‘From highs to lows: a cautionary tale of nitrous oxide recreational use leading to sub-acute combined degeneration of the cord’

Ayman Osman1,*, Dalia Yousif2, Simon Hickman3, William Branagh1

1Acute Medicine Department, Bolton NHS Foundation Trust, Minerva Road, Bolton BL4 0JF, United Kingdom
2Acute Medicine Department, Sandwell and West Birmingham NHS Trust, West Bromwich, Birmingham B71 4HJ, United Kingdom
*Corresponding author. Sandwell and West Birmingham NHS Trust, West Bromwich, Birmingham, B71 4HJ, United Kingdom. E-mail: ayman.osman@nhs.net

Abstract

Background: Several causes lead to subacute combined degeneration (SACD) of the spinal cord, with nitrous oxide (N2O) inhalation rapidly emerging as the leading cause of functional Vitamin B12 deficiency [1]. Case Presentation: A 28-year-old man presented with numbness in the extremities and an unstable gait despite having a normal serum Vitamin B12 level. He also disclosed the recreational abuse of N2O. Magnetic Resonance Imaging (MRI) of the cervical spine revealed abnormal signals consistent with SACD. The patient’s condition gradually improved after treatment with high dose Vitamin B12. Given the increasing number of N2O-induced SACD cases, the potential for drug abuse requires vigilance from clinicians. Conclusion: Healthcare providers are urged to inquire about a patient’s history of N2O inhalation to prevent the missed diagnosis of SACD.

Keywords: nitrous oxide; subacute combined degeneration (SACD); vitamin B12; causes; outcomes

Introduction

Nitrous oxide (N2O), also known as laughing gas or sweet air, is an inhaled anesthetic that blocks N-methyl-D-aspartate (NMDA) receptors in the brain, resulting in pain relief and altered sensory perception [2]. However, N2O can also cause euphoria by increasing the release of dopamine into the brain, leading to feelings of pleasure and reward [3]. The recreational use of N2O is a growing public health concern [4]. Between 2017 and 2020, nitrous oxide use in 16 to 24-year-olds remained relatively stable at 8.7% and 8.8%, respectively [5]. Additionally, a 2020 report by the Independent Scientific Committee on Drugs found that nitrous oxide was the second most commonly used drug among young people in the UK after cannabis [6]. As of November 8, 2023, the Psychoactive Substances Act 2016 was updated to include nitrous oxide as an illegal substance, in addition to production, supply, import, and export [7].

Case report

Here we report the case of a 28-year-old Caucasian male taxi driver with no relevant medical history. The patient was not diabetic and had no history of antidiabetic medication or proton pump inhibitor use. He was a non-vegetarian with normal bowel habits and presented to our same day emergency care unit (SDEC) with bilateral lower limb weakness, moderate paraesthesia more pronounced in the lower extremities, and reduced power in his lower limbs. He had normal upper-limb motor strength (MRC 5/5) but exhibited reduced hand strength and power (4/5) on the right side and more pronounced weakness (3+/5) on the left side of his lower limbs. Additionally, he had diminished ankle and knee reflexes, impaired proprioception, vibration sensation bilaterally below the ankles, and a positive Romberg sign with difficulty in performing tandem gait. Further questioning revealed a history of recreational nitrous oxide (N2O) use, inhaling gas from large commercial cylinders up to three times daily for a few months prior to symptom onset. Laboratory investigations showed normal vitamin B12 levels of 193 ng/L (170–730), high homocysteine levels of 120 μmol/L – 1 (normal range 5–15), serum folate of 11.5 μg/L (3.9–26.8), and normal renal function and serum electrolytes (Table 1).

Magnetic resonance imaging (MRI) of the spinal cord showed T2 high signal alteration involving the cervical and thoracic cord (lateral corticospinal tracts and dorsal columns), consistent with subacute combined degeneration (SACD) of the cord (Figs 1 and 2). The abnormality was imperceptible in the T1 sequence and no DWI of the spine was obtained. However, brain MRI was unremarkable. The patient was initially treated with intramuscular hydroxocobalamin injections of 1 mg every two days for two weeks and received physiotherapy support. He was advised to immediately stop N2O use, as continued use may worsen the neurological function. Immediate medical interventions can result in full recovery; however, if treatment is delayed for more than one—two months, achieving complete recovery may become unattainable.
Table 1. Laboratory findings and reference values

<table>
<thead>
<tr>
<th>Test (serum)</th>
<th>Result</th>
<th>Ref. Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>5.6 mmol/L</td>
<td>3.5–6.0</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>193 ng/L</td>
<td>170–730</td>
</tr>
<tr>
<td>Homocysteine</td>
<td>120 μmol/L</td>
<td>5–15</td>
</tr>
<tr>
<td>Copper</td>
<td>17.6 umol/L</td>
<td>13–26</td>
</tr>
<tr>
<td>Folate</td>
<td>11.5 μg/L</td>
<td>3.9–26.8</td>
</tr>
<tr>
<td>Sodium</td>
<td>141 umol/L</td>
<td>133–146</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.3 mmol/L</td>
<td>3.5–5.5</td>
</tr>
<tr>
<td>Chloride</td>
<td>105 mmol/L</td>
<td>98–108</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>24 mmol/L</td>
<td>22–29</td>
</tr>
<tr>
<td>Urea</td>
<td>5.4 mmol/L</td>
<td>12.5–7.8</td>
</tr>
<tr>
<td>Creatinine</td>
<td>101 umol/L</td>
<td>59–104</td>
</tr>
</tbody>
</table>

Figure 1. Axial T2 weighted sequence of the thoracic spine demonstrating abnormal T2 hyperintensity in the dorsal columns.

Figure 2. Sagittal T2 weighted sequence of the cervical spine demonstrating abnormal T2 hyperintensity in the dorsal columns extending from C2-C7/T1.

Discussion

The abuse of N2O is hazardous, particularly because of its toxic effects on vitamin B12 metabolism, which can lead to subacute combined degeneration (SACD) of the cord. SACD affects the spinal cord and peripheral nerves, causing weakness in the extremities, impaired motor function, and abnormal MRI of the spinal cord. Although various factors can cause SACD, the toxic effects of N2O on vitamin B12 metabolism are among the most significant [8]. N2O inactivates cobalt ions in vitamin B12, which are required for the biological activity of this vitamin. This inactivation leads to functional vitamin B12 deficiency, which results in reduced recycling of homocysteine to methionine and prevents the methylation of myelin proteins. This causes demyelination within the central and peripheral nervous systems, leading to neurological symptoms such as SACD [9]. The severity of the toxic effects of N2O on vitamin B12 metabolism is influenced by several factors, including the duration and frequency of gas exposure, an individual’s nutritional status, and the presence of pre-existing conditions that affect vitamin B12 absorption [10].

N2O was linked to 28 deaths in England and Wales between 2008 and 2017, primarily because of asphyxia, which can occur when large amounts of N2O are. In addition to the risk of asphyxia, there is a risk of neurological symptoms associated with SACD, with an estimated 3.4% of N2O users experiencing neurological symptoms that are consistent with SACD. The diagnosis and treatment of N2O toxicity can be challenging because of the lack of a standardized regimen. However, new guidelines from the Association of British Neurologists Clinical Practice Guide have been published to aid the management of N2O-induced SACD. This suggests that intramuscular injections of 1 mg hydroxycobalamin should be administered once every two days for at least two weeks. Treatment should be initiated as soon as a diagnosis is suspected. Clinicians should be aware of the prevalence of N2O use, particularly among young adults, and should inquire about a patient’s history of N2O inhalation to avoid missed diagnoses. Recreational use of N2O is illegal in the UK but remains prevalent. Therefore, healthcare providers must be vigilant and aware of the potential risks and side effects associated with N2O abuse, and provide appropriate care and treatment for patients who present with symptoms of N2O-induced SACD. It is worth noting that SACD resulting from copper deficiency can have a very similar neurological presentation to N2O-induced SACD. Clinicians should consider copper deficiency as a potential cause of neurological symptoms and ensure that appropriate laboratory tests are ordered. This highlights the importance of taking a comprehensive approach to diagnosis and treatment, and considering multiple potential causes of neurological symptoms. Prospective studies and randomized trials are needed to assess recovery and treatment optimization (e.g. treatment length and adjuncts).

Conclusion

This case report highlights the potential risks associated with N2O abuse, including SACD. Clinicians should be aware of this phenomenon, which occurs more frequently in acute medical settings. Early management, prompt use of diagnostic tools, and multidisciplinary N2O-SACD teams can help to avoid missed diagnoses and complications. Patients with incomplete recovery or diagnostic uncertainty should be prioritized for follow-up in outpatient neurology clinics.

Acknowledgements

The staff at The Royal Bolton Hospital, Bolton Same Day Emergency Care Unit, are gratefully acknowledged for the patient’s care.

Conflict of interest

None declared.
Nitrous oxide recreational use caused cord degeneration

Funding
The study received no funding.

Ethical approval
None needed.

Consent
Written consent was obtained from the patient for publication.

Guarantor
A.O is nominated as the guarantor and has had full access to the data.

References