

An Unexpected Cause of Hyperactive Delirium in Patients with Decompensated Nonalcoholic Cirrhosis

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Rec date: Feb 8, 2015, Acc date: Mar 10, 2015, Pub date: March 18, 2015

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Keywords: Vitamin B12 Deficiency; Delirium

Introduction

Delirium is a complex neuropsychiatric syndrome that typically involves a plethora of cognitive and non-cognitive symptoms, resulting in a broad spectrum of differential diagnosis dominated by mental disorders. The prevalence of delirium in elderly patients admitting to hospital is 5-55% [1]. Delirium is a common neuropsychiatric syndrome that may occur in several different settings and one of them is vitamin B12 deficiency. Vitamin B12 deficiency causes many cerebral cortex abnormalities such as confusion, mood and memory changes, delirium with or without hallucinations, depression and acute psychotic states [2,3]. Hepatic encephalopathy (HE) describes the spectrum of potentially reversible neuropsychiatric abnormalities seen in patients with liver dysfunction after exclusion of unrelated neurologic and/or metabolic abnormalities. The clinical manifestations of HE is characterized by cognitive and motor deficits of varying severity without specific lesions in the central nervous system. The symptoms range from minimal changes in personality to coma, including delirium [4]. Usually, in the elderly patients with cirrhosis, it is hard to differentiate two clinical situations. Here we report a case of an elderly patient with cirrhosis who experienced delirium due to vitamin B12 deficiency, but was treated as HE before.

Case Report

Sixty-six year-old white male patient was admitted to the emergency room with dyspnea and abdominal distention. The patient's medical history was remarkable for type 2 diabetes mellitus, hypercholesterolemia, coronary artery disease and chronic liver disease. Physical examination findings revealed massive ascites, hypoactive deep tendon reflexes and pretibial edema. Baseline laboratory investigations are shown in Table 1. Abdominal ultrasonography revealed small and lobulated liver with irregular contours, enlarged spleen and portal vein and moderate ascites which were all compatible with liver cirrhosis. The patient was evaluated as having decompensated cirrhosis with good hepatic synthetic functions with Child-Pugh score 7 points. After hospitalization, he showed restlessness, anxiety, irritability, inappropriate attention, visual hallucinations and sleep-awake cycle dysregulation. After a detailed neurologic examination, the diagnosis of focal syndromes which might mimic hepatic encephalopathy were excluded. Clinical and laboratory findings were not compatible with metabolic encephalopathy. The patient was considered as having HE and HE treatment with oral lactulose and L-ornithine, L-aspartate, was immediately began. However patient's clinical status was not resolved and didnot respond

therapy, so diagnosis of HE was re-evaluated. Patient's arterial ammonia level was normal and electroencephalography (EEG) was performed. EEG findings were normal, characteristic EEG patterns with HE-triphasic waves on EEG 5 per second- were absent. Psychiatric consultation was requested and the patient was diagnosed as having hyperactive delirium according to DSM-IV criteria. His serum hemoglobin level was measured as 10.7 gr/dl with a mean corpuscular volume of 110 pg and a mean corpuscular haemoglobin level of 38.3 fl. The peripheral blood smear showed nuclear hypersegmentation of neutrophils and macro-ovalocytosis. Serum vitamin B12 level was considerably low, 60 pg/ml (189-883 pg/ml). He was not a vegetarian person with usuall eating habits. Upper gastrointestinal endoscopy revealed grade 2 esophageal varices and multiple endoscopic biopsies which were obtained from atrophic appearance of gastric mucosa were found as consistent with severe atrophic gastritis after histopathological evaluation. Patient's serum antiparietal cell antibody was positive so we thought that vit B12 deficiency was due to atrophic gastritis. Treatment of the patient with parenteral vitamin B12 resulted in rapid neurological improvement within hours. Clinical presentation of delirium completely disappeared in the twentieth hour of treatment. His baseline memorial delirium assessment scale (MDAS) score was 19 and one day after the initiation of treatment, his score was 5. Dyspne and abdominal distention and edema resolved with sodium restricted diet, diuretics and human albumin replacement therapy. He was discharged from hospital with monthly parenteral vitamin B12 replacement treatment in addition to medicines used for supportive and palliative purposes.

Parameters	On admision	Reference range
Glucose	112	70-100 mg/dL
BUN	28	16.6-48.5 mg/dL
Creatinin	0.7	0.5-0.9 g/dL
ALT	14	5-33 g/dL
AST	44	5-32 g/dL
Albumin	3	3.5-5.2 g/dL
Total Bilurubin	1.02	0.1-1.2 mg/dL
Direct Bilurubin	0.6	0.1-0.3 mg/dL
Sodium	138	136-145 mmol/L
Potassium	4.1	3.5-5.1 mmol/L
Calcium	7.9	8.1-10.7 mg/dl

Phospor	2.8	2.5-4.5 mg/dl
Magnesium	1.9	1.7-2.4 mg/dl
Arterial blood ammonia	35.7	17-55 µmol/L
Hemoglobin	10.7	11.2-15.4 g/dl
Mean corpuscular volum (MCV)	110	79.4-94.8 fL
Mean corpuscular hemoglobin (MCH)	38.3	25.6-32.2 pg
White blood cells (WBC)	9.2	3.980-10.04 103/µL
Platelet	105	182-369 103/µL
Prothrombin time	16.7	11-14.2 sn
Vitamin B12	60	189-883 pg/ml

Table 1: Baseline laboratory assessments of patient.

Discussion

About 55% of all cirrhotic patients develop various psychiatric diseases including hepatic encephalopathy, anxiety disorders or delirium [5]. The early stage of hepatic encephalopathy may occur with various neuropsychiatric symptoms including a delirium state which could be also associated with other predisposing factors such as vitamin B12 deficiency [6]. In our case, the normal EEG patterns and arterial blood ammonia levels did not support diagnosis of hepatic encephalopathy. Vitamin B12 deficiency was diagnosed with macrocytic hyperchromic anemia, histological appearances of the gastric mucosa and subsequently low serum vitamin B12 level. In the presented case, all causes of delirium other than vitamin B12 deficiency such as infections, metabolic and electrolyte imbalances, trauma, central nervous system pathology, hypoxia, endocrinopathies and withdrawal syndrome were excluded. Deficiency of vitamin B12 may require years until encephalopathy develops. Cognitive impairment may be related to low serum vitamin B12 and high plasma homocysteine levels. Plausible mechanisms include

homocysteine neurotoxicity, vasotoxicity, and impaired S-adenosylmethionine-dependent methylation reactions vital to central nervous system function [7]. In this case, MDAS scores improved significantly on the first day with parenteral vitamin B12 treatment, indicating the cause of delirium was vitamin B12 deficiency. Jorge Gomez-Bernal et al reported a case with psychiatric symptoms which have been considered to be related to B12 deficiency and rapid recovery of all symptoms after the third day of B12 replacement therapy [8]. Although many psychiatric symptoms have been considered to be related to vitamin B12 deficiency, this is the first report with a short duration of delirium symptoms secondary to B12 deficiency in a patient with decompensated cirrhosis. Thus, we emphasize that physicians should keep in mind that cirrhotic patients may experience neuropsychiatric symptoms not only from HE but also due to other factors such as vitamin B12 deficiency. We think that early detection and intervention may alleviate the symptoms of delirium in cirrhotic patients.

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