CLINICAL VIGNETTE

A Case of Vitamin B6 Neurotoxicity

Mopelola Adeyemo, MD and Dave Garg, MD

Introduction

Vitamin B6 or pyroxidine is a water-soluble vitamin with several critical biologic roles in enzymatic pathways involved in amino acid metabolism.[1] Adults typically require 1-2 mg of vitamin B6 per day, which can be obtained from dietary sources. However, individuals with malabsorption, malnutrition, alcoholism or those taking medications that deplete vitamin B6 are more likely to have deficiencies in vitamin B6 requiring supplementation. Caution is necessary in supplementation of vitamin B6 as excess, as well as deficiency, there can have severe side effects including neuropathy leading to significant disability. While neuropathy is the most commonly reported presentation of vitamin B6 toxicity, it remains a rare cause of neuropathy and therefore is often overlooked when forming a differential. We describe a patient with progressive neuropathy over 6 years secondary to vitamin B6 toxicity.

Case

A 47-year-old male presented to clinical nutrition with a 6-year history of progressive neuropathy. Symptoms initially started in the bilateral lower extremities. Nutritional history included recent trial of gluten-free diet. He was not a vegetarian. Pertinent medical history included ocular migraines and binge drinking. He denied lower extremity weakness. On physical examination, he had intact mental status, cranial nerves, strength, sensation and normal gait.

Preliminary laboratory evaluation included vitamin B12, which was 260 pg/ml (reference 254-1060 pg/ml; Table). Licer chemistries and A1C were normal. Thyroid testing, antinuclear antibody, and IgA antibodies were also normal. Cerebral spinal fluid (CSF) analysis for Guillen Barre Syndrome was negative along with CSF testing for encephalitis. PCR testing for Lyme disease was negative; however, western blot was positive.

Initial management included vitamin B12 supplementation due to low-normal vitamin B12 (Table 1). At this time patient self-initiated additional vitamins resulting in a daily total of 250 mg of vitamin B1, 61.5 mg of vitamin B6, 2000 mcg of vitamin B12, 1000-2000 mg of vitamin C, 5000 IU daily of vitamin D, 4000 mg of magnesium, and 680 mcg of folate. He was also treated with 2 months of doxycycline given the positive Lyme disease western blot. While lower extremity symptoms resolved with vitamin B12 treatment, the patient soon developed progressive upper extremity neuropathy. He had no clinical improvement with treatment of Lyme disease. An MRI brain was unremarkable and MRI cervical spine revealed mild degenerative changes of the cervical spine without high grade or foraminal narrowing. Nerve conduction studies were normal.

The patient's vitamin B6 level was first tested five years after symptom onset and was found be elevated at 326.6 nmol/L (reference 20-125 nmol/L; Table). He presented to Clinical Nutrition one year later, at which time, his supplements containing vitamin B6 were stopped. The patient had gradual improvement in upper extremity neuropathy with improving vitamin B6 levels, until documented normalization of vitamin B6 at 84.2 nmol/L two months following discontinuation.

Discussion

Vitamin B6 or pyridoxine plays a role in many critical biologic functions including brain development during pregnancy and immune function. The amount required per day varies with age, with typical daily requirements being ~1-2mg per day. Vitamin B6 is naturally found in many foods including poultry, fish, organ meats, fruits, potatoes and other starchy vegetables. Most people will receive adequate levels of Vitamin B6 via their food; however, certain conditions may make this more challenging, including end stage renal disease, malabsorption, autoimmune diseases like inflammatory bowel disease, and alcohol dependence. However, the advent of modern vitamin supplementation, has largely rectified B6 deficiencies. However, Vitamin B6 toxicity can result from supplementation. No consensus exists on maximum daily intake of vitamin B6, however caution should be taken when exceeding 25 mg daily for a prolonged period, as levels above 50 mg/day have been associated with serious neurological side effects such as progressive peripheral neuropathy and sensory ataxia.[2-4]

For example, Tynes at el. described a 30-year-old male, who underwent sleeve gastrectomy, followed by omega-loop bypass and biliopancreatic diversion over 4 years, who presented with progressive neuropathy, immobilizing fatigue, and vitamin B6 levels more than 6 times above normal. The patient had been taking a combination of his recommended bariatric multi-vitamin supplementation containing 2 mg of vitamin B6 per day as well as 2-3 energy drinks per day containing 10-15 mg vitamin B6 per day, over several years.[4] With cessation of the energy drinks and transition to a multivitamin with reduced vitamin B6 content, the patient had complete resolution of his symptoms.

Our patient similarly presented with neuropathy related to excess supplementation of vitamin B6. Now that supplements are so ubiquitous with more than 50% of US adults taking supplements,[5] vitamin B6 toxicity is becoming a greater concern. Only after expanding the differential and considering excess supplementation as a cause of his symptoms were we then able to diagnose vitamin B6 toxicity. This case highlights the importance of performing careful medication reconciliation that includes review of supplements and their dosages. It also stresses the need to include vitamin B6 toxicity, as well as deficiency, in the differential when evaluating neuropathy in order to avoid delaying diagnosis. Fortunately, as in our case, cessation of vitamin B6 supplementation generally leads to resolution of sensory symptoms.

Table. Laboratory values from symptom onset to 2 months after vitamin B 6 discontinuation

	Reference range	Initial labs	Repeat labs 5 years later	1 month after holding vitamin B6	2 months after holding vitamin B6
Vitamin B6	20 – 125 nmol/L		326.6 (H)	218.4 (H)	84.2
Vitamin B12	254 -1,060 pg/mL	260	802	751	
Vitamin B1	70 - 180 nmol/L		324 (H)	188 (H)	
Vitamin D	20 - 50 ng/mL			55 (H)	
H- High lab value					

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