Progressive Myelopathy Due to Chronic Alcoholism: Case Report

Kronik Alkolizme Bağlı Progresif Myelopati

Mustafa SEÇKİN,[a]
Yeşim BECKMANN[a]

[a]Department of Neurology,
Atatürk Training and Research Hospital,
İzmir

Geliş Tarihi/*Received:* 29.11.2012
Kabul Tarihi/*Accepted:* 26.02.2013

Yazışma Adresi/*Correspondence:*
Mustafa SEÇKİN
Atatürk Training and Research Hospital,
Department of Neurology, İzmir,
TÜRKİYE/TURKEY
seckin.dr@gmail.com

ABSTRACT Chronic alcoholism is a significant health problem. Although brain and peripheral nervous system complications of alcohol are well known, toxic effect of alcohol on spinal cord has been rarely reported. Chronic alcohol exposure can cause myelopathy and the toxic effect of alcohol must be considered a possible mechanism of the spinal cord damage in patients with the history of chronic alcoholism. Many alcohol addicts have sedentary lifestyles and inactivity of these individuals may cover the symptoms of myelopathy. That is why gait difficulties related to myelopathy must be monitored carefully to prevent irreversible spinal cord damage by early diagnosis. In this study, we present two cases with myelopathy due to chronic ethanol use. Both patients did not seek medical care until they started to have apparent gait difficulty. Considering the frequency of alcoholism in public, it is strongly possible that myelopathy in alcoholic individuals is more common than reported.

Key Words: Alcoholism; gait disorders, neurologic; spinal cord

ÖZET Kronik alkolizm önemli bir sağlık problemidir. Alkolün beyin ve periferik sinir sistemi üzerindeki etkilerinin iyi bilinmesine rağmen, alkolün spinal kord üzerindeki toksik etkileri nadiren bildirilmiştir. Alkole kronik maruziyet miyelopatiye neden olabilir ve kronik alkolizm öyküsü olan hastalarda alkolün toksik etkisi spinal kord hasarının olası bir nedeni olarak düşünülmelidir. Pek çok alkol bağımlısı sedanter yaşam sürmekte ve bu bireylerin inaktivitesi miyelopatinin neden olduğu semptomları maskeleyebilmektedir. Bu nedenle, erken tanı ile irreverzibl spinal kord hasarının önlenmesi için miyelopati ile ilişkili yürüme bozuklukları dikkatlice takip edilmelidir. Bu çalışmada, kronik etanol kullanımına bağlı miyelopati gelişen iki olgu sunuyoruz. Her iki hasta da belirgin yürüme bozukluğu gelişinceye kadar tıbbi yardım aramadılar. Alkolizmin toplumdaki yaygınlığı göz önünde bulundurulduğunda, alkolik bireylerde miyelopati sıklığının bildirilen olgulardan daha fazla olması beklenmektedir.

Anahtar Kelimeler: Alkolizm; yürüyüş bozuklukları, nörolojik; omurilik

Turkiye Klinikleri J Neur 2013;8(2):66-72

Alcohol has been consumed by humans for thousands of years. Chronic and excessive alcohol consumption has effects on various central and peripheral nervous system functions.[1] The etiology of myelopathy involves specific infections, demyelination, vitamin B12 deficiency, tumors, syringomyelia, Chiari malformation, amyotrophic lateral sclerosis, rheumatoid artritis, spondilitic myelopathy, lupus erythematosis, paraneoplastic syndromes, radiation, brucellosis, and sarcoidosis.[1,2] However, toxic effect of chronic alcoholism on the spinal cord has been rarely

investigated.[3] The other few publishments about the relationship between alcohol consumption and spinal cord damage have focused on acute effect of alcohol intake rather than chronic use.[4,5]

Despite high prevalence of alcoholism, the effects of alcohol on spinal cord have been ignored by researchers and clinicians.

There is no special diagnostic tool for myelopathy related to chronic alcoholism. Therefore, the other reasons of myelopathy must be excluded for accurate diagnosis. In this study, we present two cases with myelopathy due to chronic ethanol use. The patients did not seek medical care until they started to have apparent gait difficulty. Since these cases had no notable liver dysfunction and all other possible diagnoses were ruled out we suggest that a direct toxic effect of alcohol must be considered as a possible mechanism of spinal cord damage.

CASE REPORTS

CASE 1

A 63 year-old man with a history of chronic alcoholism for 40 years was admitted to our clinic due to difficulty in gait and tremor in hands. The patient suffered from gait disturbance which progressively worsened over 6 months. He was unable to walk independently and fell easily to either side. His past history was significant for alcohol consumption (current alcohol intake 1 liter raki 45% volume, 45 g/day) for the last 40 years. He had no nutritional deficiency. He had no relevant past medical and family history of any neurological diseases. On mental examination, he appeared awake and oriented. Mini-Mental State Exam score was 28/30. On memory testing, the patient displayed a slow rate of acquisition. Remote memory was good with cues. He interpreted proverbs concretely and made several perseverations when asked to perform frontal systems tasks. He had normal language and perfect naming but an impaired word-list generation. There were not visuospatial difficulties. Cranial nerves II through XII were normal, as were motor bulk, power, and tone. His examination revealed a spastic paraparesis with normal upper extremity function. He had 3+/5 weakness (Medical Research Council rating scale) in both legs. Reflex examination revealed marked hyperreflexia in the lower extremities with spasticity. No atrophy was noted in the muscles. Babinski sign was positive in bilateral lower extremities. Pain and temperature sensation, discrimination, stereognosis, and graphesthesia were preserved. A dermatomal level indicating sensory loss could not be detected. Both proprioception and vibration senses were found to be impaired in the lower extremities. Romberg's sign was positive. He had spastic gait and difficulty in maintaining balance because of proprioceptive loss. Besides spastic paraparesis, the patient had intention tremor in his hands and head during admission and follow-up period. Muscle tone, strength and reflexes of the upper extremities were normal. He denied change in bowel or bladder function. On admission, all vital signs were normal. His complete blood count, partial tromboplastin time, electrolytes, glucose level (102 mg/dL), hemoglobin A1c (3.2%), iron (158 mcg/dL), total iron binding capacity (TIBC 298 mcg/dL), transferrin saturation (35%), and ferritin (222 ng/ml) values were normal. Liver function tests were normal and the results were as follows: Aspartate transaminase (AST): 21 U/L, Alanine transaminase (ALT): 18 U/L, Gamma glutamyl transpeptidase (GGT): 19 U/L, Alkaline phosphatase (ALP): 37 U/L, total bilirubin: 1.02 mg/dL, direct bilirubin: 0.4 mg/dL, total protein: 8.4 g/dL, albumin: 5.1 g/dL, globulin: 3.3 g/dL, ammonia: 12 mcg/dL, urinary copper excretion: 20 μg/day, serum copper: 94 μg/dL, and serum ceruloplasmin: 22 mg/dL. Hepatitis markers (anti-HAV, HBsAg, anti-HBs, anti-HBc, HBeAg, anti-HBe, anti-HCV, anti-HEV) were negative. Blood vitamin B12 (412 pg/ml) and folate (7.02 ng/ml), vitamin E (10 mg/L) values were in normal ranges. Serum methylmalonic acid level (0.08 μmol/L) and serum homocysteine (6.8 μmol/L) were all normal. Serum and cerebrospinal fluid (CSF) antibodies to *Human immunodeficiency virus (HIV), Human T-cell lymphotropic virus type I (HTLV-1), Treponema pallidum, Borrelia burgdorferi* were negative. Tumor markers as carcinoembryonic antigen (CEA) (3.7 U/mL), alphafetoprotein (AFP) (4.1 ng/mL), carbohydrate antigen 19-9 (CA19–9) (12.7 U/mL),

Prostate-specific antigen (PSA) (1.00 ng/ml) were investigated and the results were negative. Titers of class-specific rheumatoid factors (IgM RF, IgG RF, IgA RF), antinuclear antibody (ANA), antinuclear cytoplasmic antibodies (ANCA), antids-DNA, antiphospolipid antibodies (APA), complement components C3 and C4, cryoglobulins were in normal limits. Serum level of angiotensin-converting enzyme (ACE) was not increased. The urine drug screen was negative, except for an alcohol level of less than 10 mg/dL. CSF showed normal cell counts, glucose and protein level. Oligoclonal band was not detected and immunglobulin G (IgG) index was in normal limits. HIV, *Herpes simplex, Mycobacterium tuberculosis* were not detected in the CSF by means of viral, acid-fast bacterial cultures and polymerase chain reaction (PCR) test. Brucella-agglutinating antibodies were negative in the blood and CSF. Thorax computed tomography (CT), abdominal and testicular ultrasonography (USG), and liver magnetic resonance imaging (MRI) were considered as normal. Spinal somatosensory evoked potentials for median and posterior tibial nerves revealed prolonged latencies.

Electrophysiological investigations indicated mixed type sensorimotor polyneuropathy in the lower extremities. The patient was evaluated with the 1,5 tesla brain and spinal MRIs protocol using pre and post-contrast T1, T2-weighted and, fluid attenuated inversion recovery (FLAIR) sequences. Brain MRI demonstrated diffuse atrophy of the cerebellar and cerebral hemispheres. Cervical, thoracic and lumbasacral MRI findings were normal. With abstinence from alcohol and resumption normal diet, the patient was treated with intravenous fluids, thiamine and multivitamins, and physical therapy. An antispastic agent, baclophen 10 mg/day was given and the dose was increased to 20 mg/day in the second week of hospitalization (reference dose 5-80 mg/d). In the clinical course, pyramidal and cerebellar signs persisted while spasticity slightly relieved.

CASE 2

A 43 year-old man was admitted to our clinic because of walking disability. His gait progressively worsened over 2 years. He had a history of chronic alcohol abuse (current alcohol intake 1 liter raki 45% volume, 45 gr/day) for the last 20 years. He was a well-nourished person. There was no family history of neurologic diseases, and he had no previous medical disorders either. On neurological examination, he was awake and oriented. Mini-Mental State Exam score was 30/30. The results of neuropsychological tests including memory, language, frontal system tasks, and visuospatial abilities were normal. Cranial nerves II through XII were normal, as were motor bulk, power, and tone. Neurological examination revealed a paraparesis (3+/5 weakness) in both legs. Tendon reflexes were severely increased in the lower extremities with spasticity. No atrophy in the muscles of upper and lower extremities was observed. Babinski sign was positive in bilateral lower extremities. Vibratory and postural sensation were decreased in the lower extremities. Pain and temperature sensation, discrimination, stereognosis, and graphesthesia were preserved. Romberg's sign was positive. He presented with spastic gait and difficulty in maintaining balance because of proprioceptive loss. In addition to pyramidal and sensorial findings he had bilateral dysmetria and dysdiadokinesis in the hands. Muscle tone, strength and reflexes of the upper extremities were normal. He denied change in bowel or bladder function. The general examination was normal. His complete blood count, partial thromboplastin time, electrolytes, glucose level (105 mg/dL), hemoglobin A1c (3.8%), iron (120 mcg/dL), TIBC (300 mcg/dL), transferrin saturation (45%), and ferritin (200 ng/mL) values were normal. Laboratory data of liver function tests disclosed no abnormality and the results were as follows: AST: 19 U/L, ALT: 21 U/L, GGT: 14 U/L, ALP: 40 U/L, total bilirubin: 1.00 mg/dL, direct bilirubin: 0.2 mg/dL, total protein: 8.0 g/dL, albumin: 4.8 g/dL, globulin: 3.2 g/dL, ammonia: 15 mcg/dL, urinary copper excretion: 12 µg/day, serum copper: 87 µg/dL, and serum ceruloplasmin: 27 mg/dL. Anti-HAV IgG assay was positive and other hepatitis markers (anti-HAV, HBsAg, anti-HBs, anti-HBc, HBeAg, anti-HBe, anti-HCV, anti-HEV) were negative. Blood vitamin B12 (486 pg/mL) and folate (7.48 ng/mL), vitamin E (12

mg/L) values were in normal ranges. Serum methylmalonic acid level (0.08 μmol/L) and serum homocysteine (6.8 μmol/L) were all normal. Serologic tests of serum and CSF for HIV, HTLV-1, *Treponema pallidum, Borrelia burgdorferi* were negative. CEA (5.1 U/mL), AFP (4.9 ng/mL), CA19–9 (1.78 ng/mL), PSA (15.0 ng/mL) were studied as tumor markers and the results were negative. Titers of class-specific rheumatoid factors (IgM RF, IgG RF, IgA RF), ANA, ANCA, Antids-DNA, APA, C3 and C4, cryoglobulins and serum levels of ACE were not increased. Drug screen was negative in the urine. CSF contained normal cell counts, glucose and protein level with the absence of oligoclonal band and IgG index. HIV, *Herpes simplex, Mycobacterium tuberculosis* were not detected in the CSF. Brucella-agglutinating antibodies were negative in the blood and CSF. His thorax CT, abdominal USG, liver MRI, testicular ultrasound were normal. Spinal somatosensory evoked potentials for median and posterior tibial nerves could not be obtained. Electromyography was normal. MRI scan of the brain and spinal cord were considered as normal. He was treated with folic acid, thiamin and baclophen 20 mg/day (baclophen reference dose 5-80 mg/d). He did not give a significant response to the treatment except for slight regression in spasticity. At discharge and follow-up he still had unsteadiness and reported that he has refrained from drinking alcohol.

DISCUSSION

Myelopathy is known to occur with specific infections, notably herpes zoster, HTLV-1, HIV, tuberculous, syphilis and brucellosis.[1] Myelopathy due to infections was excluded in our cases because there was no serologic and systemic signs of infection. Myelopathy may develop on the basis of demyelination, as in certain cases of multiple sclerosis.[2] The diagnosis of inflammatory myelopathy was excluded with the absence of specific MRI and CSF findings in our cases. Other afflictions that may present as progressive myelopathy include infection, vitamin B12 deficiency, tumors, syringomyelia, Chiari malformation, amyotrophic lateral sclerosis, rheumatoid artritis, spondilitic myelopathy, lupus erythematosis, paraneoplastic syndromes, radiation, brucellosis, and sarcoidosis[1]. Normal MRIs of our patients' spinal cords excluded such etiologies involving compression or expansion of the spinal cord (epidural cord compression, intrinsic cord tumor, syringomyelia, infarction). Vitamin B12, folate and vitamin E deficiency were also absent in our patients. Electromyographic evaluation of patients excluded lower motor neuron involvement as seen in amyotrophic lateral sclerosis. Sarcoidosis may present as an intramedullary spinal cord mass. CSF is usually abnormal (increase in cells, protein and IgG concentration) and ACE enzyme level is increased. Chest CT generally demonstrates hilar adenopathy and MRI shows intramdeullary lesion with a nodular enhancement of the meninges.[6] A number of other rare granulomatous conditions have on occasion caused an intrinsic or extrinsic compressive myelopathy including brucellosis. The diagnosis is suspected if the systemic signs and brucella-agglutinating antibodies are apparent at the same time. We excluded neurosarcoidosis and brucellosis in our patients because of normal CSF, serum ACE, chest CT and spinal MRI findings. Systemic lupus erythematosus was considered in the differential diagnosis of myelopathy. It is presumed to arise from a microvasculitis of the spinal cord.[7] The patients had no antiphospholipid antibodies, pleocytosis and elevation of CSF protein which are characteristics in the diagnosis of microvasculitis of the spinal cord such as systemic lupus erythematosus. A subacute necrotic myelitis has been reported in association with paraneoplastic syndromes. The clinical syndrome consists of a rapidly progressive painless loss of motor and sensory tract function, usually with sphincter disorder.[1] The tumor workup included CT or MRI scans of the chest and abdomen, and testicular USG as well as tumor markers but no tumor was visible in our patients. We were not able to obtain anti-neuronal antibody assay that may act as a diagnostic marker of paraneoplastic syndromes.

In contrast to the acute and reversible pharmacological effects of ethanol, prolonged alcohol abuse leads to persistent and potentially irreversible

neurologic deficits. In any given patient, the sites of neuronal injury and, hence, the clinical presentations, are probably governed by genetic, nutritional, and other environmental factors. The neurologic disorders may occur in isolation, or, more commonly, multiple syndromes may be present in a single patient. An increasing amount of evidence has accumulated to suggest that excessive ethanol is toxic to the nervous system. In addition to the acute and reversible pharmacological effects of ethanol, prolonged alcohol use leads to persistent and potentially irreversible neurologic deficits. Virtually any level of the nervous system is vulnerable.[7,8] The primary site of action of alcohol appears to be the exicitable membranes.[9] Although no concencus has been reached on the mechanisms underlying the ethanol-induced loss of neurons, neuronal death is a prominent damage in chronic ethanol intake. Recent research has shown that moderate alcohol exposure can induce angiogenesis through induction of vascular endothelial growth factor.[10] It was once thought that ethanol affected neurons directly by an unknown mechanism on cell membranes. More recently it has been shown that ethanol, under experimental conditions, has wide-ranging effects on important cellular and neuronal constituents, including lipid membrane, receptors for GABA N-methyl-D-aspartate and 5-hydroxytryptamine, ion channels, G-proteins, second messengers, and gene expression.[11-14] Another effect of alcohol on central nervous system is the depression of extracellular levels of GABA and increase in the NMDA induced NO levels.[15] It is also suggested that ethanol impairs insulin stimulated mitochondrial function in immature cerebellar granule neurons and this is associated with increased expression of the p53 and CD95 pro-apoptosis genes.[16] In another study it was shown that ethanol induced decrease of the expression of glucose transport protein in the central nervous system and this is a predisposing condition to apoptosis as a mechanism of neuronal death in the cerebellum and hipocampus.[17] Cerebellar degeneration related with alcoholism is a well known effect of ethanol. However, all previously published studies on the effects of alcohol on spinal cord are limited with small numbers of cases. Previous experimental studies found that acute alcohol intoxication may alter the long-term outcome of standardized spinal cord injury resulting in increased spinal cord necrosis and impaired functional recovery. These findings confirm that increased post-contusion hemorrhage results when spinal cord contusion injury occurs in the presence of acute intoxication, and suggest that increased intramedullary hemorrhage may contribute to previously observed increases in anatomic damage and impaired functional recovery with alcohol intoxication.[4,5,18,19] Kokobun et al. reported that chronic alcoholics with spasticity had conduction disturbance in the posterior column and/or the medial lemniscus, which was considered to be due to alcoholic myelopathy and/or a brainstem lesion.[20] Myelopathy may develop as a result of nutritional deficiency and secondary to metabolic disturbances, such as hepatic disease. It has been reported that progressive myelopathy is a rare complication of chronic liver disease with portal hypertension and is characterised with progressive and irreversible paraparesis.[21] Neuropathological studies of the patients with hepatic myelopathy have demonstrated demyelination of the lateral corticospinal tracts with various degree of axonal loss. It has been hypothesised that ammonia and other neurotoxins may pass the liver by spontaneous or surgical portosystemic shunts. This mechanism may cause myelopathy as well as hepatic encephalopathy.[22,23] However, in one report, five well-nourished, alcoholic patients without cirrhosis had progressive myelopathy.[3] The detailed examination of liver functions were also normal in our patients. The cases herein we present have typical features of progressive myelopathy together with cerebellar findings due to alcoholism. All the causes that might be responsible for the etiology of myelopathy were excluded. In the first patient, nerve conduction velocities of the upper extremities were in normal limits and latency of N20 potential was prolonged. In the second patient electromyography was normal. These findings support the diagnosis of myelopathy. However, P40 potential was not obtained. This could be the result of polyneuropathy

in the lower extremities. We consider that chronic alcoholism is the probable reason of myelopathy in these cases because of the existence of upper motor neuron symptoms without any other etiological factors, with normal cranial MRI and pathological electrophysiological findings. The absence of portacaval shunting or notable liver dysfunction in these cases suggests that a direct toxic effect of alcohol must be considered a possible mechanism of spinal cord damage. The three areas which appear most sensitive to alcohol are the cortex, cerebellum, and peripheral nerves. In our opinion, many other areas in nervous system are sensitive to alcohol, including spinal cord, but to a lesser extent.

This is a paper dealing with two single cases of patients with chronic alcohol intake and presentation of a combination of cerebellar symptoms and assumed pathology within the spinal cord. Based on the clinical and neurophysiological and neuroimaging findings a progressive myelopathy related to chronic alcoholism can be diagnosed after exclusion of more common potential causes of spastic paraparesis. Nevertheless, there are still a number of open questions and further experimental and clinical trials are recommended to establish the alcohol's effect on spinal cord. The damage on spinal cord may take a longer period with very slow progression. Altough chronic alcoholism is a significant public health problem myelopathy due to alcoholism has been rarely reported. When slow progression of spinal damage is combined with sedentary lifestyle and inactivity of alcohol addicts, symptoms of myelopathy may be ignored until they become apparent. Physicians should pay more attention to the gait difficulties in alcoholic individuals. We suggest that alcohol addicts must be informed and monitored for gait difficulties related to myelopathy so that irreversible spinal cord damage can be prevented by early diagnosis depending on the initial symptoms of myelopathy and exclusion of the other reasons. Considering the prevalence of alcoholism in public, it is strongly possible that myelopathy in alcoholic individuals is more common than reported.[24]

REFERENCES

1. Victor M, Ropper AH. Adams and Victor's Principles of Neurology. 8th ed. New York: McGraw-Hill; 2005. p.1058-61.
2. Bakshi R, Kinkel PR, Mechtler LL, Bates VE, Lindsay BD, Esposito SE, et al. Magnetic resonance imaging findings in 22 cases of myelitis: comparison between patients with and without multiple sclerosis. Eur J Neurol 1998; 5(1):35-48.
3. Sage JI, Van Uitert RL, Lepore FE. Alcoholic myelopathy without substantial liver disease. A syndrome of progressive dorsal and lateral column dysfunction. Arch Neurol 1984;41(9): 999-1001.
4. Anderson TE. Effects of acute alcohol intoxication on spinal cord vascular injury. Cent Nerv Syst Trauma 1986;3(3):183-92.
5. Forchheimer M, Cunningham RM, Gater DR Jr, Maio RF. The relationship of blood alcohol concentration to impairment severity in spinal cord injury. J Spinal Cord Med 2005;28(4): 303-7.
6. Levivier M, Balériaux D, Matos C, Pirotte B, Brotchi J. Sarcoid myelopathy. Neurology 1991;41(9):1529-30.
7. Propper DJ, Bucknall RC. Acute transverse myelopathy complicating systemic lupus erythematosus. Ann Rheum Dis 1989;48(6):512-5.
8. Diamond I, Messing RO. Neurologic effects of alcoholism. West J Med 1994;161(3):279-87.
9. Wallgren H. Effects of alcohol on biochemical processes in the central nervous system. Psychosom Med 1966;28(4):431-42.
10. Gu JW, Elam J, Sartin A, Li W, Roach R, Adair TH. Moderate levels of ethanol induce expression of vascular endothelial growth factor and stimulate angiogenesis. Am J Physiol Regul Integr Comp Physiol 2001;281(1):R365-72.
11. Signore AP, Yeh HH. Chronic exposure to ethanol alters GABA(A) receptor-mediated responses of layer II pyramidal cells in adult rat piriform cortex. J Neurophysiol 2000;84(1): 247-54.
12. Yang X, Criswell HE, Breese GR. Ethanol modulation of gamma-aminobutyric acid (GABA)-mediated inhibition of cerebellar Purkinje neurons: relationship to GABAb receptor input. Alcohol Clin Exp Res 2000;24(5): 682-90.
13. Yoshimoto K, Ueda S, Kato B, Takeuchi Y, Kawai Y, Noritake K, et al. Alcohol enhances characteristic releases of dopamine and serotonin in the central nucleus of the amygdala. Neurochem Int 2000;37(4):369-76.
14. Nishida A, Zensho H, Hisaoka K, Miyata M, Yamawaki S. Differential display of ethanol-induced gene in N18TG2 cells. Alcohol Clin Exp Res 2000;24(3):348-51.
15. Manto M, Laute MA, Pandolfo M. Depression of extra-cellular GABA and increase of NMDA-induced nitric oxide following acute intra-nuclear administration of alcohol in the cerebellar nuclei of the rat. Cerebellum 2005;4(4):230-8.
16. de la Monte SM, Neely TR, Cannon J, Wands JR. Ethanol impairs insulin-stimulated mitochondrial function in cerebellar granule neurons. Cell Mol Life Sci 2001;58(12-13): 1950-60.
17. Fattoretti P, Bertoni-Freddari C, Casoli T, Di Stefano G, Giorgetti G, Solazzi M. Ethanol-induced decrease of the expression of glucose transport protein (Glut3) in the central nervous system as a predisposing condition to apoptosis: the effect of age. Ann N Y Acad Sci 2003;1010:500-3.

18. Singh SP, Gao Y, Kunapuli SP, Ravindra R. Ethanol inhibits G-protein-mediated glucose uptake by C6 glioma cells. Neuroreport 1999; 10(3):595-9.
19. Narita M, Miyoshi K, Narita M, Suzuki T. Changes in function of NMDA receptor NR2B subunit in spinal cord of rats with neuropathy following chronic ethanol consumption. Life Sci 2007;80(9):852-9.
20. Kokubun Y, Oishi M, Takasu T, Sakamaki S. Somatosensory evoked potentials in chronic alcoholics with spasticity. Arch Neurol 1988; 45(3):318-21.
21. Mendoza G, Marti-Fàbregas J, Kulisevsky J, Escartín A. Hepatic myelopathy: a rare complication of portacaval shunt. Eur Neurol 1994; 34(4):209-12.
22. Campellone JV, Lacomis D, Giuliani MJ, Kroboth FJ. Hepatic myelopathy. Case report with review of the literature. Clin Neurol Neurosurg 1996;98(3):242-6.
23. Utku U, Asil T, Balci K, Uzunca I, Celik Y. Hepatic myelopathy with spastic paraparesis. Clin Neurol Neurosurg 2005;107(6):514-6.
24. Mirsal H. [Alcohol dependence; epidemiology, etiology and prognosis]. Turkiye Klinikleri J Psychiatry-Special Topics 2010;3(3):15-9.