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Case Report

Wernicke-Korsakoff syndrome complicated by subacute beriberi neuropathy in an alcoholic patient

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ABSTRACT

Thiamine (vitamin B1) deficiency is a common condition in alcohol abusers, which can lead to damage of both the peripheral and the central nervous systems. Here we describe the case of an alcoholic patient who presented with acute onset of ataxia, severe weakness of the four limbs, and hypoesthesia and dysesthesia of the distal portion of the upper and lower extremities. The clinical picture also included mental confusion and amnesia. A diagnosis of Wernicke-Korsakoff syndrome was made based on clinical symptoms and brain RMI findings. Electromyography and electroneurography revealed signs of subacute axonal sensory-motor polyneuropathy that were compatible with a rare acute presentation of beriberi. Patient immediately received parenteral thiamine administration, which resulted in rapid clinical amelioration of ataxia and confusion and also in a significant improvement of motor and sensory deficits. The association between Wernicke-Korsakoff syndrome and acute axonal polyneuropathy is a very rare condition that could make less recognizable the clinical picture of a thiamine deficiency. However, the diagnosis of thiamine deficiency should be suspected in every alcoholic patient presenting with acute onset symptoms of central and/or peripheral nervous system involvement. This because the immediate replacement treatment can be life-saving and reverse the clinical symptoms.

1. Introduction

Thiamine deficiency (TD) classically presents as Wernicke's encephalopathy (WE), which is clinically characterized by the triad of ophthalmoplegia, ataxia and confusion. This pathological condition may be associated with the Korsakoff's syndrome (KS), an amnestic disorder characterized by anterograde and retrograde amnesia. Nutritional polyneuropathy, also called beriberi, represents another typical clinical manifestation of thiamine (vitamin B1) hypovitaminosis. Beriberi polyneuropathy (PN) is usually chronic, though rarely it can have an acute-subacute course [1]. TD is considered to be rare in the western world, where it is observed mainly in alcoholic patients. However, due to an increase of alcohol abuse in the industrialized countries, it is conceivable that neurological symptoms of hypovitaminosis B1 will be seen increasingly often.

2. Case report

Here we describe the case of a 53-year-old man who was admitted to the emergency room in January 2016 for subacute onset of confusion and walking difficulties that forced him to bed. In his medical history the patient had a major depressive episode in 1998. It was around this time when he began abusing alcohol (1–2 liters of wine/day). Family members of the patient reported that he presented with irregular sleep-wake cycle, also associated with episodes of nocturnal psychomotor agitation and diurnal confusion, during the last few weeks. Irregular eating and poor nutrition with weight loss in the last few months were also reported.

Gait disturbances were due to weakness of the lower limbs and balance impairment which occurred less than one month before, and then rapidly worsened in the next few weeks. The patient also complained muscle pain, cramps at the lower extremities, and burning paresthesias in hands and feet. The neurological examination showed disorientation in time and space as well as attention deficit. The cranial nerve exam was normal except for a hypophonic voice. No alterations in eye movements or nystagmus were detected. Patient was unable to sit, stand and walk due to truncal ataxia and severe muscular weakness of the lower limbs. Although to a less extent, proximal and distal weakness was also present in the upper limbs. Areflexia, hypotonia and distal muscular atrophy were recorded in all four limbs. Sensory examination showed thermodolorific and tactile hypoesthesia of the extremities, mainly in the lower limbs, and also decreased vibration sense below the level of the knees. Finally, the patient exhibited bilateral dysmetria on finger-to-nose and heel-to-knee testing that worsened

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Table 1
Values of neural conduction measurements recorded at first assessment and at 6-month follow-up.

Nerve	First NCS	6-month follow-up NCS	Normal values
Median – left			
DML (ms)	3.1	3.0	≤ 4.0
CMAP Amp (mV)	4.0	8.9	≥ 5.0
MNCV (m/s) BE – Wrist	45.2	52.7	≥ 49
II Dig DSL (ms)	–	2.4	≤ 3.5
SNAP (μV)	–	8.6	≥ 20
SNCV (m/s)	–	60.4	≥ 47
Ulnar – left			
DML (ms)	2.4	2.1	≤ 3.3
CMAP Amp (mV)	2.9	9.3	≥ 5.0
MNCV (m/s) BE – Wrist	47.5	53.2	≥ 50
MNCV (m/s) AE – BE	49.0	55.0	
V Dig DSL (ms)	1.9	1.9	≥ 47
SNAP (μV)	7.0	7.6	≥ 17
SNCV (m/s)		63.8	≥ 50
Tibial – left			
DML (ms)	5.6	3.8	≤ 5.6
CMAP Amp (mV)	0.3	3.8	≥ 5.0
MNCV (m/s) Knee – Ankle	41.8	40.0	≥ 40
Peroneal – left			
DML (ms)	–	5.1	≤ 5.8
CMAP Amp (mV)	–	0.6	≥ 2.0
MNCV (m/s) BK – Ankle	–	41.4	≥ 40
MNCV (m/s) AK – BK	–	42.0	
Sural – left			
SNAP (μV)	–	8.5	≥ 8.0
SNCV (m/s)	–	41.0	≥ 40

AE: above elbow; AK: above knee; Amp: amplitude; BE: below elbow; BK: below knee; CMAP: compound motor action potential; DML: distal motor latency; Dig: digit; DSL: distal sensory latency; Lat: latency; NCS: nerve conduction study; MNCV: motor nerve conduction velocity; SNCV: sensory nerve conduction velocity; SNAP: sensory nerve action potential.

when the eyes were shut.

Routine blood tests (including complete blood count, conventional renal and liver function tests, folic acid and B12 vitamin levels, ammonium and thyroid function measurements) and urine tests were all within normal limits except for a slight decrease in serum albumin levels (3.1 g/dL). The search for anti-ganglioside and anti-neuronal antibodies was negative, and the cerebrospinal fluid (CSF) analysis revealed only a slight increase in the protein levels (60 mg/dL), with normal white blood cell count (5 cells/mmc) and absence of oligoclonal bands. The patient underwent an electroencephalogram (EEG), that showed a generalized slow (theta) activity, and a electromyography/electroneurography (EMG/ENG) examination. This latter showed a significant decrease in the amplitude of sensory nerve action potentials (SNAP) and compound motor action potentials (CMAP) or even absence of motor and sensory responses (Table 1). No signs of demyelization or motor conduction blocks were recorded. High-amplitude fibrillation potentials and positive sharp waves were recorded bilaterally in the brachioradialis, first interosseus, vastus lateralis and anterior tibialis muscles, predominantly in the distal muscles of the four limbs. Based on EMG/ENG findings a diagnosis of subacute axonal sensory-motor polyneuropathy was made. Computed Tomography (CT) scan of the brain was also performed, which was normal. Thus patient underwent a brain Magnetic Resonance Imaging (MRI) which showed areas of abnormally high signal on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images adjacent to the third ventricle bilaterally and in correspondence of the midbrain roof and the periaqueductal region (Fig. 1A). Based on clinical and instrumental findings, we made a diagnosis of WE associated with subacute axonal polyneuropathy, and a treatment with parenteral administration of 100 mg thiamine per day was immediately started and continued for 7 days. Patient also received intravenous immunoglobulin (400 mg/kg for five days) remaining the possibility of a primary immune-mediated polyneuropathy.

Already 24–48 h after thiamine administration confusion and truncal ataxia significantly improved, thus enabling the patient to sit without support. Although to a less extent, also the strength of the four limbs gradually improved over the next days. Two weeks later, at discharge from the hospital, the patients was able to stand and take a few steps with a single support. After the state of mental confusion was improved, a neuropsychological test battery was carried out that revealed a severe amnestic syndrome characterized by inability to form new memories, loss of past memories, and confabulation, so that a diagnosis of Wernicke-Korsakoff syndrome (WKS) was made. Oral thiamine supplementation of 300 mg/day was continued for about six months after discharge from hospital and then stopped as the patient was no longer dependent on alcohol and followed a various dietary regimen. At a follow-up examination performed eight months later, the patient was able to walk without support, presenting only mild signs of gait ataxia and steppage. Weakness significantly improved at legs and disappeared at the upper limbs. Global hypoesthesia and dysesthesia at distal extremities were recorded and a mild dysmetria was shown only at the lower limbs. Though the amnestic symptoms also improved over time, they were still present having a significant impact on patient's social life and working ability. At a first follow-up MRI performed 10 days from admission the previously described lesions decreased (Fig. 1B), to be no longer apparent at a 6-month follow-up (Fig. 1C). A 6-month follow-up electroneurographic assessment showed a marked improvement in motor and sensory conduction parameters (Table 1), while electromyography of the same muscles as before showed no signs of denervation, but only reinnervation predominant in the distal muscles confirming regenerating processes.

3. Discussion

The patient we describe presented with a very rare association of WKS and subacute sensory-motor axonal PN. To our knowledge very few cases have been reported so far, in which a WKS occurred in strict temporal relationship with an acute polyneuropathy, and only in one single case by Ishibashi et al. TD was due to alcohol abuse [2]. However, differently from our case, in the patient by Ishibashi et al. [2] the polyneuropathy was "reversible" as the symptoms and the electrophysiological abnormalities rapidly recovered.

Our patient fulfilled the European Federation of Neurological Societies (EFNS) criteria for clinical diagnosis of WE, requiring a least two of the following: dietary deficiencies, eye signs, cerebellar dysfunction, and altered mental status or mild memory impairment. The diagnosis was further supported by the distinctive MRI findings and by the rapid clinical response to treatment with parenteral thiamine, though this was administered at a lower dose than that, up to 1500 mg daily, proposed by some authors [3]. Although thiamine levels were not assessed in our patient, it is to note that finding of low thiamine level is not a mandatory criterion for the diagnosis.

A peculiarity of the present case is the subacute course of the polyneuropathy that occurred in strict temporal relationship with the other symptoms of WKS. Neuropathy due to thiamine deficiency usually develops gradually over a period of at least few months. However, patients have been described in whom the peripheral nervous system involvement mimicked a Guillain-Barrè Syndrome [1]. This may pose a problem for the treatment choice as an immune-mediated pathophysiology cannot be rule out at all. Thus, in our case an intravenous immunoglobulin treatment was also performed. However, some clues suggested that the neuropathy was likely due to a nutritional deficiency. Among these, clinical symptoms such as myalgia, cramps and burning paresthesias in the extremities that occurred in a chronic alcoholic patient together with other typical manifestations of TD, and electrophysiological findings of acute axonal neuropathy. It is