Recreational Nitrous Oxide and Pernicious Anemia–Associated Vitamin B_{12} Deficiency in a Patient Presenting With Sensorimotor Polyneuropathy

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Cobalamin (vitamin B_{12}) deficiency is common in the general population and may lead to acute neurologic symptoms.[1,2] Autoimmune atrophic gastritis, or pernicious anemia, is the most common cause of B_{12} deficiency.[3] Although nitrous oxide is a rare cause of B_{12} deficiency, it has emerged as a popular drug of abuse.[4,5] Here, we report a case of sensorimotor polyneuropathy secondary to B_{12} deficiency associated with recreational nitrous oxide use and pernicious anemia.

Case Report

A 26-year-old man with a medical history of chronic sensorimotor polyneuropathy and nitrous oxide use disorder (classified under other [or unknown] substance-related disorders in the *DSM-5*) was admitted to the hospital in December 2019 for worsening sensorimotor symptoms.[6]

The patient had first developed symptoms of rapidly progressive numbness, weakness, and ataxia about 1 year prior, at which point he was admitted to the general neurology service and diagnosed with acute inflammatory demyelinating polyneuropathy. He received 2 g/kg of intravenous immunoglobulin in 4 divided doses over 4 days with some improvement in symptoms. At that time, he also reported a history of "whippit" (inhaled nitrous oxide) abuse and was noted to have a low-normal serum vitamin B_{12} level of 399 pg/mL (reference range, 123–730 pg/mL) with elevated methylmalonic acid (1.55 µmol/L [reference: < 0.4 µmol/L]) and homocysteine (23 µmol/L [reference: < 13 µmol/L]). He was therefore treated with oral vitamin B_{12} supplementation.

Over the ensuing year, he received another course of intravenous immunoglobulin and oral vitamin B_{12} supplementation, but the weakness progressed, and he developed worsening neuropathic pain in his lower extremities. In the months leading up to his December admission, he also had several presentations to the emergency department for abdominal pain, nausea, and vomiting. These symptoms were attributed to cannabis use, as workup with computed tomography of his abdomen and pelvis with contrast, amylase, lipase, and hepatic function panel were unrevealing. He reported use of cannabis since high school and smoked most days of the week for the last 10 years.

On presentation in December 2019, he was alert and oriented with normal vitals. His examination was notable for weakness more prominent in his lower than in his upper extremities, reduced reflexes, absence of proprioception, and decreased vibration sense in his lower extremities. Laboratory results were notable for a low-normal serum vitamin B_{12} level (388 pg/mL), elevated methylmalonic acid and homocysteine levels (4.36 and > 65 µmol/L, respectively), mild normocytic anemia, low iron level, and positive intrinsic factor antibodies. Chemistry panel, thyroid panel, and ammonia, folate, vitamin B_6, zinc, copper, and thiamine levels were within normal limits. Urinalysis results were within normal limits, and urine drug screen was positive only for tetrahydrocannabinol. The serum toxicology screen was negative. Magnetic resonance imaging of the brain, cervical and thoracic spine without contrast was negative for any cord signal abnormality. Nerve conduction study and electromyography showed distal, axonal sensorimotor polyneuropathy.

On the basis of this evaluation, the working diagnosis was vitamin B_{12} deficiency due to inhaled nitrous oxide and pernicious anemia presenting with sensorimotor polyneuropathy. He was thus treated with daily vitamin B_{12} intramuscular injections (1,000 mcg) for about 1 month, followed by continued weekly injections. This treatment resulted in normal methylmalonic acid and homocysteine levels and reduction in abdominal and extremity pain at 4-month follow-up.

Discussion

Pernicious anemia is the most common cause of vitamin B_{12} deficiency, while nitrous oxide abuse is an emerging but rare culprit.[3,4] There have been relatively few documented cases of combined recreational nitrous oxide and pernicious anemia-induced polyneuropathy.[4,7,8]

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The presentation of vitamin B_{12} deficiency may be vague, resulting in a combination of hematologic, neurologic, or psychiatric symptoms.[2] Although vitamin B_{12} deficiency is characterized by low B_{12} levels, elevated homocysteine and methylmalonic acid are more sensitive indicators of disease.[9] Since our patient had persistent symptoms of neuropathy despite oral supplementation of vitamin B_{12}, we obtained an intrinsic factor antibody test that led to the diagnosis of pernicious anemia.[10] Although high-dose oral vitamin B_{12} treatment may be as effective as intramuscular repletion, intramuscular therapy was superior in this case.[11–13]

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