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A case report: Non-alcoholic Wernicke encephalopathy associated with polyneuropathy

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Abstract

We report a rare case of non-alcoholic Wernicke encephalopathy (WE) with polyneuropathy. A 24-year-old woman who had recently served a 4-month prison sentence and underwent a short period of dieting manifested slow response, weakness, language disorder and amnesia. Brain magnetic resonance imaging (MRI) revealed typical lesions of WE. Examination of nerve conduction velocity revealed sensory-motor axonal polyneuropathy. The patient was immediately treated with thiamine. Neurological symptoms were alleviated in a few days and abnormal signals were markedly decreased in a follow-up MRI 1 week later. Polyneuropathy symptoms ameliorated during hospital therapy and significantly improved after 4 months. This case suggests that WE may be associated with polyneuropathy in non-alcoholic patients. Early thiamine treatment in symptomatic patients may improve prognosis.

Keywords

Polyneuropathy, Wernicke encephalopathy

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Introduction

Wernicke encephalopathy (WE) is an acute disorder of the central nervous system caused by thiamine deficiency, characterized as a clinical triad of acute mental confusion, ataxia, and ophthalmoparesis.[1] WE was first described in 1881 by Carl Wernicke. Although WE is typically observed in alcoholics,[2] it can also arise in pathological contexts other than alcohol abuse.[3,4] Recent studies have provided evidence that WE can also be caused by an unbalanced diet,

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frequent vomiting,[5] bariatric surgery and anorexia nervosa.[6,7] WE with polyneuropathy is well-known as a complication of thiamine deficiency resulting from chronic alcohol abuse.[8] However, there are few reports of WE with polyneuropathy in non-alcoholic patients. In the present case, the patient was on a diet for a short period, suggesting that she may have experienced thiamine deficiency caused by malnutrition. Prompt administration of thiamine by intravenous injection can reverse WE, but peripheral neuropathy typically requires a long recuperation period. A delay or lack of treatment may lead to irreversible dementia or even death. In the present case, the final observation supported the diagnosis of a non-alcoholic case of WE with polyneuropathy, and ruled out other diseases.

Case report

A previously healthy 24-year-old woman was admitted to our hospital after serving a 4-month prison sentence and undergoing a short period of dieting only in prison. Before admission, the patient experienced slow response, weakness, difficulty speaking and amnesia for 13 days. The patient's personal history revealed that she did not have a habit of alcohol abuse. Psychological examination revealed bradypsychia, language disorder and ptosis. Ocular movement examination revealed horizontal and vertical gaze-evoked nystagmus. In addition, the patient exhibited diplopia. Tendon reflexes were diminished, and severe muscle weakness was found in the distal end of upper and lower limbs (+0/+0). Muscle strength of the proximal upper and lower limbs was slightly better than that of the distal limbs (+3/+1). Sensory examination revealed stocking and glove anesthesia, and nerve conduction velocity (NCV) examination revealed sensory-motor axonal polyneuropathy (Table 1). A series of magnetic resonance imaging (MRI) scans of the patient's brain, particularly axial T2-weighted fluid attenuated inversion recovery (FLAIR) imaging, revealed abnormal white matter hyperintensities in the periaqueductal gray (Figure 1(a)–(c)), mammillary body (Figure 1(c)), thalamus (Figure 1(d)), front lateral ventricle (Figure 1(e)) and cortex (Figure 1(f)). Most other laboratory results were normal. Only the level of serum thiamine was slightly reduced (64.263 ng/L), but was still in a normal range (50–220 ng/L). WE with polyneuropathy was diagnosed on the basis of the patient's typical clinical symptoms, radiological findings and the

Table 1. Nerve conduction velocity at diagnosis.

	DL (ms)	Amp (mV)	NCV (m/s)
Right ulnar nerve CMAP			
Wrist–ADM	2.10	10.3	
UE–wrist	5.69	11.6	63.2
AE–UE	6.92	10.6	69.1
Right median nerve CMAP			
Wrist–APB	3.13	7.5	
Elbow–wrist	7.17	7.0	61.9
Right tibial nerve CMAP			
Ankle–AH	–	NR	
Left common peroneal nerve CMAP			
Ankle–EDB	–	NR	
Right common peroneal nerve CMAP			
Ankle–EDB		NR	
Right ulnar nerve SNAP			
Finger V–wrist	1.74	35.8	54.6
Right median nerve SNAP			
Finger III-wrist	1.86	20.3	72.6
Right superficial peroneal nerve SNAP			
Ankle–acrotarsium	–	NR	
Right sural nerve SNAP			
Sura–Extramalleolus	–	NR	

DL, distal latency; Amp, amplitude (peak-to-peak); CMAP, compound motor actin potential; ADM, abductor digiti minimi; UE, under elbow; AE, above elbow; APB, abductor pollicis brevis (muscle); AH, abductor hallucis; NCV, nerve conduction velocity; NR, no response; EDB, extensor digitorum brevis; SNAP, sensory nerve action potential.

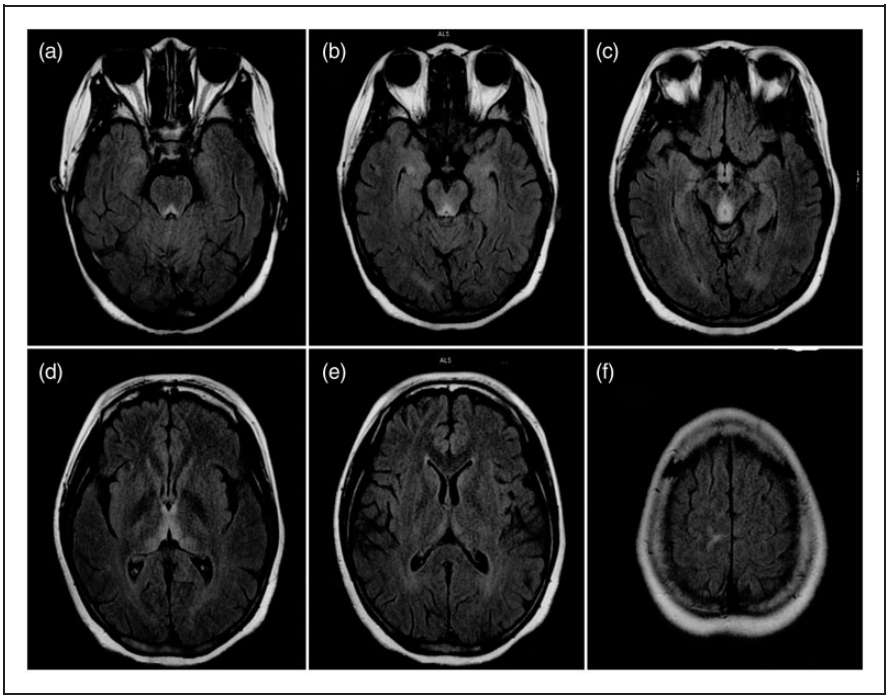

Figure 1. Axial FLAIR images showing the periaqueductal gray (a, b, c), the mammillary body (c), thalamus (d), the front lateral ventricle (e) and the cortex (f). These areas typically show white matter hyperintensities in Wernicke encephalopathy.

results of NCV. Thiamine (200 mg twice daily, intravenously, 30 mg three times daily, orally) was immediately administered. The initial thiamine treatment showed positive effects, and the clinical symptoms of language dysfunction, memory loss, disorientation and bilateral ptosis were alleviated. However, paralysis and amnesia lingered. A subsequent MRI scan performed 1 week later revealed an obvious signal change in initial areas in FLAIR images. In contrast with the first scan, this scan showed that obvious white matter hyperintensities in the periaqueductal gray were no longer present (Figure 2(a)–(b)). However, slightly increased signals were still detected in the periaqueductal gray and the mammillary body (Figure 2(c)), thalamus (Figure 2(d)), the front lateral ventricle (Figure 2(e)) and the cortex (Figure 2(f)), though these were all ameliorated compared with the initial scan. After 13 days, NCV examination revealed a slight improvement (Table 2). After 1 month, the patient still exhibited amnesia and paralysis, but both had improved. Furthermore, the patient's mental state had largely recovered. During the follow-up period (4 months), muscle strength tests revealed a substantial improvement. Muscle strength in the upper limbs had completely recovered (+5) and lower limb muscle strength returned slowly (+4). The patient had recovered enough to live independently.

The patient and her parents provided written informed consent to report this case, and the report was approved by the ethics committee of the First Hospital of Jilin University, Changchun, China (reference No.2016-357).

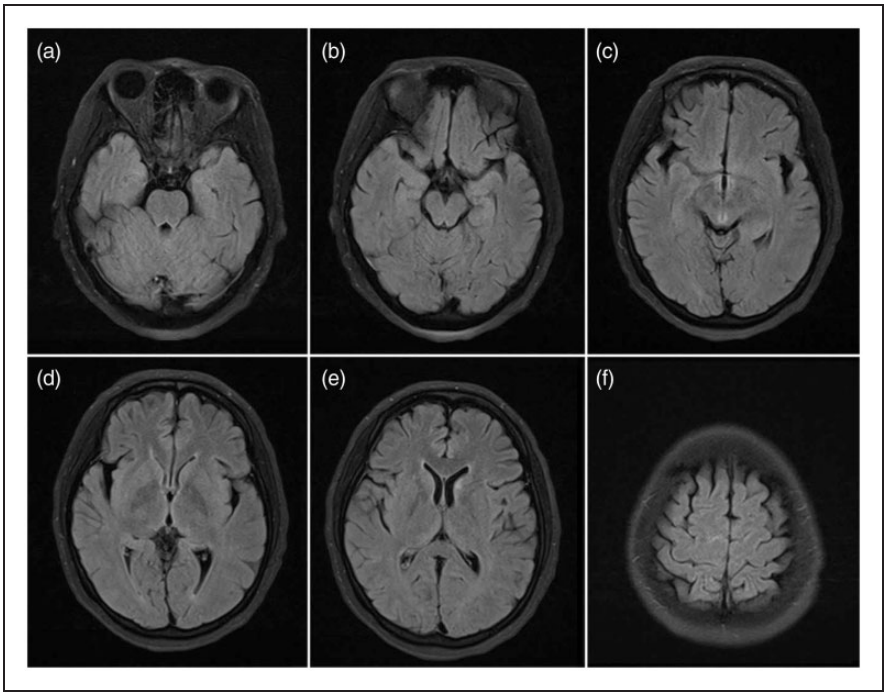

Figure 2. One week after treatment, axial FLAIR images demonstrated a more obvious improvement in the periaqueductal gray (a, b) and thalamus (d) compared with other brain regions. The remaining images showed some remaining damage in the periaqueductal gray and the mammillary body (c), the front lateral ventricle (e) and the cortex (f), although the damage was slightly alleviated in each of these areas.

Discussion

WE is a relatively common neurological condition, typically caused by short-term deficiency of thiamine in alcoholics.[3,4,9,10] However, WE can also arise from other causes, such as the surgical treatment of gastrointestinal diseases,[5,11–13] hyperemesis gravidarum,[1,5,14–16] AIDS,[17–19] Crohn's disease,[20–22] anorexia nervosa,[23,24] fasting, starvation, malnutrition and unbalanced diets.[1,21,22] WE is associated with several common clinical manifestations, including gastrointestinal symptoms, eye signs, cerebellar signs, seizures, frontal lobe dysfunction, amnesia and altered mental state.[1] This is known as the classical triad of mental confusion, ataxia and ophthalmoparesis. Importantly, only 8.2% of patients exhibit all features of the classical diagnostic triad,[1] which is more frequent in alcoholics than non-alcoholics. In the present case, the patient did not exhibit alcoholism. However, she experienced 4 months of prison life and a short period of dieting, which may have caused malnutrition and thiamine deficiency. The patient showed bradypsychia, language disorder, ptosis, diplopia and gaze-evoked nystagmus. These symptoms were one part of the diagnostic basis for WE. Meanwhile, the patient manifested two signs of the classical triad that are rare in non-alcoholics, encephalopathy and nystagmus. Ataxia, the other typical symptom, was not observed, was considered to be covered by paralysis.

Understanding the precise mechanisms of WE could be valuable for improving the accuracy of diagnosis and provision of

Table 2. Nerve conduction velocity after 13 days.

	DL (ms)	Amp (mV)	NCV (m/s)
Right ulnar nerve CMAP			
Wrist–ADM	2.05	11.9	
UE–wrist	5.94	7.7	55.3
AE–UE	7.44	8.8	73.3
Right median nerve CMAP			
Wrist–APB	3.13	4.1	
Elbow–wrist	7.48	4.9	58.6
Right tibial nerve CMAP			
Ankle–AH	–	NR	
Right common peroneal nerve CMAP			
Ankle–EDB	–	NR	
Right ulnar nerve SNAP			
Finger V–wrist	1.93	18.4	57.0
Right median nerve SNAP			
Finger III–wrist	2.10	19.8	57.1
Right superficial peroneal nerve SNAP			
Ankle–acrotarsium	–	NR	

DL, distal latency; Amp, amplitude (peak-to-peak); CMAP, compound motor actin potential; ADM, abductor digiti minimi; UE, under elbow; AE, above elbow; APB, abductor pollicis brevis (muscle); AH, abductor hallucis; NCV, nerve conduction velocity; NR, no response; EDB, extensor digitorum brevis; SNAP, sensory nerve action potential.

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 α-ketoglutarate dehydrogenase complex.[14,19,24] These enzyme complexes are also key rate-limiting enzymes, involved in the metabolism of lipids, glucose and amino acids. Thiamine deficiency can cause metabolic disturbance in vulnerable brain regions. Damage caused by metabolic disturbance can result in oxidative stress, excitotoxicity of neurons, inflammatory responses, decreased neurogenesis, destruction of the blood–brain barrier, lactic acidosis and weakening astrocyte function.[14,19] 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.[4,14,19,24] 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.[1] Generally, typical lesions are located in the thalamus, periaqueductal area and the mammillary body. Atypical lesions have been observed in the cerebellar vermis, intralaminar nuclei, inferior colliculus and cerebral cortex. In the present case, high intensity signals were observed in these typical and atypical areas using FLAIR imaging. The lesions observed on FLAIR images were consistent with the vulnerable regions described above, suggesting that our patient may have exhibited relevant abnormal brain function and neurological symptoms.

The measurement of serum thiamine is useful in the diagnosis of patients with WE, but its limitations should be acknowledged. Because WE is typically caused by thiamine deficiency, thiamine levels would be expected to be below the normal range in WE patients. However, normal thiamine levels have been reported in many previous cases of WE. Despite this, European Federation of Neurological Societies (EFNS) guidelines still recommend a timely thiamine test using high-performance liquid chromatography for differential diagnosis whenever WE is suspected.[1] In the present case, the patient's level of serum thiamine was not below the normal range in the initial examination.

Diagnosis of WE is usually dependent on clinical symptoms, changes in medical imaging results, and the measurement of

thiamine.[1,25,26] 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 impairment.[1] As discussed above, our patient experienced a short term of dieting, and exhibited two typical symptoms, encephalopathy and nystagmus. In addition, there were obvious changes in radiological imaging results. Despite the patient's normal serum thiamine levels, a primary diagnosis of WE arising from nutritional deficiency was established on the basis of these indications.

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. However, because of ethical concerns in controlled studies, no uniform standards for dosage and frequency have been developed. The patient in our case was given 200 mg three times/day by intramuscular injection, and 30 mg three times/day orally. The patient's symptoms were rapidly improved within 1 week, and the number of lesions was markedly decreased in follow-up FLAIR imaging.

Polyneuropathy can also result from nutritional thiamine deficiency or alcoholism, and may lead to sensory, motor, and autonomic dysfunction, as well as paralysis and anesthesia. The mechanisms of polyneuropathy are generally considered to involve axonal degeneration and segmental demyelination. Thiamine deficiency inhibits the activity of pyruvate dehydrogenase in peripheral nerves, which affects Adenosine Triphosphate (ATP) supply.[14] Reduction of ATP is associated with decreased Na+-K+-ATP-ase activity, which is important for maintaining a balance between depolarization of the peripheral nerves and excitability of the axons.[5,14] Impairment occurs when this balance is disrupted. There is evidence that polyneuropathy is more severe in distal limbs, and that myelin damage is more serious than axonal damage.[4,5] In general, peripheral nerve damage in alcoholic thiamine deficiency leads to more serious and more complex symptoms than in non-alcoholic thiamine deficiency.[28] Our patient exhibited several unique features. First, she manifested relatively serious damage without alcoholism. Second, the patient's axonal damage, indicated by decreased muscle strength and anesthesia, were more serious than commonly observed with demyelination. Our patient was diagnosed with polyneuropathy via physical examinations and NCV.

Serious short-term thiamine deficiency often leads to WE, while mild to moderate prolonged deficiency tends to preferentially cause damage to peripheral nerves. This does not imply that these diseases cannot occur together. One study reported that 11% of WE cases are associated with peripheral nerve lesions in alcoholics.[8] The present case verifies that both WE and polyneuropathy can also be caused by factors unrelated to alcohol, such as nutritional thiamine deficiency. Future studies will be required to identify the precise mechanisms underlying the coexistence of two diseases.

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Declaration of conflicting interests

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

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