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Wernicke's Encephalopathy in an Adolescent Who Leads a High Risk Lifestyle

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Abstract We report an adolescent who led a high risk lifestyle with ketamine abuse, unhealthy eating habits, smoking and social drinking. He developed prominent mental status changes, unsteady gait and paranoid ideations after an episode of viral illness. The diagnosis of Wernicke's encephalopathy was established on the MRI findings of symmetrical high signal intensity in bilateral medial thalami, associated with reduction of red blood cell transketolase activity. There was prompt clinical, radiological, and biochemical improvement after thiamine therapy. Psychological testing during convalescence identified residual working memory deficits. We review recent updates in the diagnosis and management of this medical emergency. Emergency physician should be aware of this neuropsychiatric syndrome in predisposed adolescents, as early instillation of thiamine is vital to reverse the potentially fatal disorder.

Key words Adolescents; Thalamus; Thiamine; Wernicke's encephalopathy

Introduction

Wernicke's encephalopathy (WE) is an acute neuropsychiatric syndrome resulting from thiamine (vitamin B1) deficiency. The disorder is characterised by mental status changes, ataxia and ocular abnormalities such as ophthalmoplegia or nystagmus. The classic triad is however found only in 16% of patients.[1] WE is a medical emergency which requires prompt treatment to prevent neurological morbidity and possible mortality. Unfortunately, the condition is most often recognised only in autopsy, especially in nonalcoholic individuals.[2] The estimated mortality of WE is 17%, and 80% of survivors will develop Korsakoff's syndrome, characterised by severe loss of working memory with relative preservation of reference memory.[3]

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Case Report

A 16-year-old boy was admitted for acute confusion state and nonsense speech for one day. He had mild upper respiratory tract symptoms preceding the confusion. He was afebrile all along, with no history of head injury. Prior to admission, he had been leading a high risk lifestyle, including ketamine abuse, social drinking and smoking. His eating habit was unhealthy; he often missed meals and ate junk food instead. His past health was otherwise unremarkable.

On admission, the boy was found to be disoriented, lethargic and anorexic. There were nocturnal delirium and visual hallucinations. He failed the serial seven subtraction test, and only recalled one object in the five-minute recall test. The vital signs and hydration status were otherwise normal. He had no fever, no meningitic signs and neurological examination was unremarkable. Ophthalmological and cardiac examinations were normal. His body weight and height fell in the 50th percentiles. There was no other feature of nutritional deficiency such

as pallor, dermatitis, paraesthesia or rickets.

Initial investigation including complete blood picture, glucose, venous blood gas, ammonia, liver and renal function tests, anti-nuclear antibody, complement C3 and cold agglutinin titre were normal. Blood paracetamol and salicylate levels were also unremarkable. Chest radiograph was normal. Nasal pharyngeal aspiration was positive for influenza B antigen. Paired serology revealed two-fold increase for influenza B, and no increase for herpes simplex, influenza A, measles, mycoplasma pneumoniae and varizella zoster virus. Urine toxicology was negative for recreational drugs. Cerebral spinal fluid (CSF) showed normal white cell count, normal glucose level and slightly raised protein level 0.63 g/L (reference 0.15- 0.5 g/L). CSF gram stain and culture was negative. Polymerase chain reaction (PCR) was negative for influenza B and herpes simplex virus. CSF lactate, oligoclonal bands and immunoglobin level were normal. Blood lactate, very long chain fatty acids, acylcarnitine profiles and ceruloplasmin were normal. Blood for thrombotic screening was also normal. Electroencephalography (EEG) was unremarkable. Urgent computer tomography (CT) of brain showed hypodense areas in bilateral thalami and a small hypodense area in right cerebellum. Magnetic resonance imaging (MRI) of brain performed on day 10 revealed signal enhancement on bilateral medial thalami without signal change in the mammillary bodies (Figure 1).

In view of the initial suspicion of encephalitis, he was empirically put on intravenous acyclovir and cefotaxime. This was followed by apparent stabilisation of mood and improvement in confusion, but he remained lethargic with slow cognition. Vital signs were all along stable, and he was discharged after completion of the course of antimicrobials. Nine days after discharge, he was readmitted for malaise, delirium and poor appetite. He denied any alcohol intake or drug abuse. Neurological examination was normal, but serial seven subtraction test demonstrated a poor executive memory. Baseline blood investigations were again unremarkable.

Based on the clinical features and MRI findings, a presumptive diagnosis of WE was made. He was immediately started on intravenous thiamine 500 mg every eight hours for three days, followed by 250 mg daily for another three days. There was dramatic improvement in his mood, cognition and memory functions. His speech became coherent and relevant, and there was no more delirium at night. Pretreatment red blood cell (RBC) transketolase activity was reduced to 29 umol/min.L (reference 41-83 umol/min.L). Dietetics estimation of thiamine intake before admission was below the recommended daily allowance of 1.2 mg.[4]

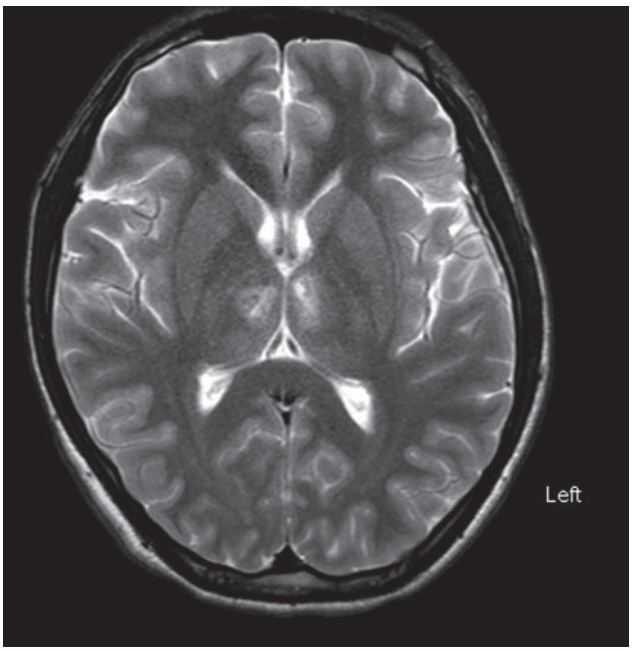

Figure 1 T2 weighted image of MRI brain on admission reveals symmetrical high signal intensity over bilateral medial thalami.

The patient was subsequently discharged on oral thiamine 30 mg daily. Five days later, he was admitted again for unstable mood and suicidal ideation. Neurological examination remained unremarkable. He was again given intravenous thiamine infusion as in the previous regimen. His condition improved over the next few days with no further apathy or stupor. Repeated RBC transketolase level was normal (43 umol/min.L). During convalescence, psychological testing by the Wechsler Adult Intelligence Scale III revealed poor scores in digit span, suggestive of weakness in working memory function. He was discharged with oral thiamine 50 mg twice daily. He remained stable clinically two months after discharge, and was competent in a summer job working in a café. Follow-up MRI brain at six weeks revealed complete resolution of the thalamic lesions (Figure 2). Pattern shift visual evoked potential revealed mild prolonged P100 on the left side; nerve conduction study was normal.

Discussion

Thiamine is present in a wide variety of food, particularly rich in whole grains, oatmeals, brown rice, potatoes,

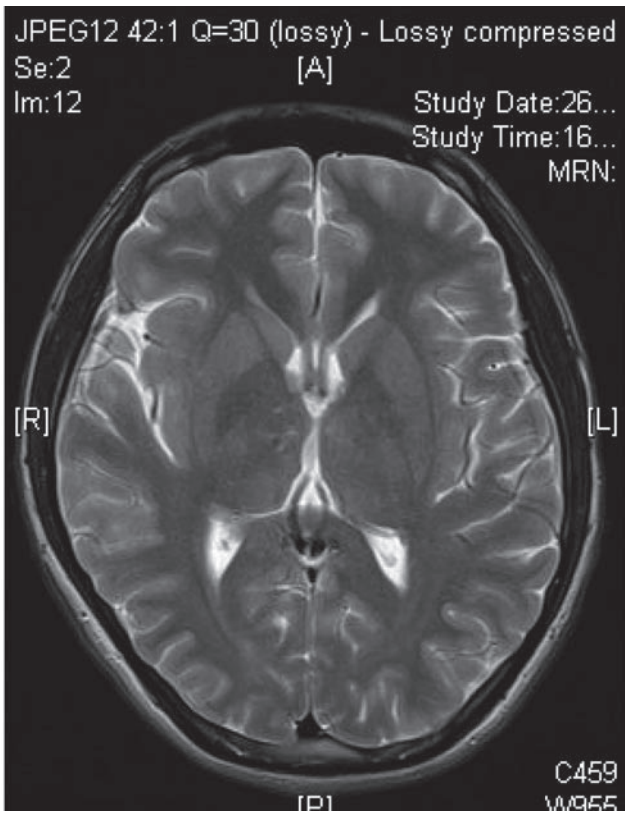

Figure 2 Resolution of the thalamic lesions six weeks after thiamine administration.

oranges, liver, and eggs. Reference daily intake for males older than fourteen is 1.2 mg.[4] Thiamine pyrophosphate is an essential coenzyme in several biochemical pathways in the brain, involving the regulation of ATP synthesis, maintenance of myelin sheath and production of neurotransmitters.[5] Body stores of thiamine are only sufficient for up to 18 days.[6] After one week of thiamine deficiency, there is decrease in transketolase activity in the pentose-phosphate pathway, affecting cellular energy metabolism.[7,8] More prolonged deficiency results in lactate accumulation, acidosis and irreversible neuronal apoptosis.[9]

WE is caused by thiamine deficiency as a result of any nutritionally deficient state, not only confined to chronic alcoholism. Unfortunately, WE confirmed at autopsy has been missed in nearly 80% of adult cases and 60% of paediatric cases during clinical examination.[2] The clinical features reported are mostly nonspecific, including mental status changes, gait disturbance, stupor, hypotension, hypothermia, seizures, hearing loss, hallucinations and behavioral changes.[10] As illustrated in this case, in adolescents the early features are often difficult to differentiate from acute psychotic disorders or organic brain disorders secondary to substance abuse. In a review of 31 paediatric patients, the commonest underlying disorders preceding the onset of WE were malignancies, gastrointestinal disease and food allergy. Less common preceding disorders included primary malnutrition, congenital heart disease, dieting, hyperemesis gravidarum, and tuberculosis. Common preceding events were vomiting, carbohydrate load, infection, parenteral nutrition and chemotherapy.[2] In the present report, we identified chronic malnutrition from underlying high risk lifestyle and unhealthy eating habit to be a significant risk factor for development of WE. In adolescents from this predisposed population who present with acute neuropsychiatric syndromes, enhanced physician awareness is vital for early clinical diagnosis and timely instillation of treatment.

MRI is the single most useful tool in making the diagnosis, with specificity of 93% and sensitivity of 53%, compared to 13% for CT brain.[11] Typical findings include high signal symmetrical intensity alternation on T2 weighted images in the thalami, mamillary bodies, periaqueductal region, floor of fourth ventricle, tectal plate and periaqueductal areas. These changes can be reversed after successful thiamine replacement.[12] In the present case, the characteristic mental state changes (including working memory deficit) and the typical radiological features help the clinician to differentiate WE from other encephalopathic syndromes with unique MRI changes, including acute necrotising encephalopathy, acute demyelinating encephalomyelopathy, and recreational drug abuse with cocaine, methamphetamine or heroin.[12,13] The negative CSF PCR study supported influenza B as a precipitating rather than a causative agent for encephalopathy. The initial normal EEG probably reflects the low sensitivity of EEG to detect early neuropsychiatric disturbances.

The presumptive diagnosis of WE can be confirmed by measuring blood thiamine levels (not available locally) or the erythrocyte transketolase activity.[10] As the results will only be available after a few days, the assay is of limited value for emergency diagnosis. Nonetheless, biochemical study helps in confirmation among ambiguous cases, and aids monitoring of treatment response.[14]

WE is a medical emergency, and clinical suspicion should prompt immediate thiamine administration even before radiological and laboratory results are available.[13] Unfortunately, there is lack of randomised controlled trials to guide the optimal dose and duration of treatment.[10,14] We adopt an empirical regimen of 500 mg thiamine

hydrochloride in 100 ml normal saline infused over 30 minutes, three times per day for three days, followed by 250 mg infusion daily over the next 3-5 days or until clinical improvement ceases. Thiamine should be given before or concomitantly with intravenous glucose, as glucose alone can precipitate WE in thiamine deficient patients. Upon recovery, oral thiamine at 30 mg twice daily may be continued for several months.[10] Side effects are generally mild, including local irritation and pruritis. Anaphylactic risk is rare.[10,14]

In conclusion, the emergency diagnosis of WE remains clinical, to be supported by a dramatic response to thiamine treatment and paraclinical MRI changes.[10] In paediatric age group, heightened suspicion of this under-recognised disorder is vital, especially in predisposed adolescents with a high risk lifestyle.

References

1. Harper CG, Giles M, Finlay-Jones R. Clinical signs in the Wernicke-Korsakoff complex: a retrospective analysis of 131 cases diagnosed at necropsy. J Neurol Neurosurg Psychiatry 1986;49:341-5.
2. Vasconcelos MM, Silva KP, Vidal G, Silva AF, Domingues RC, Berditchevsky CR. Early diagnosis of pediatric Wernicke's encephalopathy. Pediatr Neurol 1999;20:289-94.
3. Victor M, Adams RD, Collins GH. The Wernicke-Korsakoff syndrome: a clinical and pathological study of 245 patients, 82 with post-mortem examinations. Contemp Neurol Ser 1971; 7:1-206.
4. Institute of Medicine, Food and Nutrition Board. Dietary reference intakes for thiamine, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline. National Academy Press, Washington DC, 1998.
5. Manzo L, Locatelli C, Candura SM, Costa LG. Nutrition and alcohol neurotoxicity. Neurotoxicology 1994;15:555-65.
6. Tanphaichitr V. Thiamin. In: Shils ME, Olson JA, Shike M, Ross AC, eds. Modern Nutrition in Health and Disease, 9th edn. Baltimore MD: Williams and Wilkins, 1999:381-9.
7. Butterworth RF. Cerebral thiamine-dependent enzyme changes in experimental Wernicke's encephalopathy. Metab Brain Dis 1986;1:165-75.
8. Hakim AM, Pappius HM. Sequence of metabolic, clinical, and histological events in experimental thiamine deficiency. Ann Neurol 1983;13:365-75.
9. Navarro D, Zwingmann C, Hazell AS, Butterworth RF. Brain lactate synthesis in thiamine deficiency: a re-evaluation using ^{1}H-^{13}C nuclear magnetic spectroscopy. J Neurosci Res 2005; 79:33-41.
10. Sechi GP, Serra A. Wernicke'e encephalopathy: new clinical settings and recent advances in diagnosis and treatment. Lancet Neurol 2007;6:442-55.
11. Antunez E, Estruch R, Cardenal C, Nicolas JM, Fernandez-Sola J, Urbano-Marquez A. Usefulness of CT and MR imaging n the diagnosis of acute Wernicke's encephalopathy. AJR Am J Roentgenol 1998;171:1131-7.
12. Arora A, Neema M, Stankiewicz J, et al. Neuroimaging of toxic and metabolic disorders. Semin Neurol 2008;28:495-510.
13. Sazgar M, Robinson JL, Chan AKJ, Sinclair DB. Influenza B acute necrotizing encephalopathy: a case report and literature review. Pediatr Neurol 2003;28:396-9.
14. Donnino MW, Vega J, Miller J, Walsh M. Myths and misconceptions of Wernicke's encephalopathy: what every emergency physician should know. Ann Emerg Med 2007;50: 715-21.