INTERNAL MEDICINE

□ CASE REPORT □

Alcoholic Myelopathy and Nutritional Deficiency

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Abstract

A patient with chronic alcoholism presented with myelopathy and low serum folate and cobalamin levels. A 42-year-old alcoholic man had gait disturbance for 4 months. A neurological examination revealed marked spasticity with increased deep tendon reflexes and extensor plantar responses of the lower limbs. His cobalamin level was decreased and his serum folate level was particularly low. His plasma ammonia level was not increased. Abstinence and folic acid and cobalamin supplementation stopped the progression of his neurological deficits. This case indicates that nutritional deficiency should be monitored closely in patients with chronic alcoholism who present with myelopathy.

Key words: alcoholism, cobalamin, ethanol, folate, folic acid, myelopathy

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Introduction

The neurological disorders related to alcohol abuse are diverse and affect the brain, spinal cord, peripheral nervous systems, and muscles (1, 2). In addition to the direct toxicity of ethanol and its metabolites, concomitant nutritional deficiencies may also contribute to the pathogenesis, complicating the neurological manifestations in chronic alcoholics (1, 3). Damage to the spinal cord (myelopathy) has been reported in patients with alcoholism (4, 5). As portosystemic blood shunting associated with liver cirrhosis causes hepatic myelopathy (5-9), it has been considered to be the major cause of myelopathy in chronic alcoholics. In 1984, Sage et al. reported 5 patients with so called alcoholic myelopathy without substantial liver disease (4). This report clearly indicated the direct toxicity of ethanol (or its metabolites) as a cause of myelopathy in these alcoholic patients because their nutritional status, including their folate and cobalamin status, was good. Since then, the possible contribution of nutritional deficiency has not been extensively examined in alcoholics with myelopathy (2). However, vitamin deficiency, particularly folate deficiency, has often been reported to occur in chronic alcoholics (3, 10).

In the present report, we describe the case of a patient with chronic alcoholism who presented with myelopathy with decreased serum folate and cobalamin levels and discuss the need to recognize nutritional deficiency in alcoholic patients with myelopathy.

Case Report

A 42-year-old man reported the onset of a gait disturbance 4 months prior to his admission to our hospital. He had no noteworthy family history. He had been drinking 1.8 L shochu (a clear liquor distilled from sweet potatoes, rice, or buckwheat) per day and took meals irregularly for 9 months after losing his job. He principally ate instant noodles, which were fortified in thiamine and riboflavin but not in folic acid or cobalamin. The patient's gait disturbance gradually worsened, and he became almost bed-ridden 1 month before his admission. One day before his admission to our hospital, he became inarticulate and drowsy.

A neurological examination on admission revealed that the patient was lethargic and had dysarthria and horizontal gaze nystagmus. Mild weakness was observed diffusely in the lower limbs but was absent in the upper limbs. A slight reduction of tactile sensation was noted in the distal portions of the lower limbs, whereas the sensations of vibration and joint position were preserved. He complained of distal numbness from the level of the thigh on both sides. The patient's deep tendon reflexes, including his Achilles tendon

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Table. Laboratory Findings.

	On admission	1 month later	Normal values
Plasma			
Total protein (g/dL)	6.7	6.5	6.5-8.0
Albumin (g/dL)	4.2	3.9	3.7-5.0
Aspartate transaminase (IU/L)	35	17	0-41
Alanine transaminase (IU/L)	18	26	0-45
g-Glutamyl transpeptidase (IU/L)	89	74	8-45
Alkaline phosphatase (IU/L)	366	359	115-359
Lactate dehydrogenase (IU/L)	272	146	100-250
Ammonia (mg/dL)	35	ND	38-70
Blood urea nitrogen (mg/dL)	8	13	8-20
Creatinine (mg/dL)	0.51	0.62	0.5-1.2
Sodiun (mEq/L)	137	142	135-144
Potassium (mEq/L)	3.5	4.4	3.2-4.9
Magnesium (mg/dL)	2.4	ND	1.9-2.5
Serum			
Cobalamin (pg/mL)	187	656	≥ 200*
Folate (ng/mL)	1.3	≥ 20	≥ 3.0*
Copper (μg/dL)	113	ND	70-132
Whole blood			
White blood cell (no/mm^3)	9,200	8,600	3,800-8,500
Red blood cell (no/mm^3)	4.22	4.18	3.60-5.00 × 10^6
Hemoglobin (g/dL)	14.2	13.7	11−16
Mean corpuscular volume (fl)	94.8	97.1	80-100
Mean corpuscular hemoglobin (pg)	33.6	32.8	26-33
Mean corpuscular hemoglobin concentration (g/dL)	35.5	33.7	32-36
Platelet (no/mm^3)	271	224	160-410 × 10^6
Thiamine (ng/dL)	34	124	≥ 20*

ND, not determined.

*Based on a previous report (21).

reflexes, showed hyperreflexia in both the upper and lower limbs. Extensor plantar responses were observed on both sides. Ankle clonus was also observed. Autonomic involvement, such as orthostatic hypotension, gastrointestinal tract dysmotility, dysuria, paridrosis, or dyscoria, was not noted.

The patient's laboratory data revealed a considerably reduced serum folate level (1.3 ng/mL; normal, ≥3.0 ng/mL) (Table). His serum cobalamin level was also reduced (187 pg/mL; normal, ≥200 pg/mL). On the contrary, his serum copper level was within the normal range, and neither anemia nor macrocytosis was observed. His whole blood thiamine level was normal. Although a mild increase of γ-glutamyl transpeptidase was noted, his plasma ammonia level was not increased (35 μg/dL; normal, 38-70 μg/dL). The patient was negative for anti-human T-cell lymphotropic virus-1, anti-DNA, and anti-nuclear antibodies. A cerebrospinal fluid examination revealed a normal cell count and increased protein levels (75 mg/dL; normal, 15-45 mg/dL).

The results of nerve conduction studies for the median, ulnar, tibial, peroneal, and sural nerves and somatosensory-evoked potentials of the median nerve, which were performed as reported previously (11, 12), revealed normal findings. The central motor conduction time, as assessed using the previously described methods (13, 14), was normal in the median nerve but prominently prolonged in the tibial nerve (24.3 ms; normal, <15 ms). Cranial and spinal cord magnetic resonance imaging revealed no abnormalities. Brain atrophy was not apparent. Abdominal ultrasound indicated fatty liver with no ascites.

Although thiamine (fursultiamine, 75 mg per day) and cobalamin (mecobalamin, 1,500 μg per day) supplementation was initiated immediately after admission, only a slight improvement in the patient's conscious disturbance was observed. The administration of folic acid (15 mg per day) was initiated 5 days later, which led to the further recovery of the patient's consciousness. The patient performed a trail making test (a measure of cognitive function) in 74.9 seconds before folic acid supplementation (age-adjusted normal value, 22-36 seconds), and 24.3 seconds 28 days later. Although we did not observe the progression of the patient's gait disturbance, there was no substantial change in the spasticity of the lower limbs at 2 months after the patient's admission.

Discussion

We herein describe the case of a patient with chronic alcoholism who manifested myelopathy with low serum folate and cobalamin levels (his serum folate level was particularly low). The patient exhibited gait disturbance due to spasticity of the lower limbs. That the central motor conduction time in the upper limbs was normal, while that of the lower limbs was prolonged may indicate spinal cord abnormalities. In addition to the findings suggestive of myelopathy, our patient had consciousness disturbance. Although we did not analyze the nature of nystagmus that was seen in our patient

in detail, it may be related to brain abnormalities. Nutritional deficiencies, including folate and cobalamin deficiencies, have known to affect various areas of the nervous system, and multiple sites may be concomitantly involved (15-18).

Most previous reports on spastic paraparesis in chronic alcoholics reported that hepatic myelopathy occurred due to portosystemic blood shunting, which resulted from liver cirrhosis (2). The features of hepatic myelopathy are characterized by progressive spastic paraparesis and the scarcity of sensory deficits, similar to those of our patient (5, 9). However, our patient did not have increased blood ammonia levels, which would suggest that any portosystemic shunting was not substantial. A previous study described 5 cases of alcoholic myelopathy in well-nourished myelopathy patients without substantial liver disease (4). These patients also showed spastic paraparesis that was similar to that observed in patients with hepatic myelopathy (4). As the serum folate and cobalamin levels were reportedly normal in these patients with so-called alcoholic myelopathy, the direct toxicity of ethanol (or its metabolites) was emphasized. On the contrary, the possible contribution of nutritional deficiency, particularly folate and cobalamin deficiency as was observed in our patient, has not been extensively examined in chronic alcoholics with myelopathy (2). Although the direct toxicity of ethanol (or its metabolites) was not completely ruled out as a cause of myelopathy in our patient, the improvement in the patient's conscious disturbance that was observed after vitamin supplementation indicates the presence of vitamin deficiency. Although further studies are needed to elucidate the nutritional status of alcoholic patients with myelopathy, this case report will contribute to the earlier recognition of nutritional deficiency in such patients.

Folate is a B-vitamin that is present in fresh green vegetables, citrus fruits, legumes, and liver but it is easily denatured by heat during cooking (19, 20). Chronic alcohol intake decreases the folate level by inhibiting the absorption of folate from the intestines, reducing its hepatic stores, and increasing its urinary excretion (10). An unbalanced diet associated with chronic alcoholism may also contribute to reduced folate intake. Folate deficiency causes a variety of neurological manifestations that poorly correspond to megaloblastic anemia (21). These features include neural tube defects in embryos, (22), dementia (23), depression (24), optic neuropathy (25), peripheral neuropathy (21), and myelopathy (26, 27). Myelopathy due to folate deficiency is known to lead to the subacute combined degeneration of the spinal cord (26, 27), which is also prominent in individuals with cobalamin deficiency (28). As the features of subacute combined degeneration usually include deep sensory loss (predominantly in the lower limbs) (26), the relative preservation of the sensory functions in our patient seems atypical. However, previous studies of patients with folate deficiency have highlighted the incidence of pyramidal tract damage (29). Hence, the influence of folate deficiency on the clinical manifestations of our patient is possible. Folate deficiency may also contribute to consciousness disturbance as it has been reported to be closely related to cognitive decline (17).

In 1998, the fortification of cereal-grain products with folic acid was initiated in the USA and Canada to prevent neural tube defects; this action was followed by many countries. However, there are still many countries, including East Asia and European nations, which have not implemented folic acid fortification. Moreover, a recent study suggested that the level of folate intake remains below the level recommended for the prevention of neural tube defects in subgroups of the population, even in countries with such mandatory fortification (30, 31). Thus, folate deficiency remains a major public health problem throughout the world, and it is considered to be more prevalent in alcoholics.

As for cobalamin, which was mildly reduced in our patient, the major causes of deficiency are the impaired absorption caused by achlorhydria and the impairment of intrinsic factors due to atrophic gastritis or gastrectomy (32). However, alcoholism has not been regarded as a cause of cobalamin deficiency. Cobalamin deficiency induces megaloblastic anemia, cognitive decline, myelopathy, and neuropathy, all of which are indistinguishable from the symptoms induced by folate deficiency (18, 21, 28). Because cobalamin deficiency may be present along with other B-vitamin deficiencies (21), the cobalamin levels should also be monitored carefully in patients with nutritional deficiency.

An impediment to the definitive diagnosis of nutritional deficiency is that laboratory evidence must be obtained before vitamin supplementation or dietary modification is prescribed. As previous studies have suggested that irreversible neurological deficits might remain in patients with myelopathy due to nutritional deficiency (17, 26), the early diagnosis and treatment of nutritional deficiency in alcoholic patients with myelopathy is important. Physicians should therefore be aware of the possibility of nutritional deficiency, particularly B-vitamin deficiencies, as a cause of myelopathy in patients with chronic alcoholism and should monitor their nutritional status carefully. In particular, folate deficiency may frequently contribute to neurological deficits in patients with alcoholism-associated myelopathy, and the relationship between folate deficiency and alcohol intake should be carefully considered.

The authors state that they have no Conflict of Interest (COI).

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