Case Report
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Seizures Related to Vitamin B6 Deficiency in Adults

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Vitamin B6 is closely associated with functions of the nervous, immune, and endocrine systems. Its deficiency may result in neurological disorders including convulsions and epileptic encephalopathy. Until today, this has only been reported in infants, children, and critically ill adult patients. We report a case of a 36year-old man with chronic alcoholism who presented with seizures after gastrointestinal disturbance. His seizures persisted even after treatment with antiepileptic drugs, but eventually disappeared after administration of pyridoxine. Hence, vitamin B6 deficiency may cause seizures in adult patients with chronic alcoholism. **(2015;5:23-24)**

Key words: Vitamin B6 deficiency, Seizure

Introduction

Vitamin B6 is part of the vitamin B group complex and can serve as a cofactor in the metabolism of glucose, amino acids, and lipids. Since it is essential for neurotransmitter synthesis, its deficiency causes various neurological disorders.[1] Seizures associated with vitamin B6 deficiency are usually observed in pediatric patients and these are characterized by refractoriness to antiepileptic drugs and a positive response to pyridoxine administration.[2] Here, we report a case of adult-onset seizures associated with vitamin B6 deficiency and discuss the pathophysiological mechanism.

Case

A previously healthy 36-year-old man visited our hospital because of recurrent loss of consciousness and convulsions. He had had poor nutritional intake, nausea, and vomiting for about 6 weeks. He was a heavy drinker with a reported alcohol intake of more than two bottles per day of Soju (Korean whiskey) for 10 years. Recently, he had reported drinking more than three bottles per day without meals. He continued to drink without abstinence.

Upon physical and neurological examination, no specific abnormalities were observed. Complete blood count revealed that his hemoglobin level was as low as 9.4 g/dL. Mean cell volume was slightly elevated (104.7 fL, normal value 80-100 fL), but the mean corpuscular hemoglobin concentration was normal (33.6 g/dL, normal value 32-36 g/dL). White blood cell and platelet counts were normal. Liver function tests revealed aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase levels of 59 IU/L(normal value 0-40 IU/L), 8 IU/L (normal value 0-40 IU/L), and 234 IU/L (normal value 42-128 IU/L), respectively. Chest X-ray radiographs and an electrocardiogram revealed no abnormalities. Brain magnetic resonance imaging and an electroencephalogram also showed no abnormalities.

The patient had a generalized tonic-clonic seizure in the emergency room prior to admission. The seizure ceased after administration of 4 mg of lorazepam and 1 g of valproate. After one day, another seizure developed and 800 mg of controlled-release carbamazepine was administered. Vitamin B6 levels were measured to be 4.4 nM/L (normal value: 20-202 nM/L), serum homocysteine levels

Table 1. Serum Laboratory test at admission

	Value	Measure	Normal range
Complete blood count			
WBC count	4.91	x 10^3/μL	4.0-10.0
RBC count	2.68 ▼	x 1,000,000/μL	4.0-6.0
Hemoglobin	9.4 ▼	g/dL	13.0-18.0
MCV	104.7 ▲	fL	80.0-100.0
MCH	35.2 ▲	Pg	20.0-35.0
MCHC	33.6	g/dL	32.0-36.0
PLT	193	x 10^3/μL	130.0-450.0
Liver function test			
AST	59 ▲	IU/L	0-40
ALT	8	IU/L	0-40
ALP	234 ▲	IU/L	42-128
T-bilirubin	1.5 ▲	Mg/dL	0.2-1.2

Table 2. Serum Vitamin level at admission and follow up

	Value	Measure	Normal range
Serum Vitamin level at admission			
Vitamin B1	79.8	ng/ml	59-213
Vitamin B6	4.4 ▼	nMol/L	20-202
Vitamin B12	262	ng/ml	180-914
Homocystein	>65 ▲	μMol/L	5.0-13.9
Serum Vitamin level at 2 months later			
Vitamin B6	59.3	nMol/L	20-202

were 65 μM/L (normal value 5.0 ~ 13.9 μM/L) and vitamin B1 level was normal (79.8 ng/mL).

The patient abstained from alcohol and had regular meals after admission. Pyridoxine (12 mg/day) and carbamazepine were administered for 2 months. Since discharge, the patient has been seizure-free for over 6 months. Follow-up vitamin B6 levels were also normalized (59.3 nM/L).

Discussion

Vitamin B6 is a water-soluble vitamin with the active form being pyridoxal 5'-phosphate (PLP).[3] PLP is essential for the metabolism and synthesis of amino acids, gluconeogenesis, hematopoiesis, hormone regulation, immunologic functions, and synthesis of neurotransmitters.[4] Importantly, PLP is a crucial cofactor in the synthesis of γ-aminobutyric acid (GABA) from glutamate because of its involvement in the mechanism of decarboxylation. Therefore, PLP deficiency results in the lowering of seizure thresholds by impairing the synthesis of GABA.[5]

In this case, Wernicke's encephalopathy and hepatic encephalopathy must be differentiated. Our patient showed no physical or laboratory findings compatible with those disorder, i.e. profound alteration of mentality before and after seizures, no stigmata of chronic liver disease, no significant abnormalities on liver function test and platelet counts, and normal thiamin level. Our patient had seizures without abstinence period, which was not compatible with alcohol withdrawal seizures.

Our patient has been seizure free for 4 months with nutritional supply only. This finding suggests that the seizures of our patient were probably associated with vitamin B6 deficiency, not with an epileptic brain disorder.

The most common cause of seizures associated with vitamin B6 deficiency in adults is isoniazid (INH) toxicity.[5] INH hyrozone, a metabolite of INH, inhibits pyridoxine phosphokinase, which is involved in the process of converting pyridoxine to pyridoxine phosphate. This induces the reduction of PLP and GABA and thereby increases the excitability of nerve cells.[5]

Vitamin B6 deficiency-associated seizure caused by mechanisms other than INH toxicity are rarely reported in adults.[6,7] Gerlach et al.[6] reported three patients with status epilepticus who showed refractoriness to antiepileptic drugs and low levels of PLP. All of them were admitted to an intensive care unit in critical condition. In that report, all three patients were chronic alcohol drinkers with alcohol-associated liver disease. Low concentrations of PLP in patients with chronic alcoholic liver disease may result from a dietary deficiency coupled with an intact PLP metabolizing enzyme, aldehyde oxidase.[8] Hyperhomocysteinemia may also induce seizures, but its mechanism is not well understood.[9]

Our patient, who previously had recurrent seizures despite treatment with antiepileptic drugs, became seizure-free after normalization of vitamin B6 levels. We propose that a differential diagnosis for vitamin B6 deficiency needs to be considered in patients with chronic alcoholism and nutritional deficiencies who show refractoriness to antiepileptic drugs.

References

1. Ahmad I, Mirza T, Qadeer K, Nazim U, Vaid FH. Vitamin B6: deficiency diseases and methods of analysis. *Pak J Pharm Sci* 2013;26:1057-69.
2. Yeghiazaryan NS, Zara F, Capovilla G, Brigati G, Falsaperla R, Striano P. Pyridoxine-dependent epilepsy: an under-recognised cause of intractable seizures. *J Paediatr Child Health* 2012;48:E113-5.
3. Food Standards Agency. Safe Upper Levels for Vitamins and Minerals. Report of the Expert Group on Vitamins and Minerals [Internet]. May 2003. Available from: http://www.food.gov.uk/multimedia/pdfs/vitmin2003.pdf.
4. Gospe SM Jr. Current perspectives on pyridoxine-dependent seizures. *J Pediatr* 1998;132:919-23.
5. Kook DH, Cho SY, Lee KY, Lee IG, Lee JS. A case of acute isoniazid intoxication in childhood. *J Korean Child Neurol Soc* 2006;14:358-62.
6. Gerlach AT, Thomas S, Stawicki SP, Whitmill ML, Steinberg SM, Cook CH. Vitamin B6 deficiency: a potential cause of refractory seizures in adults. JPEN J Parenter Enteral Nutr 2011;35:272-5.
7. Schulze-Bonhage A, Kurthen M, Walger P, Elger CE. Pharmacorefractory status epilepticus due to low vitamin B6 levels during pregnancy. *Epilepsia* 2004;45:81-4.
8. Ohgi N, Hirayama C. Vitamin B6 status in cirrhotic patients in relation to apoenzyme of serum alanine aminotransferase. *Clin Biochem* 1988;21:367-70.
9. Coppola G, Ingrosso D, Operto FF, et al. Role of folic acid depletion on homocysteine serum level in children and adolescents with epilepsy and different MTHFR C677T genotypes. *Seizure* 2012;21:340-3.