Clinical Case Report

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Hypothalamic sydrome as an initial presentation of Wernicke encephalopathy

A case report

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Abstract

Rationale: Wernicke encephalopathy (WE) is a syndrome characterized by an acute or subacute onset of ataxia, ophthalmoplegia, and mental status changes. To our knowledge, hypothalamic syndrome is rare in WE.

Patient concerns: A 73-year-old female patient with acute cerebral infarct, who showed initial symptoms of vomiting, nausea, ataxia, and subsequent anorexia, was treated with parenteral nutritional supplement for 20 days. Nevertheless, the patient still developed refractory hyponatremia despite the appropriate sodium supplement given for a week following parenteral nutritional supplement. In fact, after 14 days of parenteral nutritional supplement, the patient gradually showed hypotension and apathy. Hyponatremia, hypotension, anorexia and apathy were signs of hypothalamic syndrome.

Diagnoses: Finally, the patient was diagnosed as WE by head magnetic resonance imaging, which showed symmetrical lesions in T2-weighted imaging images and FLAIR high signal intensity in the periaqueduct, hypothalamus, thalamus, mammiliary bodies, medulla oblongata, and vermis cerebelli.

Interventions: The patient was given thiamine supplementation.

Outcomes: The patient regained consciousness within 3 days. The sings of hyponatremia, hypotension, and apathy were relieved subsequently.

Lessons: When patients develop unexplained hypothalamic syndrome, we should think of the possibility of WE. The concomitant presence of hyponatremia, hypotension, anorexia, and apathy in WE is rare. Therefore, this case is reported here for discussion.

Abbreviations: CNS = central nervous system, CSWS = cerebral salt-wasting syndrome, MRI = magnetic resonance imaging, SIADH = syndrome of inappropriate antidiuretic hormone secretion, WE = Wernicke encephalopathy.

Keywords: hypothalamic syndrome, thiamine, Wernicke encephalopathy

1. Introduction

Hypothalamic syndrome is caused by a variety of processes, including developmental abnormalities, primary tumors of the central nervous system (CNS), vascular tumors, systemic tumors affecting the CNS, and granulomatous diseases. Hypothalamic syndrome is characterized by endocrine and metabolic disorders, along with vegetative nerve dysfunction, dysregulation of body temperature, diet and sleep disorders, sexual dysplasia, neuropsychiatric changes, and epilepsy.

WE is an acute or subacute neuropsychiatric disorder triggered by thiamine (vitamin B1) deficiency. First described by Carl Wernicke in 1881, WE is featured by signs and symptoms such as altered mental status, ataxia, and ocular signs, including nystagmus and ophthalmoplegia. However, the above so-called classical symptoms of WE may only be present in about 16% to 38% of the patients[1,2] and are relatively rare in nonalcoholic WE. WE is most frequently associated with alcoholism, although the incidence of nonalcoholic WE is becoming higher under conditions of nutritional insufficiency, such as hyperemesis gravidarum,[3] bariatric surgery, Crohn disease, prolonged parenteral feeding, or even a hunger strike.[4] The diagnosis is confirmed in 0.4% to 2.8% of autopsies, yet maybe overlooked in 68% of patients with alcoholism and 94% of patients without alcoholism.[5]

To the knowledge of the authors, WE rarely causes hypothalamic syndrome. Therefore, a rare case of WE-induced hypothalamic syndrome is reported here for discussion.

2. Case report

A 72-year-old female was admitted to our hospital with acute cerebellar infarction and signs of nausea, vomiting, ataxia, and

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Written informed consent was obtained from the patient for publication of this case repot and any related images.

The authors report no conflicts of inerest.

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subsequent anorexia. The medical history of the patient included hypertension and arrhythmia, although it was unclear whether the patient ever experienced atrial fibrillation. The patient had no diabetes, coronary heart disease, hyperlipidemia, and no history of smoking and alcohol abuse. During physical examination, the patient was conscious, fluent in speech, with both eyeballs showing horizontal nystagmus. The limb muscle tone of the patient was normal, with signs of ataxia in left upper and lower limbs. Other items of the physical examination showed normal results. The routine blood test, liver and kidney function, electrolytes, blood glucose, and blood coagulation results of the patient were also normal. The head magnetic resonance imaging (MRI) of the patient showed bilateral cerebellar infarction (Fig. 1).

During hospitalization the appetite of the patient became worse. After 1 month of hospitalization, the dizziness, nausea, and vomiting of the patient were not alleviated. The patient then received another head MRI examination. No other abnormalities were found in this head MRI, except the marks of previous cerebral infarction. After being treated with benzaisol and ondansetron, the above symptoms of the patient gradually improved. Nevertheless, the appetite of the patient got worse and hence intravenous administration of nutritional support was needed. The patient eventually developed hyponatremia after 1-week administration of parenteral nutrition supplement, including high glucose, although the supplement of vitamins was not sufficient. The blood sodium level of the patient was 121 to 128 mmol/L despite the use of an appropriate sodium supplement. The blood osmolality and urine osmolality of the patient were 256 and 685 mOsm/Kg, respectively. On day 14 of parenteral nutrition supplement, the patient presented with hypotension and apathy. The blood pressure of the patient dropped to 95/60 mmHg and stayed there after all antihypertensive drugs were stopped. The patient developed consciousness disorder on day 20 of parenteral nutrition supplement and was uncooperative in examination. Neurological examination of the patient showed slower pupillary response to light and more obvious signs of nystagmus with paralysis of bilateral abduction nerves. Blood tests showed that the white blood cells, C-reactive protein, and procalcitonin of the patient were all elevated, although the signs of fever were absent. The analysis of arterial blood gas indicated respiratory alkalosis and lactic acidosis. The patient showed a pH value of 7.31, an oxygen partial pressure of 157 mmHg, a carbon dioxide partial pressure of 13 mmHg, and a lactic acid concentration of 6.2 mmol/L. Chest computed tomography showed signs of mild inflammation in both lungs. Routine urine test and routine stool test did not show signs of infection. The patient received head MRI again for fear of cerebral infarction relapse. The MRI showed symmetrical lesions in T2-weighted imaging images and FLAIR high signal intensity in the periaqueduct, hypothalamus, thalamus, mammiliary bodies, medulla oblongata and vermis cerebelli, which were consistent with the diagnosis of WE (Fig. 2). On the same day, the patient quickly fell into lethargy. At the time, the blood pressure of the patient reached as low as 60/40 mmHg, with a heart rate of 130 bpm, a pH value of 7.31, an oxygen partial pressure of 65 mmHg, a carbon dioxide partial pressure of 13 mmHg, and a lactic acid concentration of 6.2 mmol/L in the arterial blood. Subsequently, the patient was intubated and sent to intensive care unit, where an electroencephalograph examination showed diffuse low-amplitude theta waves.

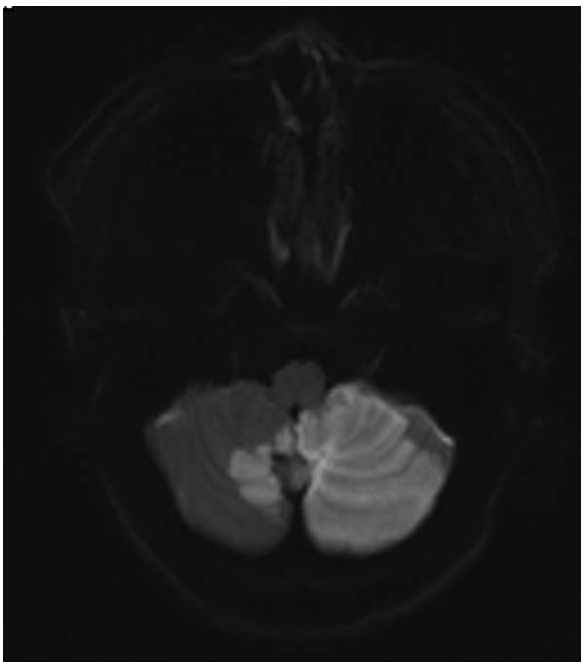

Figure 1. Brain MRI DWI showing the bilateral cerebellar infaction (arrow). DWI = diffusion-weighted imaging, MRI = magnetic resonance imaging.

The patient was given 300 mg of intramuscular thiamine per day for two weeks, followed by 100 mg of intramuscular thiamine per day for another two weeks and then 300 mg of oral thiamine tablet per day. At the same time, the patient received anti-infection treatment and vasopressors. Within 3 days, the patient became alert and her blood sodium level returned to normal without the use of sodium supplementation. The blood pressure of the patient was stabilized after one-week administration of vasopressors, although her signs of nystagmus did not disappear until 45 days of thiamine supplementation was given. Mini-Mental State Examination indicated impaired memory functions. Unfortunately, the patient was not examined with head MRI again after thiamine supplementation, so it is not clear whether the intracranial lesions have improved. Nevertheless, the signs of severe pneumonia of the patient were alleviated more than 1 month later.

3. Discussion

The patient in this study was first admitted because of acute cerebral infarction characterized by dizziness, nausea, vomiting, nystagmus, and ataxia. Therefore, WE was not considered until the typical signs of WE were revealed by head MRI, which was given when the patient showed signs of consciousness disturbance and nystagmus. Therefore, an opportunity for early treatment was missed. Ataxia, ophthalmoplegia, and mental confusion are characteristic symptoms of WE. Therefore, the possibility of WE should not be excluded prematurely in patients of posterior circulation infarction showing signs of repeated nausea, vomiting, and anorexia, especially in patients given intravenous nutrition supplement without thiamine supplementation.

Thiamine is an essential vitamin with critical roles in glucose metabolism. Thiamine cannot be synthesized in human body and hence is mainly derived from food. Without supplement, the thiamine reserve in the body can only last for about 18 days.[6]

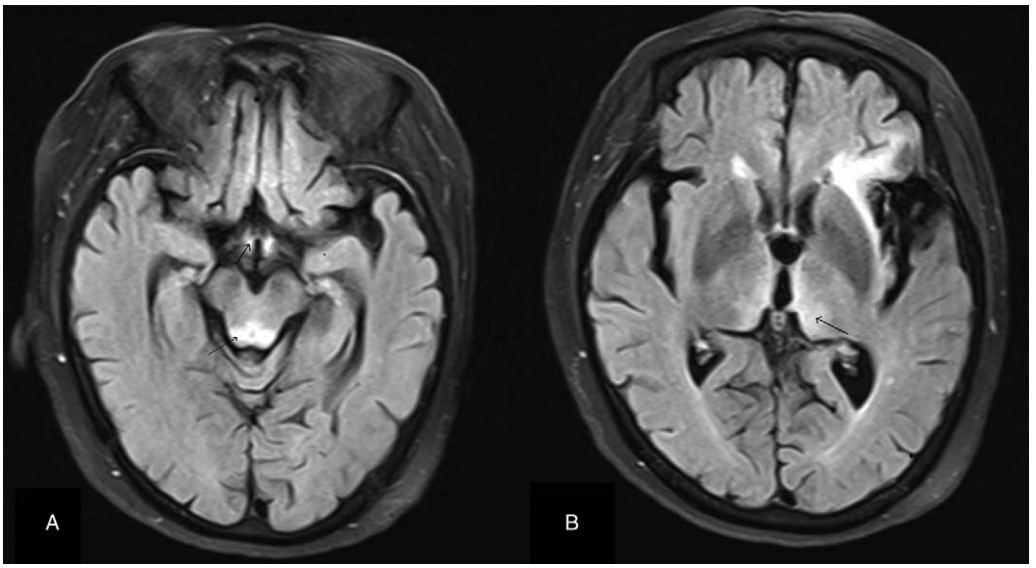

Figure 2. Brain MRI FLAIR demonstrating the symmetric lesions of hyperintensity at the periaqueduct and mammiliary bodies (A, arrow) and thalamic areas (B, arrow). FLAIR = fluid attenuated inversion recovery, MRI = magnetic resonance imaging.

Without thiamine, glucose is metabolized through less-efficient anaerobic pathways, which in turn produce lactic acid during glucose metabolism. Acidosis affects periventricular structures and accounts for the clinical presentations of WE.[5] Eventually, lactic acidosis may lead to circulatory failure. The patient in this study was not offered thiamine supplementation when intravenous nutrition supplement was given, whereas high intravenous glucose accelerated the consumption of thiamine. Finally, the patient developed WE featured by disturbance of consciousness and circulatory failure that could not be explained by pulmonary infection.

In this study, the patient developed refractory hyponatremia, hypotension, anorexia, and apathy, all of which were signs of hypothalamic syndrome, in the early stage of WE. Such hypothalamic symptoms are rare in WE. As far as the authors know, hyponatremia and hypotension were only reported in some WE cases, respectively.[7–9] Therefore, as a very rare example, this case showed all above symptoms. Therefore, this case was reported here to highlight the possibility of WE when patients with nutrition supplemental deficiency developed hypothalamic syndrome.

To our knowledge, 1 report of WE in the literature indicated syndrome of inappropriate antidiuretic hormone secretion (SIADH),[9] whereas another WE report revealed cerebral salt-wasting syndrome (CSWS),[8] although both cases showed hyponatremia. However, SIADH shows dilutional hyponatremia, a decreased urine volume, and euvolemia or hypervolemia because of the excessive release of antidiuretic hormone, whereas CSWS shows hyponatremia, serum hypoosmality, concentrated urine, and natriuresis with dehydration. The patient in this study showed intractable hyponatremia with normal urinary sodium, normal osmotic pressure in the early stage of WE. In addition, despite the use of appropriate sodium supplement, the hyponatremia of the patient was not improved. Therefore, the diagnosis of SIADH seemed more suitable for this patient as all symptoms of the patient were caused by hypothalamic damage. After thiamine supplement was given to the patient, blood sodium returned to normal.

Hypotension is an uncommon sign of WE. After hyponatremia, the patient of this study showed hypotension and lactic acidosis, and finally experienced circulatory failure. Hypotension is associated with hypothalamic damage, although lactic acidosis can also accelerate circulatory failure.

Anorexia is one of the causes of nutrition supplemental disorders and also a manifestation of WE. Thiamine deficiency may induce anorexia by inhibiting hypothalamic adenosine monophosphate-activated protein kinase activity in animal experiments.[10] The patient of this study showed poor appetite after developing repeated nausea and vomiting, although her appetite got even worse after nausea and vomiting were alleviated. It is speculated that anorexia might be an early manifestation of WE in this patient.

Some studies have reported a mortality of 17% in patients with acute WE. Therefore, the possibility of WE shall not be excluded prematurely when unexplained signs of refractory hyponatremia, hypotension, anorexia, and apathy are observed in patients with nutrition supplemental disorders because an early diagnosis and treatment of WE can avoid the onset of more serious events.

Author contributions

Conceptualization: Jun Zhang.
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Supervision: yanshu wang.
Writing – original draft: SHA ZHU.
Writing – review & editing: Jun Zhang, Xianzeng Liu.

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] Zuccoli G, Gallucci M, Capellades J, et al. Wernicke encephalopathy: MR findings at clinical presentation in twentysix alcoholic and nonalcoholic patients. AJNR Am J Neuroradiol 2007;28:1328–31.

[3] Morishma T, Aoyama M, Lida Y, et al. Lactic acid increases aquaporin 4 expression on the cell membrane of culturedrat astrocytes[J]. Neurosci Res 2008;61:18–26.
[4] Sechi G, Serra A. Wernicke's encephalopathy:new clinical settings and recent advances in diagnosis and management. Lancet Neurol 2007;6: 442–55.
[5] Day Gregory S, Martin del Campo C. Wernicke encephalopathy: a medical emergency. Canad Med Asso J 2014;186:295.
[6] Yang FG, Yao HG, Jin YG. Wernicke's encephalopathy. J Clin Neurol 2012;25:78–80.
[7] Shi W, Xiaojun H, Suju D, et al. Refractory hypotension in a patient with Wernicke's encephalopathy. Alcohol Alcohol 2012;47:48–51.
[8] Min Jeong H, Soon Chul k, Chan Uhng J, et al. Cerebral salt-wasting syndrome in a child with Wernicke encephalopathy treated with fludrocortisone therapy. Medicine 2016;95:36–9.
[9] Cooles PE, Borthwick LJ. Inappropriate antidiuretic hormone secretion in Wernicke's encephalopathy. Postgrad Med J 1982;58:173–4.
[10] Liu M, Alimov AP, Wang H, et al. Thiamine deficiency induces anoxia by inhibiting hypothalamic AMPK. Neuroscience 2014;267: 102–13.