A Case Report of Subacute Degeneration of the Spinal Cord due to Chronic Nitrous Oxide Use with Review of the Literature

Babajide Adenekan
Specialist Registrar, Emergency Medicine, Department of Emergency Medicine, Wythenshawe Hospital, Manchester, United Kingdom

Debkumar Chowdhury
Specialist Registrar, Emergency Medicine, Department of Emergency Medicine, Wythenshawe Hospital, Manchester, United Kingdom

Abstract
Subacute degeneration of the spinal cord (SACD) is an acute medical emergency that requires early detection and management to limit worsening neurological deficit. With the increase in the usage of recreational drugs including nitrous oxide whippets, the incidence of the condition is noted to be rising. Currently it is the second most commonly used recreational drug used in the United Kingdom amongst 18–24-year-olds. Here we present a young gentleman with weakness and numbness following chronic usage of nitrous oxygen whippets.

Introduction
Subacute degeneration of the spinal cord (SACD) is a disease that affects the dorsal and lateral columns of the spinal column primarily due to demyelination. This often occurs in individuals who are deficient in Vitamin B12, causing neurological and haematological manifestations. Vitamin B12 is an active cofactor in the synthesis of deoxyribonucleic acid (DNA) and myelin [1]. Subacute combined degeneration of the spinal cord can be caused by inadequate oral intake of vitamin B12, poor absorption of vitamin B12, or by the use of medications such as metformin, proton pump inhibitors, and nitrous oxide [2]. There is a growing use of nitrous oxide as a recreational drug in the form of whippets [3]. Good clinical history and physical/neurological examination is vital in establishing the diagnosis. Rapid institution of treatment and involvement of relevant teams is also vital. Like most other acute presentation of complication of illicit drug use, the emergency department is the first point of call [4]. A high level of suspicion is needed among emergency physicians to ensure immediate treatment.

Case presentation
We present the case of a 28-year-old gentleman with progressively ascending numbness and weakness in the upper and lower limbs to the emergency department for the previous 2 days. However, due to the weakness in the lower limbs, there was associated with problems related to co-ordination. These symptoms were not preceded by any gastrointestinal or cardiorespiratory symptoms. He admitted to chronic use of Nitrous oxide whippets recreationally over the past one year with increasing use of same in the preceding four weeks prior to presentation. Examination of the upper limbs revealed normal tone, reduced power, more in the flexion than extension, absent reflexes globally in the upper limbs. Patient described reduced sensation in the hands. Proprioception was lost at the interphalangeal joints but maintained at the metacarpophalangeal joints. There was constant dysdiadochokinesia in the hands.

Lower limb examination revealed normal tone, reduced power in the flexion and extension, reduced sensation, proprioception lost in big toe but maintained at ankle. Impaired coordination was also noted. Rhomberg’s was positive. Our patient had an abnormal ataxic gait. He could not do heel to toe walk. Investigations revealed normal Vit B12 and folate. The potential differential diagnoses with the above symptoms

More Information
DOI: 10.59324/ejmhr.2024.2(2).21

Keywords:
SACD, neurological deficit, nitrous oxide whippets, chronic usage.

This work is licensed under a Creative Commons Attribution 4.0 International License. The license permits unrestricted use, distribution, and reproduction in any medium, on the condition that users give exact credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if they made any changes.
• Ascending idiopathic demyelinating polyneuropathy- whilst this is a potential diagnosis, MRI imaging would be pertinent to exclude this potential diagnosis. The absence of extensors plantars and hyper-reflexia would make this diagnosis less likely.
• Cerebrovascular accident- given the relatively young age and in the absence of cardiovascular risk factors, this diagnosis was noted to be unlikely given the clinical picture.
• Subacute demyelination of the spinal cord (SACD)- was noted to be most probable diagnosis given the history of recurrent use of nitrous oxide whippets

Further discussion with Neurology team alluded to concerns of SACD due to nitrous use rather than Guillain Barre syndrome. He was commenced on I/M Hydroxocobalamin and admitted for MRI whole spine. This later showed some demyelination in the posterior column of the spinal cord.

**Imaging in SACD**

Magnetic Resonance Imaging (MRI) is the gold standard imaging modality in the diagnosis of SACD. The typical radiological appearance of dorsal spinal cord hypointensity on T1-weighted images and hyperintensity on the T2-weighted images which highlight the ensuing demyelination [3].

![Image 1: Increased Intensity in Spinal Cord in Saggital Section](image1)

![Image 2: Normal Appearance of Spinal Cord](image2)

![Image 3: Axial Images T2 Hyperintensities Seen Bilaterally in the Dorsal Column](image3)
On sagittal images (Image 1), there is a minimal widening of the affected spinal cord with increased signal intensity on T2W images for a variable segment at the posterior aspect. On axial images (Image 2) paired T2 hyperintensities are seen bilaterally as “inverted V” or “inverted rabbit ears” patterns in the expected anatomic location of the dorsal columns as seen [2,3].

As highlighted the changes in appearance of the MRI spine in patients with SACD (our patient) (Image 1) in comparison with an essential normal MRI spine (Image 2).

Discussion

The mechanism of subacute combined degeneration of the spinal cord due to chronic nitrous oxide use is due to functional B12 deficiency. Nitrous oxide causes oxidation of cobalt ion of Vitamin B12 hence making it unavailable as a co-enzyme in the synthesis of myelin hence subacute combined degeneration [2]. With an increasing incidence of recreational drug use, cases similar to this will become more prevalent. It is important to be able to differentiate the aetiology of the clinical symptoms as the management often differs. The history of chronic nitrous use was vital in channeling the appropriate treatment as compared to other infectious causes. It is essential that a multi-disciplinary approach is undertaken in a timely fashion to ensure that further neuronal damage is avoided. There also needs to be emphasis on lifestyle modifications to prevent further damage. Vitamin B12 deficiency of unclear aetiology should raise suspicion for nitrous oxide toxicity as early initiation of replacement therapy with vitamin B12 can improve neurological function [2].

Investigations

In cases where SACD is suspected, biochemical testing including testing for Vitamin B12 and Methylmalonic acid (MMA). If the Vitamin B12 levels are noted to low, there is less use of measuring the MMA level. In addition, the homocysteine levels can be measured. Although the sensitivity of Vitamin B12 levels can be low, in the majority of nitrous oxide SACD- have both levels elevated [5].

In terms of imaging, MRI Cervical and thoracic spine are the gold standard mode of investigations. In a select number of cases nerve conduction studies and electromyography can be carried out especially if the diagnosis is not clear.

Treatment of SACD

The mainstay treatment for SACD is with Vitamin B12 supplementation, the delivery depends on the severity of symptoms, the underlying aetiology, availability and patient preferences amongst other aspects [6]. Timely treatment needs to be given to limit deterioration in neurological function this includes development of bladder incontinence.

Characteristics that are associated with good prognostic outcome [7,8].

- Age < 50 years
- Short disease course
- Absence of sensory deficits
- Absence of Romberg’s sign
- Absence of Babinski’s signs
- Involvement of ≤ 7 spinal segments on MRI
- Presence of spinal cord oedema
- Contrast enhancement of the spine
- Absence of spinal cord atrophy

Our patient had several of the above good prognostic factors.
Nitrous oxide and SACD
Due to the increasing incidence of nitrous oxide related SACD through its recreational use, Paris et al in 2023 have suggested an algorithmic pathway highlighted below (See Figure 4) to highlight the potential treatment strategies [9]. The symptoms from nitrous oxide related SACD are similar to standard SACD symptoms [6]. Despite of a rising incidence of nitrous oxide related SACD, the diagnosis of this condition can be challenging and thereby necessitates a multi-disciplinary approach from the outset. The admitting clinician needs to be aware of conditions such as Crohn’s disease, previous gastric resection that predispose patients to low serum B12 levels that which would lead to development of SACD type symptoms [9].

Pathway for patients with suspected N2O-SACD. In the Emergency Department, the focus is on immediate treatment with I.M. hydroxocobalamin, time-critical.

Conclusion
As in our patient, the Emergency department might be the first presentation for patients with neurological manifestations of SACD due to chronic nitrous use. Recognition of this pattern from the history and physical examination should trigger immediate institution of treatment and liaison with specialist services (neurologist).

Inpatient admission is also required for patient with severity of symptoms for further investigations and management.

Patient education is important as to the severity of the diagnosis and help offered with drugs and alcohol services to help stop the continuous use of nitrous oxide to ensure treatment success.

Acknowledgement
The authors would like to sincerely thank the patient for kindly allowing to share his clinical presentation for the wider learning.

Ethical Statement
The authors have identified no ethical concerns in undertaking this article.

Conflict of Interest
There are no conflicts of interest highlighted by the authors.

References