

Wernicke's Encephalopathy in a Non-alcoholic Man:

Case Report and Brief Review

AMAN MUNIR, M.D.¹, SYED A. HUSSAIN, M.D.², DAMANPAUL SONDDHI, M.D.², JOSEPH AMEH, M.D.²,
AND FRED ROSNER, M.D.^{3,4}

Abstract

Wernicke's encephalopathy, a serious neurological disorder caused by thiamine deficiency, is most commonly found in chronic alcoholics. We present a typical case of Wernicke's encephalopathy in a non-alcoholic man. Our patient presented with altered mental status, slurred speech, fever, vomiting and headache of one-week duration. An infectious etiology of the symptoms was ruled out by spinal fluid cultures. The patient improved dramatically within 24 hours of administration of thiamine.

Key Words: Wernicke's encephalopathy, thiamine, chronic alcoholism, malnutrition, glucose.

Introduction

WERNICKE'S ENCEPHALOPATHY (WE) is a serious neurological disorder caused by thiamine deficiency and is most commonly found in chronic alcoholics (1, 2). Typically, patients have the "classic triad" of symptoms: oculomotor abnormalities, gait disturbance and global confusional state. However, some patients may not exhibit this triad. The diagnosis is then based on clinical suspicion and rapid reversibility of symptoms after administration of thiamine, or autopsy demonstration of the characteristic lesion (3, 4). We report a case of Wernicke's encephalopathy in a non-alcoholic man.

Case Presentation

A 34-year-old African-American man presented with altered mental state, fever, slurring of speech, vomiting and headache of one-week duration. The patient denied alcohol or drug abuse, protracted vomiting, starvation, hospitalizations or abdominal surgery and indicated that he ate a normal diet. He also denied any history of sexually transmitted diseases or promiscuity. He had had occasional headaches, but had never

been seen by a doctor for this complaint. He claimed to be well otherwise. On examination, the patient was alert, but disoriented. His temperature was 102°F; his pulse and blood pressure were normal. He had bilateral ophthalmoplegia with vertical nystagmus, weakness of both lower extremities and gait ataxia. There was no neck rigidity or tenderness. No other focal neurological deficit was present. Complete blood count and serum electrolytes, including magnesium, were within normal limits. The liver function tests showed normal enzymes and serum bilirubin levels with a low normal albumin.

In view of the normal hemoglobin level (14.9 g/dL), serum folate was not done. Urine toxicology was negative. Although the patient declined to have an HIV test, he had normal CD4 counts with a normal CD4/CD8 ratio. Computerized tomography (CT) scan and magnetic resonance imaging (MRI) of the brain were normal. The patient was admitted to the intensive care unit with the differential diagnoses of meningitis, cerebrovascular event or Wernicke's encephalopathy. He was empirically given cephtriaxone, vancomycin, and acyclovir because of fever, vomiting, altered mental state and lower extremity weakness, which suggested the possibility of meningitis or encephalitis. Cerebrospinal tap results were normal and all antibiotics were stopped immediately after the spinal fluid cultures were reported as negative. He was also given 100 mg of thiamine intravenously and started on oral

¹Junior Resident, ²Senior Resident, and ³Director, Department of Medicine, Mount Sinai Services at Queens Hospital Center, Jamaica, NY; and ⁴Professor of Medicine, Mount Sinai School of Medicine, New York, NY.

Address correspondence to Fred Rosner, M.D., Queens Hospital Center, 82-68 164th Street, Jamaica, NY 11432.

thiamine supplementation of 100 mg daily. Within 24 hours the patient improved dramatically. He became alert and fully oriented. The ophthalmoplegia and vertical nystagmus resolved and the leg weakness improved markedly, with some residual ataxia. The patient was discharged home with continued outpatient physiotherapy.

Discussion

Wernicke's encephalopathy is a common but preventable disorder due to thiamine deficiency. Alcoholics account for most cases, but thiamine deficiency may infrequently occur in patients with hyperemesis, starvation, hemodialysis (5), cancer, acquired immune deficiency syndrome (AIDS), magnesium depletion (6), gastropasty/gastric bypass surgery (7), rapid weight loss (8, 9), anorexia nervosa, refeeding syndrome and prolonged intravenous feeding (8, 10). Body stores of thiamine are only sufficient for up to 18 days (11). Thus, depletion can occur rapidly with restricted intake or prolonged vomiting. The Canadian recommendation for thiamine intake is 1.1 mg per day, whereas the American recommendation is 1.4 mg per day (1, 11, 12).

Thiamine is a co-factor of several enzymes, including transketolase and pyruvate dehydrogenase (13). Activity of the latter enzyme, a rate-limiting tricarboxylic acid cycle enzyme, is significantly reduced in autopsied brain tissue of Wernicke's encephalopathy patients and from rats treated with a central thiamine antagonist, pyrimethamine (13). In animal studies, evidence suggests that such enzyme deficits result in focal lactic acidosis, cerebral energy impairment and depolarization of neurons resulting from increased glutamate in vulnerable brain structures. This depolarization may result in n-methyl-d-aspartate receptor-mediated excitotoxicity as well as increased expression of immediate early genes such as *c-fos* and *c-jun*, resulting in apoptotic cell death (13). Another mechanism may involve free radicals and alterations of the blood-brain barrier (13).

Anatomical abnormalities in WE occur mainly in periventricular regions of the diencephalon, midbrain, brainstem and superior vermis of the cerebellum. In acute cases of WE, the lesions consist of symmetrical discoloration with petechial hemorrhages (4). Amnesia is related to lesions of the medial dorsal nuclei of the thalamus. Shrinkage of the mamillary bodies can also be seen (14).

Symptoms and signs indicative of WE usually include vomiting, nystagmus (horizontal more than vertical), medial and lateral rectus muscle palsies leading to unilateral or bilateral ophthalmoplegia, fever, ataxia and progressive mental deterioration that evolves to a global confusional state, coma, and death. Other manifestations of a nutritional deficiency, such as polyneuropathy, may also occur. Tachycardia and orthostasis may be related to an impaired autonomic nervous system or coexistent cardiovascular beriberi. The true prevalence of WE at autopsy is about 3% (3, 4, 15), much higher than what is diagnosed clinically in the general population (0.06–0.13%). Acute WE should be suspected in all alcoholics with neurological symptoms, especially those with evidence of calorie or protein malnutrition and peripheral neuropathy (16). The classic triad of oculomotor abnormalities, gait disturbance and global confusional state occurs only in one-third of the patients. The diagnosis of WE is based on the clinical suspicion and rapid reversal of symptoms after the administration of thiamine. Decreased serum activity of erythrocyte transketolase and MRI (sensitivity 53% and specificity 93%) may be helpful in confirming the clinical diagnosis (16). Typically, there is an increased T₂ signal of the paraventricular region of the thalamus and peri-aqueductal regions of the midbrain. There can also be enhanced T₁ weighted spin-echo (SE) sequences after intravenous gadolinium administration in the acute phase of WE (17). Normal MRI does not exclude the diagnosis of WE. On the other hand, the sensitivity of the CT scan in detecting the characteristic lesion of WE is extremely low (13%), so it is not useful in the diagnosis of this entity (16).

WE is a medical emergency and requires the immediate administration of thiamine in a dose of 50–100 mg, either intravenously or intramuscularly. Doses should be given daily, to build up the body reserves until the patient is able to resume a normal diet. The central nervous system is almost entirely dependent on glucose for its energy requirements. Thiamine is an important co-factor needed in several steps of glucose utilization. Therefore, loading of glucose in a thiamine-deficient person can precipitate a neurological crisis (WE) or can cause rapid worsening of mild symptoms. To avoid this complication, thiamine should always be given prior to any intravenous glucose administration whenever this diagnosis is suspected (18). Patients who recover show im-

provement of oculomotor palsies within hours of thiamine administration. Ataxia improves more slowly. About one-half the patients recover incompletely and are left with a slow, shuffling wide-based gait and inability to take one step in quick succession after the other. Apathy, drowsiness and confusion diminish gradually. As these symptoms recede, an amnesic state with impairment in recent memory and learning may become more apparent in some cases (Korsakoff's psychosis).

Summary

WE is uncommon in non-alcoholics, but not rare. One should have a high index of suspicion in patients with hyperemesis, starvation, dialysis, cancer, magnesium depletion, AIDS, gastropasty/gastric bypass surgery, rapid weight loss, anorexia nervosa, refeeding syndrome or prolonged intravenous feeding. Our patient had none of the aforementioned conditions. The recommended treatment is the administration of thiamine, and most patients respond within 24–36 hours.

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