Nonalcoholic Wernicke's encephalopathy

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ABSTRACT

Wernicke's encephalopathy (WE) is a serious neurologic condition resulting from thiamine deficiency. The majority of cases involve alcoholism; however, nonalcohol-associated WE does occur and is under-recognized. We discuss a case of a 22-year-old man with a history of Crohn's disease who presented to our emergency department with multiple neurologic complaints related to WE.

RÉSUMÉ

L'encéphalopathie de Wernicke (EW) est une affection neurologique grave, qui résulte d'une carence en thiamine. Dans la majorité des cas, la maladie est associée à l'alcoolisme, mais il arrive qu'elle ne le soit, et, dans ces cas, l'affection est mal reconnue. Sera exposé ici le cas d'un jeune homme de 22 ans, qui avait des antécédents de maladie de Crohn et qui a consulté au service des urgences pour de nombreux troubles neurologiques liés à l'EW.

Keywords: nutritional deficiency, thiamine deficiency, Wernicke's encephalopathy

INTRODUCTION

Wernicke's encephalopathy (WE) is often thought of in the context of alcoholism and neurologic abnormalities. The relationship with other diseases that lead to thiamine deficiency is less often recognized in a patient who presents with a variety of neurologic complaints. However, it is imperative that WE is diagnosed and treatment is started as quickly as possible. This case report illustrates how the diagnosis may initially be difficult and that it is necessary to consider WE in the differential diagnosis when presented with a patient with risk factors for the disease.

CASE REPORT

A 22-year-old male presented to the emergency department after he witnessed seizure-like activity lasting 30 seconds. The episode was followed by a postictal state. There had been no prior history of seizures.

For several days, he had been noted to have mild perseveration of speech with intermittent dysarthria. He had presented to the emergency room three times within a 2-week period with various complaints. Initially, he was seen for fatigue and presyncope. At that time, he denied fevers, chills, dyspnea, anorexia, or change in bowel habit. His vital signs showed a low blood pressure and a slight tachycardia, which both patient and records had noted to be "normal" for him. Blood work, electrocardiogram, chest x-ray, and physical exam were unremarkable. He was discharged home. Four days later, he was seen for vertigo that was similar to an episode several months earlier. He noted nausea and vomiting with the vertigo, but no hematemesis, fever, chills, vision changes, or other neurologic symptoms. Blood work at this time was unremarkable, and physical exam yielded an appropriate neurologic exam. Dix-Hallpike testing yielded latent vertigo with nausea and rotatory nystagmus on the left positioning. He was diagnosed with benign paroxysmal positional vertigo and referred to an ear, nose, throat (ENT) physician as an outpatient.

He returned several days later with persistent vertigo and new onset binocular horizontal diplopia. A friend presented with the patient and stated that he had been repeating himself on the phone earlier that day. He was

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CJEM 2016;18(4):309-312 DOI 10.1017/cem.2015.27

noted to be quite thin and pale, though this was stated to be his baseline appearance. He was alert and oriented. He exhibited bilateral sixth nerve palsy. The remainder of the neurologic exam was unremarkable with the exception of clear ataxia. An unenhanced CT head was conducted and was normal. Neurology was subsequently consulted and arranged MRI brain and follow-up within several days. Prior to the appointment, he returned with witnessed seizure-like activity.

Evaluation at the time of the seizure yielded a very pale and thin young man. He was afebrile with similar vital signs to previous visits. His general physical exam was normal; however, his neurologic exam demonstrated horizontal ophthalmoparesis with preservation of vertical eye movement. Nystagmus was noted with extremes of gaze. There was no ptosis. In the emergency department, he had a witnessed generalized tonic-clonic seizure lasting approximately 45 seconds in which he was given lorazepam 1 mg IV and phenytoin 500 mg IV.

The patient underwent a lumbar puncture, and an urgent MRI and neurology consultation was arranged. In light of the patient's frail appearance, ophthalmologic symptoms as well as confusion in the differential diagnosis included encephalitis, meningitis, and WE. He was given a high dose of IV thiamine and acyclovir. The MRI subsequently showed symmetric increased T2 signal and restricted diffusion without enhancement in the posterior aspect of the pontomedullary junction, circumferentially within the periaqueductal gray, within the inferior colliculus, mammillary bodies, medial thalami, and hypothalamus. There was also increased T2 signal seen along the lateral aspect of the right frontal lobe. These findings were most consistent with Wernicke's encephalopathy.

The patient was ultimately admitted under the neurology service, given a high dose of intravenous thiamine, and observed in the intensive care unit. The cerebrospinal fluid was acellular with normal protein and glucose, and the electroencephalogram showed diffuse disturbance of cerebral cortical function. He was continued on phenytoin and had no further seizures. He also received changes in his Crohn's regimen to attempt better control and dietetics consultation to address malnutrition. He was discharged home on thiamine 100 mg orally once daily and with close follow-up from the neurology and gastrointestinal services.

DISCUSSION

WE is a neurologic condition as a consequence of thiamine (vitamin B_1) deficiency. It was first described by Carl Wernicke in 1881; he noted the classic triad of altered mentation, ataxia, and ocular signs in association with brain lesions on autopsy.[1] The prevalence of WE brain lesions is 0.4% to 2.8%, with most of those affected having a history of alcoholism.[2,3]

Chronic alcoholism is the most well known association with WE. WE is also seen in individuals with malnutrition from a variety of factors, including malabsorption, poor dietary intake, dialysis-related loss of thiamine, increased metabolic demand, gastrointestinal disease or surgery, malignancy, and hyperemesis gravidarum.[2,3] It has also been associated with non-nutritional states, such as structural lesions of the medial thalami.[4] The deficiency in thiamine results in acute and chronic changes within the brain. These changes occur in structures surrounding the third ventricle, aqueduct, and forth ventricle. Acutely, there is vascular congestion, microglial proliferation, and petechial hemorrhages. Chronically, demyelination, gliosis, and neuronal loss occur.[2]

Our patient presented initially with fatigue and vertigo and progressed to oculomotor dysfunction as well as confusion. His history of Crohn's disease and multiple bowel surgeries put him at risk for malnutrition and thiamine deficiency. Therefore, WE was considered in the differential diagnosis. Suspicion for this disorder must be high; with clinicians appreciating the presentation of nonalcohol-associated WE versus alcohol-associated WE may be different, and the classic triad of symptoms may not be apparent.

Clinical manifestations

The classic triad of encephalopathy, oculomotor dysfunction, and gait ataxia is only seen in approximately one-third of patients and is more common in alcoholics.[2,3,5] The literature has noted that the most common presentation is mental status abnormalities. Patients may exhibit profound disorientation, indifference, and inattentiveness. Without treatment, patients can progress to the more permanent Wernicke-Korsakoff syndrome (in which the confabulation does not resolve), decreased level of consciousness to coma to death.

https://doi.org/10.1017/cem.2015.27 Published online by Cambridge University Press

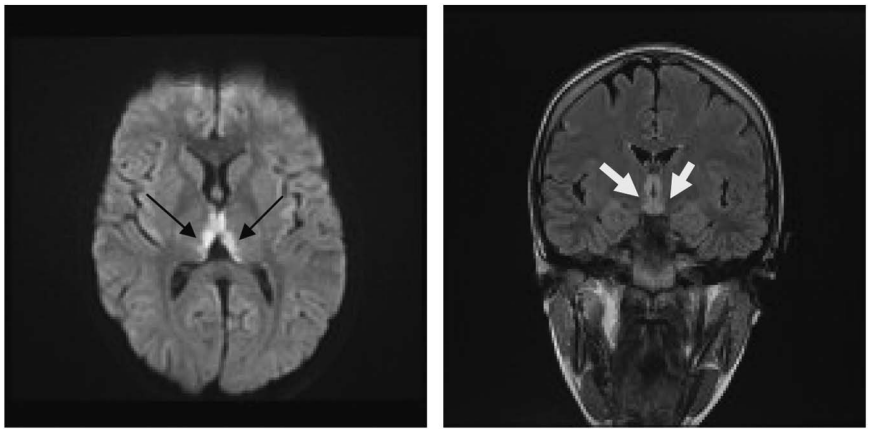

Figure 1. MRI Diffusion weighted images highlighting WE changes in bilateral thalami (black arrows in the axial Diffusion Weighted Images) of our patient. Also, note the T2 hyperintesities in the periventricular region around the third ventricle with involvement of the mammillary bodies (white arrows in the Coronal T2 weighted image on the right).

Eye signs include nystagmus as well as lateral rectus and conjugate gaze palsies.[5] In most cases, these eye signs occur together. Gait abnormalities can range from mild to severe; in mild cases, it can be seen on tandem gait, and, in severe cases, patients are unable to walk. Ataxia may precede other symptoms by a few days or weeks, whereas other symptoms may present around the same time.[2]

Patients may also present with stupor or coma, hypotension, and hypothermia. In addition, both vestibular dysfunction without hearing loss and peripheral neuropathy, particularly involving the lower extremities, are common.[2] In fact, the latter is present in upwards of 80% cases.[4]

Diagnosis

Clinical suspicion for WE should be high because clinical presentation varies and the diagnosis is largely clinical. Thiamine levels can be determined by chromatography; however, patients should be treated immediately with thiamine if WE is suspected, and treatment should not wait or be based on laboratory tests.[2,5] A similar urgency to treatment is important when considering imaging studies, and treatment should not be delayed pending such studies.[2]

Imaging studies can be useful in both ruling out other medical conditions that may mimic WE as well as showing characteristics consistent with WE. CT scan is noted to be insensitive and unreliable for WE, though it may show symmetric, low-density abnormalities in the diencephalons, midbrain, and periventricular regions.[2,3]

MRI is considered more sensitive in detecting specific changes associated with WE.[3] Imaging shows typically reversible cytotoxic edema, with symmetric increased T2 and decreased T2 signal around the aqueduct and third ventricle as well as within the medial thalamus, tectal plate, and mammillary bodies[2,5] (Figure 1). Atrophy is not seen in nonalcoholic patients; however, it is present in alcoholism. In addition, atypical findings on MRI may be seen in nonalcoholic patients, but not in alcoholic patients.[5]

Treatment

As soon as WE is suspected, treatment should be initiated. The literature is divided with regard to the optimal dose and route and treatment time.[3] One regimen recommends 500 mg of thiamine intravenously three times daily for 2 days and then 500 mg intravenously or intramuscularly once daily for 5 additional days. Following this, patients should receive 100 mg orally daily until patients are no longer considered at risk.[2] High dose thiamine is recommended because lower doses have failed to produce improvement in some patients.[2] Another regimen recommends 200 mg of thiamine intravenously three times a day until there is no further improvement in signs and symptoms.[3] Note that the first dose of thiamine should be administered prior to the administration of any carbohydrate because it can worsen WE.[2,3]

With administration of thiamine, ocular signs are generally the first to recover, resolving within hours to days. Confusion improves over days to weeks, and

https://doi.org/10.1017/cem.2015.27 Published online by Cambridge University Press

vestibular function improves within weeks. There are residual effects noted in some patients, with deficits in gait as well as cognition persisting.[2]

CONCLUSION

WE is a clinical diagnosis and should be considered in anyone presenting with confusion, ataxia, or oculomotor signs. WE is often underdiagnosed because the classical triad is not seen in the majority, especially those with nonalcoholic WE. Therefore, suspicion should be high. Treatment with high-dose thiamine should be initiated immediately; for many patients, this means administration in the emergency department setting.

Acknowledgements: A special thank you to the young man featured in this case report as well as to his family for allowing us to share this case. Unfortunately, prior to submission of this article, he succumbed to complications of Crohn's disease.

Competing interests: None declared.

REFERENCES

1. Thomson AD, Cook CCH, Guerrini I, et al. Wernicke's encephalopathy revisited. *Alcohol Alcohol* 2008;43(2):174-9.
2. Charness ME, Yuen TS. Wernicke's encephalopathy. UpToDate; 2013. Available at: http://www.uptodate.com (accessed 24 March 2013).
3. Galvin R, Brathen G, Ivashynka A, et al. EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. *Eur J Neurol* 2010;17(12):1408-18.
4. Ropper A, Samuels M, Klein J. Diseases of the nervous system caused by nutritional deficiency. In: *Adams and Victor's principles of neurology*, 10th Edition. pp 1161-85. New York: McGraw-Hill Education; 2014.
5. Zuccoli G, Pipitone N. Neuroimaging findings in acute Wernicke's encephalopathy: review of the literature. *Am J Roentgenol* 2009;192(2):501-8.

https://doi.org/10.1017/cem.2015.27 Published online by Cambridge University Press