Wernicke's Encephalopathy: Similar and Different Aspects of the Three Cases

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ABSTRACT

Wernicke encephalopathy is a neurological disorder, classically characterized by altered consciousness, opthalmoparesis, and ataxia results from thiamine deficiency. It is frequently associated with chronic alcohol abuse; however, many conditions which lead to thiamine deficiency such as gastric surgery, hyperemesis, parenteral nutrition, malnutrition may also be the cause. WE is a life-threatening condition

that requires early diagnosis and rapid initiation of intravenous thiamine therapy. In patients, findings of characteristic examinations may not always be seen; therefore, imaging methods are of great importance. In this article, we aimed to emphasize the similar and different aspects of three WE cases with typical and atypical imaging findings.

Keywords: Wernicke's encephalopathy, thiamine, confusion

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INTRODUCTION

Wernicke's encephalopathy is an acute neurological disorder results from thiamine deficiency. Classically, it is characterized by confusion, ataxia, and ocular findings (1). Autopsy studies report the prevalence of WE ranging between 0.4% and 2.8% in the general population. The diagnosis of WE may be challenging because of clinical heterogeneity and different etiologic factor. Early intravenous thiamine therapy is important (2,3). The etiological factors include malnutrition caused by chronic alcohol usage, long-term fasting, gastric surgery and iatrogenic causes related total parenteral nutrition (3). In this report, we aimed to present 3 cases followed-up with the diagnosis of WE with the aetiologies of chronic alcohol use and malnutrition after gastric surgery, and to discuss clinical and radiological features of WE in the light of these cases.

Case 1

A 62-year-old male patient was assessed due to walking incapability, vision loss and somnolence at follow-up carried out after surgery performed due to ileus. In his medical history, the patient had undergone Miles surgery because of rectum cancer 1.5 years ago, received parenteral nutritional support because of vomiting and malnutrition for 2 months and had been operated for ileus one month ago. On neurological examination, he had confusion, decreased orientation, severely limited cooperation and bilateral slight restriction of lateral gaze. The patient had no loss of strength in the upper extremities, while bilateral lower extremity strength of the patient was found as 1/5. On cranial magnetic resonance imaging (MRI); hyper intense areas were noted in periaqueductal grey matter and bilateral medial of the thalamus (Figure 1). Cerebrospinal fluid (CSF) examination revealed 97 mg/dl (15-45 mg/dl) of protein and 61 mg/dl (45-80 mg/dl) of glucose, while no cell was detected. High-dose thiamine therapy was initiated (first two days 600 mg, following five days 200 mg, and afterwards 100 mg daily) on the patient who was diagnosed as WE based on history, clinical findings and MRI findings. The patient recovered from his confusion on the second day of treatment, and his eye symptoms returned to normal after one week. Cranial MRI carried out one month later revealed that the findings were completely recovery. Patient who had no feature on the spinal imaging underwent electromyography

(EMG) examination which revealed findings of lumbosacral plexopathy effecting L1,L2,L3-4 and L4-S1 segments of bilateral lower extremities. It was thought that progressive paraparesis of the patient could be related to the paraneoplastic process or radiotherapy treatment. Motor deficit of the patient was improved with IVIG therapy administered following steroids. Control EMG examination could not be done on follow-up.

Case 2

A 32-year-old male patient was admitted to our emergency department with the complaints of imbalance, diplopia and amnesia for four days. The patient with no significant illness had a history of smoking, chronic alcohol use and malnutrition which was added in the last 15 days. On the neurological examination performed at the time of admission, pathologically his eye movements were restricted in four directions, the eyes were at the midline, eye lids were mildly pitotic, deep tendon reflexes were bilaterally hypoactive in the lower extremities and he had truncal ataxia. Diffusion weighted imaging (DWI) carried out at the admission to the emergency department revealed cerebellar vermian, and T2 FLAIR sequences revealed, around the aqueductus adjacent to the 3rd ventricle, cerebellar vermian localized, bilateral thalamic hyperintensities (Figure 2), and the patient was hospitalized for investigations and treatment. Intravenous thiamine therapy of 200 mg/day was initiated on the patient who had no additional findings detected in the routine laboratory investigations and was diagnosed as WE based on clinical and cranial MRI findings. On follow-up oral thiamine treatment was started and no significant finding was detected in lumbar spinal MRI. Intermittent intravenous thiamine replacement (100 mg/day once every two weeks) was added to oral thiamine treatment. In evaluation carried out for patient's amnesia, significant loss of short-term memory (memory scale 0/3) was observed (MMT:27/30). Eye findings were recovered except bilateral horizontal nystagmus on the 3rd day of the treatment. One week after the admission, dorsiflexion in bilateral lower extremities (0/5) and weakness in the plantar flexion (3/5) were detected in the patient with continuing truncal ataxia. In the EMG examination carried out for the loss of strength in the lower extremities (approximately 10th day),

Figure 1. Hyperintensities on axial FLAIR images: involving periaqueductal gray matter (a,b), involving bilateral medial thalamus (c); after treatment the regression of signal change in periaqueductal grey matter can be seen (d).

reduction in the amplitudes of compound muscle action potentials (CMAP) in the lower extremity nerves examined (Table 1). No marked pathology was detected in the sensory nerve conduction study except for mild reduction in the nerve conduction velocities of right median and ulnar nerves. Needle EMG study carried out 1.5 month later revealed abnormal spontaneous activity and advanced dispersion pattern in lower extremities especially in distal muscles (Table 2). mild in the dominant motor axonal polyneuropathy was found in motor fibers of the lower extremities. Lumbar puncture could not be performed since the patient refused. At follow-up, there was no significant feature in lumbar spinal MRI of the patient who was converted to oral from intravenous thiamine therapy. Cranial MRI performed one month later revealed that the existing lesions were regressed except the cerebellar vermis. Examination of the patient with ongoing thiamine treatment which was carried out at the end of the 6th months revealed that, muscular strength in the lower extremities was normal and the amplitudes of compound muscle action potential of the nerves in the lower extremity were improved compared to previous examinations. Remission was also detected in the patient's short-term memory disturbance.

Case 3

A 51-year-old male patient referred with complaints of drowsiness and imbalance for several days. The patient had consumed intensive alcohol 2 days before his complaints. The patient's history had no significant feature except smoking and alcohol habits. On neurological examination, he had confusion partially cooperation and his eye movements were restricted toward all directions. The patient had wide-based gait and truncal ataxia. Cranial MRI showed partly hemorrhagic signal changes non-enhancing after contrast administration, in bilateral cerebellar hemispheres, pons, bulbus, bilateral thalamus, and periventricular white matter that were hyperintense on T2W and FLAIR sequences (Figure 3). Routine investigations showed no significance except HIV positivity and elevated ALT. HIV encephalitis was ruled out with imaging findings and there were no clinical and laboratory findings to suggest acquired

Table 1. Nerve conduction studies performed on the tenth day of patient's hospitalization

Sensorial conduction study	Latency (ms)	Amplitude (µV)	Velocity (m/s)
R Median - 2 nd finger	2.8	17	42.9
L Median - 2 nd finger	2.5	9.3	52
R Ulnar - 5 th finger	2.1	12	47.6
R Suralis	2.7	12	44.4
Motor conduction study	Latency (ms)	Amplitude (mV)	Velocity (m/s)
R Median - APB	3.6	7.5	
	7.9	7.0	53.5
L Median - APB	3.7	7.4	
	8.2	7.0	57.8
R Ulnar - ADM	1.96	7.1	
	7.2	5.3	49.6
R Tibialis - AH	4.9	0.5	
	16.4	0.3	37.8
L Peroneal - EDB	3.5	0.7	
	12.0	0.5	45.9

R, right; L, left; APB, abductor pollicis brevis; ADM, abductor digiti minimi; AH, abductor hallucis; EDB, extensor digitorum brevis. Abnormal values were written in bold.

immunodeficiency syndrome. In the CSF study, protein was found as 110 mg / dl and glucose as 77 mg / dl, while no cell was detected in the direct examination. High-dose thiamine was initiated on the patient who was diagnosed as WE based on history, clinical and MRI findings. In the first 24 hours of treatment, the patient recovered from confusion, and eye symptoms and ataxia almost completely improved on the 5th day. The imaging findings were completely regressed one month later. The patient was discharged with thiamine therapy and followed up by the department of infectious diseases for HIV positivity.

Figure 2. Hyperintensities on axial FLAIR images: involving periaqueductal region and bilateral mammillary bodies (a), involving bilateral medial thalamus (b); after treatment complete regression of signal changes can be seen on same regions (c,d).

Table 2. Concentric needle EMG examination performed 1.5 month later

Needle EMG Examination	Pathological spontaneous activity			MUAP			
	Fibrillation	PSW	CRD	Amp	Duration	Polyphase	IP
R Deltoid	N	N	N	N	N	N	N
L Biceps	N	N	N	N	N	N	N
L Fleksor carpi ulnaris	N	N	N	N	N	N	N
R Paravertebral T12	N	N	N	N	N	N	N
L Gastrocnemius medial head	+2	N	N	N	N	N	-2
R Gastrocnemius medial head	+2	N	N	N	N	N	-2
R Peroneus longus	+2	N	N	N	N	N	-2
L Tibialis anterior	+3	1+	N	N	N	N	-2
R Tibialis anterior	+2	1+	N	N	N	N	-2
L Vastus lateralis	+2	N	N	N	N	N	-1
R Vastus lateralis	+1	N	N	N	N	N	-2
R Iliopsoas	+1	N	N	N	N	N	N

R, right; L, left; Amp, amplitude; MUAP, motor unit action potential; N, normal; PSW, positive sharp waves; CRD, complex repetitive discharge; IP, interference pattern. Abnormal values are written in bold.

DISCUSSION

Wernicke's Encephalopathy is a disorder with classical clinical picture including confusion, oculomotor disorders, and ataxia, and is caused by thiamine deficiency. All of these three findings are seen in a small number of cases at a rate of 16% (4). The major clinical finding is altered mental status. This condition consists of a wide spectrum of cognitive impairments including confusional state, apathy, memory and concentration deficits, coma and death. This picture is resulted from the affected thalamic nuclei and mamillary bodies (2). Horizontal nystagmus is the most common among the ocular disorders. The other findings that may be seen include reduced visual acuity, diplopia, paralysis of the both lateral recti or other ocular muscles, conjugate gaze palsy due to the lesions of the 3rd and 6th cranial nuclei of pontine tegmentum, decreased pupillary light reactions, papillary edema and ptosis. Balance disorders associated with cerebellar vermis and vestibular dysfunction may cause several complications ranging from mild gait disturbance to advanced ataxia with standing impairment (2,5).

In WE, besides cases with coexisting classical findings, there are also case reports with different clinical and radiological features (6,7). There

are only a few cases reporting association of acute polyneuropathy and WE (7,8). In their study, Ishibashi et al. reported 3 cases with acute axonal polyneuropathy coexisting with WE and stated that the patients recovered within weeks with thiamine therapy (7). Our second case also presented with complaints of diplopia and forgetfulness, but motor axonal polyneuropathy of the lower extremities effecting predominantly motor fibres was detected during clinical follow-up. While significant improvement was found in the loss of strength in lower extremities of the patient at the 6th month follow-up, a partial improvement was recorded in EMG findings. We think that our second case is interesting also in terms of WE accompanied by acute neuropathy. In literature chronic neuropathies accompanying WE are mostly related with underlying reason whereas acute neuropathies are reported to be rare (7,9). The cases reported emphasise that early improvement in acute neuropathy after thiamine therapy could be related to the decrease in ATP with pyruvate dehydrogenase activity due to lack of thiamine, resulting in decrease in the activity of Na/K ATPase which has a role in depolarisation of peripheral nerves (7).

Although etiologically WE is most commonly seen due to chronic alcohol use, it may also be observed following cancer, malnutrition,

Figure 3. Hyperintensities on axial T2W and FLAIR images: involving deep cerebellar white matter (a), involving supratentorial periaqueductal deep white matter (c); cerebellar confluent microhemorrhages can be seen on SWI sequence(d); after treatment complete regression of signal changes can be seen on axial FLAIR images (e,f).

gastrointestinal surgery, hyperemesis gravidarum, HIV infection and hunger strike (10-12). Evan Y. et al. stated that gastrointestinal system cancers were accounted for the majority (17/46) of 46 patients who were diagnosed with cancer and developed WE (13). There were different etiological causes in our 3 cases. Our first case had been operated due to rectal cancer and re-operated in the later period, because of ileus developed in the follow-up. During this period, he had very often vomiting and had to take TPN support for a long time. He had been exposed to more than one process that could lead to thiamine deficiency. Our other two cases had developed WE related to extensive alcohol use.

Cranial MRI is of great importance in diagnosis. In the early period T2W and FLAIR imaging shows increased signals in bilateral medial thalamus, around the third ventricle and in periaqueductal gray matter. Besides this typical appearances, atypical MRI findings have also been observed (6,9). In their study, Zuccoli G et al. reported that alcoholic WE cases showed more contrast enhancement in thalamus and mammillary body and that, besides typical MRI findings, involvement of the cerebellum, pre- and postcentral cortical areas were more commonly observed in non-alcoholic patients compared with alcoholic ones (10). In a study by Ha et al. with 24 WE patients (13 alcoholic and 11 non-alcoholic), no significant difference was found between both groups in terms of atypical imaging findings (14). Hygino et al. stated that both typical and atypical imaging findings could be seen in both groups in their study with two cases of non-alcoholic WE, showing typical imaging findings (15). Sugar and Kikugawa, contrary to Zuccoli et al. presented two alcoholic WE cases with atypical MR findings of cortical and amygdala involvement (16). It is known that petechial hemorrhage is also seen accompanying typical underlying pathological findings causing imaging features such as variable degrees of necrosis, vascular, astroglial and microglial proliferation (17). Macroscopic hemorrhage as in our case is quite rare. While MRI images of our first case showed typical features, atypical characteristics such as cerebellar involvement and hemorrhage were prominent in our third case.

Thiamine is an important vitamin for providing osmotic gradient in the cell membrane, glucose metabolism and neurotransmitter synthesis. For adults, the average daily thiamine requirement is 1.4 mg or 0.5 mg thiamine should be taken for every 1000 kcal in the diet. High dose IV thiamine is given in the treatment of WE. Although there is not a clear protocol for the dose of treatment, it is generally recommended to initiate with very high doses (14). The recommended dose is 200 mg three times a day in the first two days, 200 mg/day in 100 or 250 cc saline as infusion for 30 minutes in the next five days. There are publications recommending an initial dose of 500 mg IV/IM 3 times a day for 2-3 days in alcohol dependents (15). Clinical improvement begins within 1 week after intravenous thiamine therapy, but full clinical healing takes 1 to 3 weeks (16).

At the moment of clinical suspicion, fluid with dextrose should be avoided and intravenous thiamine infusion should be initiated. Clinical diagnosis may be challenging due to the absence of classical findings together or the development of coma in some cases. Insufficient or late treatment may lead to the development of Korsakoff Syndrome and may be mortal (11). In our 3 patients with evident confusion, WE was diagnosed based on the imaging findings and high dose thiamine treatment was initiated. It was observed that clinical picture of confusion was regressed within 24-48 hours of the treatment, and the other clinical findings improved within weeks.

Among these 3 cases, more than one etiological cause was found in the first patient, while in our second patient WE clinical triad was accompanied by axonal polyneuropathy and in our third patient, MRI findings other than the typical imaging findings that we expected to see were observed. These three cases had characteristics different from each other because of the diversity of etiological causes, the presence of atypical imaging findings, and the presence of rarely seen accompanying polyneuropathy. What made the cases similar was detection of the classic clinical triad which is rarely seen together, in all three patients.

In conclusion, WE should be considered in patients developing confusion with etiological factors of chronic alcohol use, a history of surgical operation, severe malnutrition, and in addition to the typical imaging findings, diagnosis should be supported considering possible coexisting atypical findings and very rapid intravenous thiamine treatment should be initiated.

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