

CASE REPORT

A Patient with Sub Acute Viral Hepatitis (HEV) and Nonalcoholic Wernicke's Encephalopathy: A Case Report

ISLAM MR¹, AHTESSAM MS², WAHIDUZZAMAN M³, RAHMAN H⁴, ISLAM MM⁵, NATH DK⁶

Abstract:

Wernicke's encephalopathy (WE) is an acute neurological disorder resulting from thiamine deficiency. It is mainly related to alcohol abuse but it can be associated with other conditions such as gastrointestinal disorders like hyperemesis. A 38-year-old man with acute viral hepatitis presented with severe weakness, yellow discoloration of the body, hyperemesis in addition with disorientation, horizontal and vertical gaze-evoked nystagmus. MRI of brain showed typical findings of WE. Adequate treatment with parenteral thiamine was given. Neurological symptoms (Disorientation, Nystagmus and Ataxia) ameliorated during hospital stay and radiological abnormalities markedly improved in a follow up MRI after 2 months. This case suggests that WE may be associated with hyperemesis in non-alcoholic patients. Early thiamine treatment in symptomatic patients may improve prognosis. This extraordinary presentation of WE with hyperemesis, encouraged us to present this case history.

Keywords: Hyperemesis, Thiamine, Wernicke's encephalopathy (WE) etc.

Introduction:

Glucose which is the main source of energy for many tissue especially brain which is metabolized by glycolysis pathway to produce pyruvate. Pyruvate is further degrading into acetyl Co-A which further utilized in citric acid cycle pathway thereby producing ATPs (Flow chart). Thiamine, or vitamin B1, plays an essential role in glucose metabolism & nerve cell function. Thiamine pyrophosphate (TPP) constitutes the active form of thiamine. TPP, as a coenzyme, is a necessary part of complexes such as the dehydrogenase complex and the alpha-ketoglutarate dehydrogenase complex. These enzyme complexes are key rate-limiting enzymes, involved in the metabolism of glucose. Thus thiamine deficiency can cause metabolic disturbance of glucose in vulnerable brain regions. Thiamine is found in beef, liver, dried milk, nuts, oats, oranges, pork, eggs, seeds, legumes, peas and yeast. Daily need of thiamin in adult is

1.2 mg per day. Malnutrition (due to alcohol abuse, unbalanced diet, hyperemesis, starvation, renal dialysis, cancer, AIDS, or even gastric surgery) is the main cause of thiamin deficiency. Thiamin deficiency results in diffuse polyneuropathy, high-output heart failure, and Wernicke-Korsakoff syndrome¹.

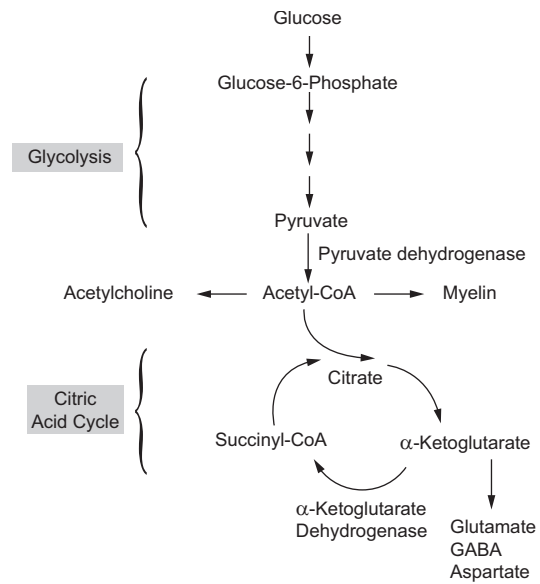
Wernicke's encephalopathy (WE) or Wernicke's disease is an acute and treatable neurological disorder due to deficiency of thiamine (vitamin B1)². In Bangladesh malnutrition (due to unbalanced diet, hyperemesis, starvation, renal dialysis, cancer, AIDS, or even gastric surgery) is the main risk, though alcohol abuse is the main cause in world wide. The characteristic clinical triad is that of Ophthalmoplegia, Ataxia, and Confusion¹. However, only one third of patients present with all three features⁶. Most patients are profoundly disoriented, indifferent, and inattentive, although rarely they have an agitated delirium related to

1. Prof. (Dr.) Md. Rafiqul islam, Professor & Chairman, Department of Neurology, BSMMU, Dhaka, Bangladesh.
2. Dr. Mohammad Saifullah Ahtesam, Medical Officer, 250 Bedded District Hospital, Kishoreganj, Dhaka, Bangladesh.
3. Dr. Md. Wahiduzzaman, Register, Medicine Department, Faridpur Medical College, Faridpur, Dhaka, Bangladesh.
4. Dr. Md. Habibur rahman, Senior Resident, Department of Neurology, BSMMU, Dhaka, Bangladesh.
5. Dr. Md. Monirul islam, Registrar, Medicine Department, Satkhira Medical College, Satkhira, Dhaka, Bangladesh.
6. Dr. Debashis Kumar nath, Senior Resident, Department of Neurology, BSMMU, Dhaka, Bangladesh.

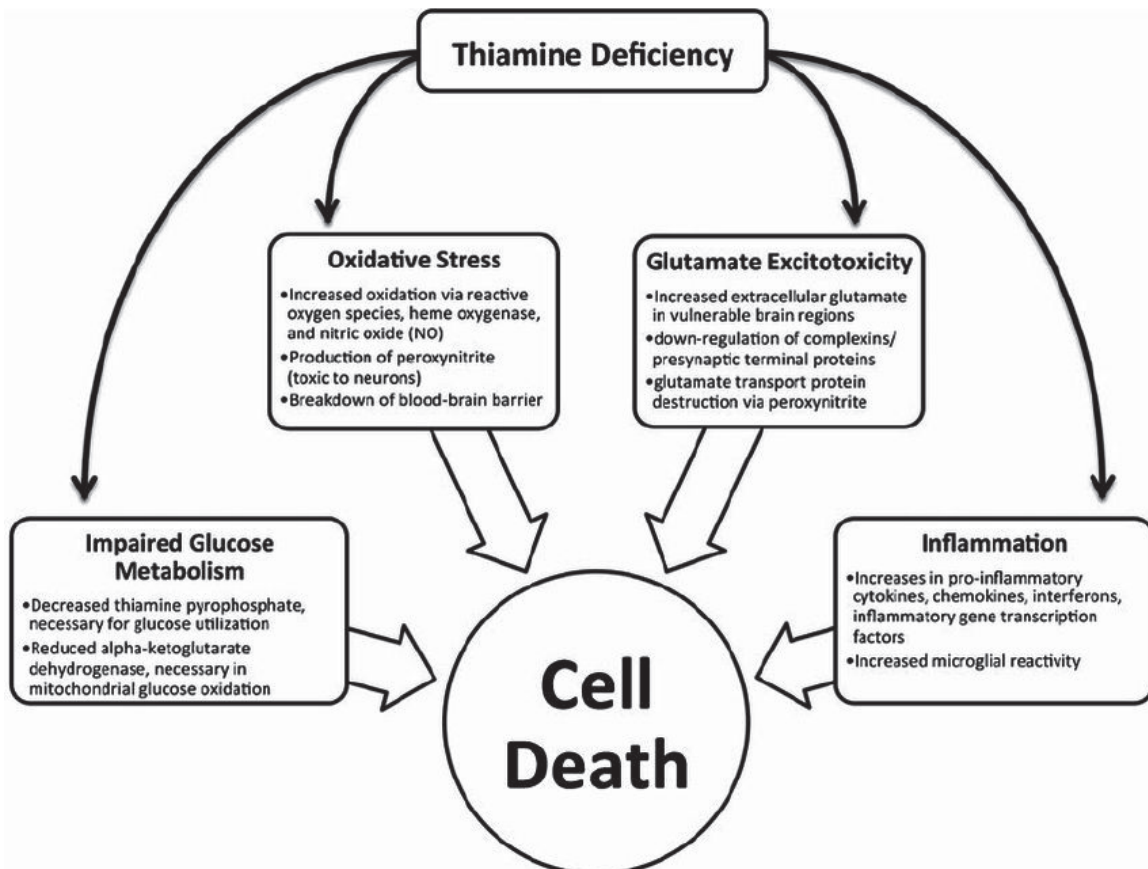
ethanol withdrawal. If the disease is not treated, stupor, coma, and death may ensue. Symptomatic thiamine deficiency in non-alcoholic patients is a less recognized and often misdiagnosed condition. The diagnosis of WE is mostly made clinically; nevertheless, magnetic resonance imaging (MRI) has been recognized as a useful adjunct in diagnosis.

WE is treatable disease with thiamine supplementation, which can lead to improvement of the symptoms and often complete resolution, particularly in those where alcohol abuse is not the underlying cause. Often other nutrients also need to be replaced, depending on the cause.

However, there are few reports of WE with Hyperemesis in nonalcoholic patients. In the present case, suggesting that he may have experienced thiamine deficiency caused by anorexia and severe vomiting.



Flowchart: Glucose metabolism



Flow chart: Pathogenesis of WE

Case report:

A previously healthy 38-year-old man was admitted to BSMMU with irrelevant talking, ataxia, drowsy & restless of last 15 days. Before admission, the patient suffering from severe anorexia, vomiting & yellow discoloration of skin for two and half - months. The patient's personal history revealed that he did not have a habit of alcohol abuse. Physical examination revealed he is disoriented, anemic, icteric, pulse 82/min, blood pressure 110/70 mmHg, and tender hepatomegaly but there was no thyroid enlargement or palpable lymph nodes. Ocular movement examination revealed horizontal and vertical gaze-evoked nystagmus. In addition, the patient exhibited diplopia, deep tendon reflexes were diminished and severe muscle weakness and positive Babinski's sign on both side. Sensory examination couldn't be evaluated due to disorientation and restlessness

He had elevated level of Bilirubin 11.2 mg/dl (normal limit ; 0.2-1.2mg/dl) , Random plasma glucose 4.7 mmol/L (reference value : <7.8 mmol/L) plasma AST 76 U/L (SGOT; normal limit: < 50 U/L) , plasma ALT 1904 U/L (SGPT; normal limit: <50 U/L), Serum Amylase 75.58 U/L (normal limit : 25-115 U/L) , Prothrombin time; patient's: 18.10sec (reference value 12-16 seconds) with INR 1.51 , Serum total protein 77 gm/L (reference value : 64 –83 gm/L), Serum Albumin 40gm/L (reference value : 37.95 – 53.99 g/L) , Gamma-GT 36.3 U/L (reference value : < 55 U/L) , Alkaline Phosphatase 495 U/L (reference value : 30 - 120 U/L) , Serum CA 19-9 5.1 U/ml (reference value : < 37 U/ml) Hemoglobin 12.4 g/dl (normal range : 15±2 gm/dl) , ESR 90 mm/ 1st hour (normal range : 0 – 10 mm/ 1st hour) , total WBC count 6000/cmm , platelet count 310000/cmm ,Serum electrolytes; Sodium 135 mmol/l , Potassium 4.8 mmol/l , Chloride 95 mmol/l , Serum Creatinine 0.71mg/dl (reference value : 0.6 – 1.4 mg/dl) Anti HEV IgM positive , Anti HBs & Anti Hbc (total) also positive , USG of whole abdomen revealed hepatomegaly with darker liver & coarse bright hepatic parenchyma , ESR 90mm/ 1st hour , Erosive gastritis on endoscopy.

Because of his inability to swallow, the patient initially received nutritional support by intravenous

infusion and after a few days a nasogastric feeding tube was placed for maintain nutrition and medication. Initially he was diagnosed as a case of subacute viral hepatitis due to HEV and the investigations concentrated to exclude chronic liver disease. Upper GIT endoscopy revealed erosive gastritis & USG of whole abdomen revealed hepatomegaly with darker liver & coarse bright hepatic parenchyma. Then the patient was examined by a neurologist and ocular movement examination revealed horizontal and vertical gaze-evoked nystagmus. In addition, the patient exhibited diplopia, absence of deep tendon reflexes and positive Babinski's sign and suspected that the patient was suffering from Wernicke's encephalopathy. Serum thiamine couldn't be measured due to unavailability but MRI of brain showed bilateral symmetrical T2WI and FLAIR hyper intense signal changes were noted in the peri-aqueductal region, dorsal brain stem, medial thalami surrounding the 3rd ventricle, post contrast showed mild enhancement of the lesion (Figure-1). Therefore, immediate treatment was given. Patient received intravenous thiamine

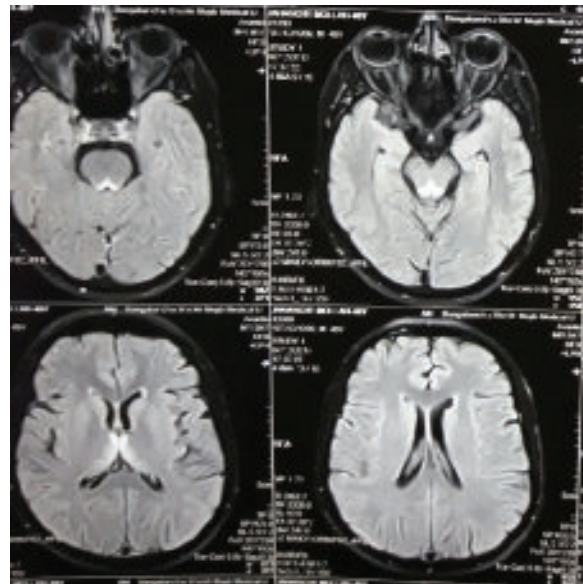


Fig.-1: Axial FLAIR images showing the periaqueductal gray (a, b), bilateral thalamus (c), the front lateral ventricle (d) These areas typically show hyper intensities in Wernicke encephalopathy

200mg per dose 8 hourly. After 3 days neurological symptoms and sign improved including ataxia and nystagmus. Total 7days intravenous thiamine was given. After 7 days he was discharged with the advice of oral thiamine 300mg daily in divided doses for 2 months. Review MRI of brain was done after 2 months and revealed disappearing previous hyper intense signal changes in the previously mentioned areas (Figure – 2).

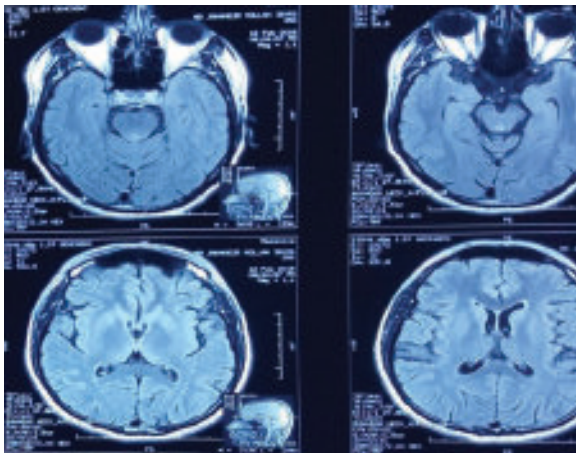


Fig.-2: Two months after treatment, axial FLAIR images demonstrated a more obvious improvement in the periaqueductal gray (a, b) and thalamus (c,) the front lateral ventricle (d).

Discussion:

WE is a relatively common neurological condition, typically caused by short-term deficiency of thiamine in alcoholics². WE can also arise from other causes, such as the hyperemesis, Crohn's disease, anorexia nervosa, fasting, starvation, malnutrition, AIDS, surgical treatment of gastrointestinal diseases and unbalanced diets²⁻⁶. WE is associated with several common clinical manifestations including eye signs, cerebellar signs, amnesia and altered mental state, seizures, frontal lobe dysfunction gastrointestinal symptoms. Classical triad WE are mental confusion, ataxia and ophthalmoparesis which is more frequent in alcoholics than non-alcoholics. In the present case, the patient did not exhibit alcoholism⁷.

Understanding the precise pathogenesis of WE could be valuable for improving the accuracy of

diagnosis and provision of appropriate treatments for the condition. Thiamine, or vitamin B1, plays an essential role in the functions of growth and development in normal cells. Thiamine pyrophosphate (TPP) constitutes the active form of thiamine. TPP, as a coenzyme, is a necessary part of complexes such as the dehydrogenase complex and the alpha-ketoglutarate dehydrogenase complex. These enzyme complexes are also key rate-limiting enzymes, involved in the metabolism of lipids, glucose and amino acids. Thus thiamine deficiency can cause metabolic disturbance in vulnerable brain regions⁸⁻⁹.

Diagnosis of WE is usually dependent on clinical symptoms, changes in medical imaging results, and the measurement of thiamine⁷. EFNS guidelines recommend that at least two of the following four signs are present in the clinical diagnosis of WE in non-alcoholics: dietary deficiencies, eye signs, cerebellar dysfunction, and either an altered mental state or mild memory impairment⁷.

The present case is a patient of acute viral hepatitis caused by Hepatitis E virus, who has intractable vomiting, severe anorexia, deep jaundice for which he was on parenteral nutrition for two months. Patient suddenly developed altered level of consciousness, imbalance & involuntary eye movements. Examinations showed patient is confused, disoriented, having gaze evoked nystagmus, bilateral lateral rectus palsy, cerebellar ataxia. These symptoms were one part of the diagnostic basis for WE.

Damage caused by metabolic disturbance from thiamine deficiency can result in oxidative stress, excitotoxicity of neurons, inflammatory responses, decreased neurogenesis, destruction of the blood–brain barrier, lactic acidosis and weakening astrocyte function In addition, selective damage to the medial and intralaminar nuclei of the thalamus, mammillary bodies, inferior colliculus, lateral vestibular nucleus, cerebellar vermis and other vulnerable areas has been observed where thiamine is processed and high levels of oxygen are consumed.

Taken together, damage to these areas is likely to lead to the related symptoms of WE. Therefore, radiographic imaging of these vulnerable areas may be valuable for diagnosing and treating WE patients. MRI can aid diagnosis of WE and can also be used in follow-up examinations to monitor prognosis. Generally, typical lesions are located in the thalamus, periaqueductal area and the mammillary body. In the present case, high intensity signals were observed in periaqueductal region, dorsal midbrain, and medial thalami surrounding the 3rd ventricle in T2 & FLAIR imaging. The lesions observed on T2 & FLAIR images were consistent with the vulnerable regions described above & clinical symptoms. The measurement of serum thiamine is useful in the diagnosis of patients with WE, but its limitations should be acknowledged. In the present case, the patient's level of serum thiamine was not measured.

The presented patient was diagnosed as acute viral hepatitis due to HEV infection evident by high serum bilirubin (11.2 mg/dl), high level of SGPT (1904 U/L), S.ALP (495 U/L) & positive IgM HEV antibody. Serum ammonia level was normal which excludes hepatic encephalopathy but EEG was not done in our patient.

As discussed above, our patient experienced severe vomiting, anorexia, received parenteral nutrition for two months and exhibited classical symptoms, encephalopathy, ataxia, ophthalmoparesis (Bilateral abducence palsy) and nystagmus. In addition, there were obvious changes in radiological imaging results. Despite the patient's serum thiamine levels unmeasured, a primary diagnosis of WE arising from nutritional deficiency due to severe vomiting, anorexia can be made from these data.

Diagnosis of WE constitutes a medical emergency. When patients do not exhibit alcohol abuse, neurological damage may be serious and acute. Therefore, immediate treatment is important.

The patient in our case was given intravenous thiamine 200 mg three times/day for 7 days then oral thiamine 100mg three times daily was prescribed for next 2 months. The patient's symptoms were rapidly improved within 1 week,

and the number of lesions was markedly decreased in follow-up FLAIR imaging.

Conclusions:

Wernicke's encephalopathy is probably an underdiagnosed condition, mainly in nonalcoholic patients. Thiamine deficiency can pass unnoticed clinically, while an established deficiency can manifest in the form of neurological symptoms other than those classically described in WE. We need to identify patients at risk due to dietary restriction or malabsorption of vitamins, since the early establishment of thiamine treatment rapidly improves acute symptoms and long-term prognosis. Prophylactic administration of vitamin supplements in such risk groups should be considered as a routine clinical practice

Declaration of conflicting interests:

The authors declare no conflicts of interest in preparing this article.

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