutrition (BMI, 18.2 kg/m²), prolonged ICU stay, and surgery led to increased requirement of thiamine. Because the patient was bedridden and on ventilator support, gait disturbances could not be assessed.

Figure 3. Coronal FLAIR images. A, Coronal FLAIR images showing bilateral and symmetrical hyperintense lesions in thalami and periaqueductal lesions (circle). There is also cortical involvement of frontal lobes showing multiple subacute infarcts (arrows). B, Coronal FLAIR images show near and complete resolution of cortical lesions and thalami after thiamine treatment. FLAIR indicates fluid-attenuated inversion recovery.

Figure 4. Axial FLAIR images. These show multiple hematomas in bilateral temporoparietal region (arrow) (A) and infarcts in thalami (circle), improving after thiamine treatment (B). FLAIR indicates fluid-attenuated inversion recovery.

Figure 5. Axial FLAIR images. A, Axial FLAIR images show symmetrical hyperintensity involving midbrain tectum, periaqueductal grey matter, superior cerebellar peduncles, and thalamus, improving after thiamine treatment (B). FLAIR indicates fluid-attenuated inversion recovery.

Nonalcoholic WE can be confirmed by MRI using FLAIR sequence with 93% specificity.^{11,12} T2 hyperintensities can be found throughout the regions of the brain with typical lesions in the thalamus, mammillary bodies, and periaqueductal area in alcoholic related WE. Vasogenic and cytotoxic edema can coexist in thiamine deficiency, mimicking hypoxic-ischemic insults.¹³ Similarly, in this case, hypoxic injury to the brain was suspected at first, especially with the history of CPR. But the patient had considerable improvement only after high-dose intravenous thiamine with resolution of previous lesions on subsequent MRI scans. The diagnosis of nonalcoholic WE was confirmed, and the other differential diagnoses of stroke, cerebral venous thrombosis, ICU neuropathy, and acute encephalitis were ruled out. Other disorders that can cause confusion, such as drug withdrawal, sepsis, and hepatic encephalopathy, were also ruled out.

Laboratory testing does not aid in the diagnosis of WE.^{2,6} In this case, total thiamine and thiamine diphosphate levels were not assessed, as they do not reflect total thiamine

stores. However, a thiamine pyrophosphate effect test can assess actual thiamine status, but due to its nonavailability at our center, this test was not done.

In our case, clinical suspicion of WE was delayed as the patient was a nonalcoholic. He was treated with high-dose thiamine on the basis of clinical features consistent with Caine's criteria (nystagmus, altered mental state)¹⁴ and Thomson grading (disorientation, confusion, unconsciousness)¹⁵ for diagnosis of WE. Guidelines published by the European Federation of Neurological Societies for the treatment of WE in alcoholics were followed for treatment, as no published guidelines exist for treatment of WE in nonalcoholics.⁵ WE should be treated promptly, as it can further lead to Korsakoff's syndrome, coma, and death. Mortality rates of WE are high, ranging from 20% to 30%.²

CONCLUSIONS

In nonalcoholic patients, this rare complication is challenging to diagnose. We should use increased doses of thiamine

supplementation in cases of underlying malnutrition, gastrointestinal surgeries, prolonged postoperative ICU stay, and TPN. Any clinical suspicion of WE should be treated promptly with thiamine supplementation to prevent permanent neurological damage. ■■

DISCLOSURES

Name: Kompal Jain, DA, DNB.

Contribution: This author helped to conceive the work, and draft the manuscript.

Name: Jasveer Singh, MD.

Contribution: This author helped interpret the case and revise the manuscript critically for important intellectual content.

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