



Neuroimaging Highlight

Nitrous Oxide-Induced Myelopathy Mimicking Longitudinally Extensive Transverse Myelitis

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A 28-year-old man presented with one week of progressive paresthesia in a stocking-glove distribution up to bilateral elbows and hips, diffuse leg weakness and myalgias, staggering gait and urination difficulty. Neurological examination revealed absent vibration sensation and proprioception in the feet more than fingers, reduced pinprick in the hands and legs up to T9, Romberg's sign, a wide-based gait with mild limb sensory ataxia, and normal remainder of the exam. Spine magnetic resonance imaging (MRI) demonstrated a long segment expansile lesion throughout the cord, predominantly affecting the dorsal columns (Fig. 1). He received high-dose corticosteroids for possible longitudinally extensive transverse myelitis (LETM). Cerebrospinal fluid analysis was unremarkable with normal glucose (3.2 mmol/L), protein (371 mg/L), leukocytes (2) and no

oligoclonal bands. Further workup revealed normal brain MRI and negative serum aquaporin-4 IgG. Notably, he recently used dimethyltryptamine and inhaled nitrous oxide (N₂O). He was diagnosed with myelopathy secondary to functional vitamin B12 deficiency from N₂O inhalation. Serum vitamin B12 (263 pmol/L), holo-transcobalamin II (52 pmol/L) and homocysteine (10.4 μmol/L) were normal. After treatment with intramuscular vitamin B12 1000 mcg daily for a week, followed by 1000 mcg weekly for 4 weeks and 1000 mcg oral daily thereafter, his symptoms improved over 3 months. 8-months follow-up MRI demonstrated near-complete resolution (Fig. 1d).

N₂O irreversibly deactivates vitamin B12 through oxidation, resulting in myelopathy characterized by spinal cord dorsal column damage through subacute combined degeneration (SACD).¹ In a

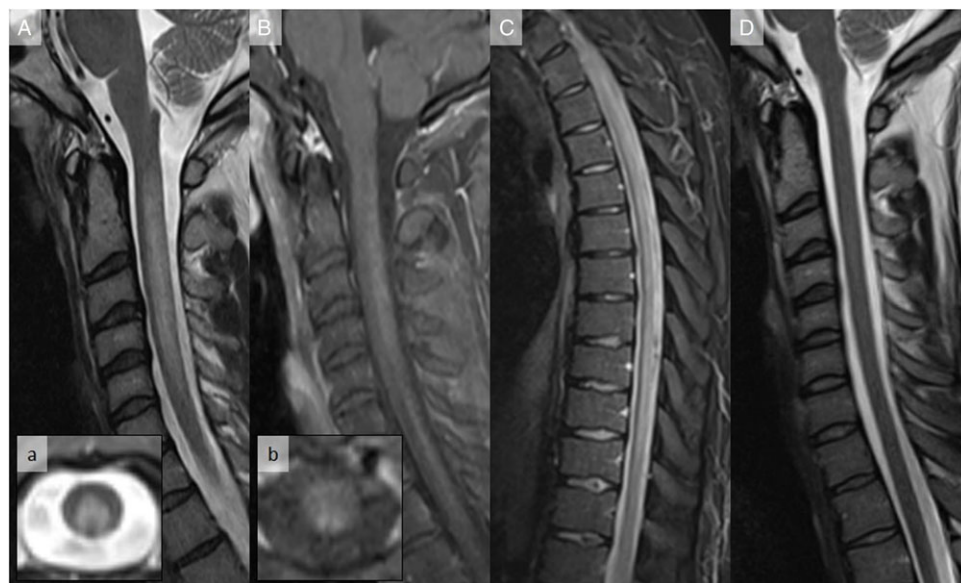


Figure 1. MRI spine, sagittal (A–D) and axial (a–b) views. Cervical T2 (A,a), T1 post-contrast (B,b), and thoracic T2 (C) sequences demonstrate extensive symmetrical cord edema in the central and posterior cervicothoracic cord centered in the dorsal columns, extending from the cervicomedullary junction to the T12–L1 intervertebral disc space. The cervical cord is expanded, measuring 1.4 cm in transverse diameter and 0.8 cm in anterior–posterior diameter, with faint enhancement of the dorsal columns from C1 to C4–5 (B,b). Axial views (a,b) reveal symmetric bilateral hyperintensities in the lateral portions of the dorsal columns (inverted V sign). Follow-up at 8 months (D) shows complete normalization of the cervical cord. MRI = magnetic resonance imaging.

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case series of 116 N₂O-myelopathy patients, common symptoms included paresthesia (85%) more often in the lower than upper limbs, unsteadiness (14%) and weakness (13%).² MRI characteristically reveals dorsal column T2 hyperintensities, with C3-C5 segments being most commonly affected, and the appearance of an inverted “V” (inverted V sign) on axial images.¹⁻⁴ Bloodwork typically reveals normal serum B12 and holo-transcobalamin and elevated homocysteine (80-90% sensitivity for N₂O-SACD).³ Treatment relies on the case literature and involves N₂O abstinence and parenteral B12 supplementation.⁵

This case demonstrates findings atypical of N₂O-myelopathy and that mimic LETM, such as cord involvement up to T12-L1, while <10% of N₂O-myelopathy cases affect T12.² Moreover, this case demonstrates significant cord swelling (0.8 cm anterior-posterior diameter), whereas a mean diameter of 0.53 ± 0.08 cm was observed in a study of 50 N₂O-myelopathy patients.⁶ Overall, it is important to consider N₂O-myelopathy even in the setting of contiguous long segment cord lesions mimicking LETM and normal homocysteine. Early recognition and supplementation can significantly improve health outcomes.

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References

1. Keddie S, Adams A, Kelso ARC, et al. No laughing matter: subacute degeneration of the spinal cord due to nitrous oxide inhalation. *J Neurol*. 2018;265:1089–95. DOI: [10.1007/s00415-018-8801-3](https://doi.org/10.1007/s00415-018-8801-3).
2. Mair D, Paris A, Zaloum SA, et al. Nitrous oxide-induced myeloneuropathy: a case series. *J Neurol Neurosurg Psychiatry*. 2023;94:681–8. DOI: [10.1136/jnnp-2023-331131](https://doi.org/10.1136/jnnp-2023-331131).
3. Paris A, Lake L, Joseph A, et al. Nitrous oxide-induced subacute combined degeneration of the cord: diagnosis and treatment. *Pract Neurol*. 2023;23:222–8. DOI: [10.1136/pn-2022-003631](https://doi.org/10.1136/pn-2022-003631).
4. Sotirchos ES, Saidha S, Becker D. Neurological picture. Nitrous oxide-induced myelopathy with inverted V-sign on spinal MRI. *J Neurol Neurosurg Psychiatry*. 2012;83:915–6. DOI: [10.1136/jnnp-2012-303105](https://doi.org/10.1136/jnnp-2012-303105).
5. McCormick JP, Sharpe S, Crowley K, et al. Nitrous oxide-induced myeloneuropathy: an emerging public health issue. *Ir J Med Sci*. 2023;192:383–8. DOI: [10.1007/s11845-022-02945-8](https://doi.org/10.1007/s11845-022-02945-8).
6. Gao H, Li W, Ren J, Dong X, Ma Y, Zheng D. Clinical and MRI differences between patients with subacute combined degeneration of the spinal cord related vs. Unrelated to recreational nitrous oxide use: a retrospective study. *Front Neurol*. 2021;12:626174. DOI: [10.3389/fneur.2021.626174](https://doi.org/10.3389/fneur.2021.626174).