Multivitamin supplements and energy drinks in pyridoxine megavitaminosis

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A 42-year-old woman with genetically confirmed but asymptomatic Huntington disease (HD) presented with a 2-year history of tingling along the lateral legs, intermittent band-like sensations in the legs that resolved with walking and worsened during rest, and searing pain from the knee down. She also noticed nocturnal leg jerking on days when she had energy drinks. She had no weakness, lower back pain, or bowel or bladder dysfunction. Family history was notable for HD in her brother and both parents. There was no significant alcohol use or other factors that may have contributed to her symptoms. Neurologic examination showed hyperreflexia in her legs but was otherwise normal (including intact perception of pinprick, light touch, and proprioception). She took duloxetine for anxiety and depression and zolpidem for insomnia. Diagnostic evaluation for multiple sclerosis, rheumatoid arthritis, and lupus was inconclusive. MRI showed mild C4–C7 posterior disk protrusions but no significant central or neural foraminal stenosis. Laboratory studies at presentation showed an elevated vitamin B₆ (B₆ or pyridoxine) level of 161.6 ng/mL (normal 2.1–21.7 ng/mL) and normal or negative complete blood count differential, metabolic profile (including fasting glucose), thyroid-stimulating hormone, vitamin B₁₂, methylmalonic acid, antinuclear antibody, and Sjögren screen. Electrodiagnostic study showed no evidence of active lumbosacral radiculopathy or large fiber neuropathy. Additional history obtained following the discovery of elevated B₆ levels revealed that the patient had consumed 2 energy drinks per day (40 mg of B₆ each) for at least a year and one multivitamin tablet per day (100 mg of B₆ each) for many years. One and a half months after stopping these sources of B₆, the patient had dramatic improvement of her symptoms with only rare and transient recurrence.

DISCUSSION

B₆ is a water-soluble vitamin important in amino acid metabolisms that has been used to treat various conditions.¹ While high doses (>2,000 mg a day) have been shown to damage dorsal root ganglia,² the effect of lower B₆ doses is not well-established. In a retrospective series of 26 patients with a mean B₆ level of 68.8 ng/mL, sensory symptoms were reported in 80.8%.³

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Practical Implications

Vitamin B₆ is widely consumed, often in high doses, via sport and energy drinks and nutritional supplements. Inadvertent vitamin B₆ overuse should be considered as a possible cause of neuro-pathic symptoms.

Another study of women taking B₆ at 117 ± 92 mg/day for 2.9 ± 1.9 years reported paresthesia, bone pains, hyperesthesia, muscle weakness, fasciculations, and numbness.⁴ It is interesting that the controls in this study were taking a similar dose but for a shorter duration of time. Thus, duration of supplementation appears to play an important role in toxicity.⁴

On the other hand, a recent study reported a lack of correlation between B₆ and neuropathy.⁵ In this study, average B₆ intake in the study group was 2.1 mg/day with average serum B₆ of 135 nmol/L, while in controls average intake was 2.8 mg/day with average serum B₆ of 165 nmol/L (normal 26–102 nmol/L).⁵ Of note, the B₆ intake and serum B₆ levels in this study were lower than in other studies that considered B₆ as a possible cause of neuropathic symptoms.^{3–6} Furthermore, this study estimated intake through a questionnaire, which may not reflect the actual intake.⁵ Inadvertent B₆ intake is possible, as supplements and many popular products like cereals, body-building supplements, energy bars, and drinks have high B₆ content.⁷ Nevertheless, this study suggests that B₆ can accumulate in the body even at low doses with persistent use.⁵ Why B₆, a water-soluble vitamin, can accumulate to toxic levels is likely related to the high protein binding of B₆ metabolites and B₆'s long half-life (~15–20 days).⁸ These factors may explain the observation that only about 93% of B₆ intake was excreted following IV B₆ infusion, and B₆ metabolite levels remained elevated during supplementation and for at least 2 months afterward.⁹ The authors also suggested that storage of B₆ does occur, presumably in the liver.⁹ How elevated B₆ levels cause nerve damage is not clearly established, but possible mechanisms include the direct toxicity of pyridoxal-5-phosphate metabolite¹⁰ and the negative effect of B₆ on levels of other B vitamins.¹¹

We believe that B₆ intoxication is the cause of sensory symptoms in our patient. This conclusion is supported by the observations that the serum level exceeds the upper limit of normal by severalfold, relief of symptoms occurred after cessation of B₆ ingestion, and no other causes could be identified. Our case is unique in that B₆ intoxication is attributable to energy drinks and supplements. Physicians and patients should be aware of the multiple sources of B₆ that can potentially lead to intoxication. With the popularity of products with high B₆ content, studies of threshold neurotoxic B₆ doses are needed.

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