Nitrous oxide myelopathy posing as spinal cord injury

Case report

GEORGE M. GHOBRIAL, M.D., RICHARD DALYAI, M.D., ADAM E. FLANDERS, M.D., AND JAMES HARROP, M.D.

Departments of Neurological Surgery and Neuroradiology, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania

The authors describe a patient who presented with acute tetraparesis and a proposed acute traumatic spinal cord injury that was the result of nitrous oxide myelopathy. This 19-year-old man sustained a traumatic fall off a 6-ft high wall. His examination was consistent with a central cord syndrome with the addition of dorsal column impairment. Cervical MRI demonstrated an isolated dorsal column signal that was suggestive of a nontraumatic etiology. The patient’s symptoms resolved entirely over the course of 48 hours.

Nitrous oxide abuse is increasing in prevalence. Its toxic side effects can mask vitamin B12 and folate deficiency and central cord syndrome. The patient’s history and radiographic presentation are key to establishing a diagnosis. (http://thejns.org/doi/abs/10.3171/2012.2.SPINE11532)

**Key Words**
- nitrous oxide
- spinal cord injury
- myelopathy
- central cord
- spine

**Abbreviations used in this paper:** NASCIS II = Second National Acute Spinal Cord Injury Study; SCI = spinal cord injury.

Central cord syndrome is a common presentation after cervical hyperextension injuries. Nitrous oxide is used as an anesthetic agent; however, it is also available as a propellant in pressurized containers such as whipped cream. It is frequently abused for its euphoric and anesthetic effects. The effects of nitrous oxide on the spinal cord have been reported in the literature, however, the unique and insidious presentation after cervical trauma has not been documented. Since the abuse of nitrous oxide is increasing in prevalence, this may be an important mechanism for SCIs and should be considered in the differential diagnosis in the acute care setting.

**Case Report**

**History and Presentation.** This 19-year-old man presented with complaints of progressive numbness and weakness in all extremities. One day earlier he had fallen over a 6-ft wall onto his back. The patient denied back pain and bowel or bladder incontinence. Additionally, he denied any relevant medical or surgical history. Over the course of 24 hours, his symptoms progressed to an inability to ambulate and numbness in his distal extremities. The patient stated that he occasionally abused oxycodone, alcohol, and “huffed” nitrous oxide canisters several times per week. Moreover, he stated he would huff as much as a 20-lb canister of nitrous oxide in 1 sitting.

**Examination.** On initial assessment, the patient had minimal neck pain, was hemodynamically stable, and had a Glasgow Coma Scale score of 15. He was alert and oriented, without apparent cognitive or language deficits. On motor examination, however, proximal weakness of 3/5 in the deltoids bilaterally and distally of 2/5 was found. In the lower extremities, the iliofossus muscle groups were weak (4–5), and the distal muscle groups were 3/5. Hyperreflexia was noted in the bilateral lower extremities. Sensation to light touch and pinprick was absent in the distal extremities as well as vibration and proprioception. The sensation loss was not dermatomal. The remainder of the neurological examination was insignificant.
Due to the history of nitrous oxide abuse, vitamin B12 and folate levels were evaluated, and the values were within the reference ranges. An MRI scan of the cervical spine did not demonstrate any acute traumatic signs such as bone fracture, ligamentous injury, or subluxation. However, the spinal cord parenchyma had significant T-2 signal abnormalities in the posterior columns from C-2 to C-7 (Fig. 1).

Treatment and Posttreatment Course. Approximately 8 hours after the patient fell, intravenous methylprednisolone was started at an outside institution according to the NASCIS II criteria, and, since the patient was making progressive improvements, the steroid therapy was maintained. Thirty-six hours after the injury, the patient noted complete resolution of his symptoms. The following day, the patient was discharged home.

Discussion

The National Institute on Drug Abuse has reported a significant increase in the number of nitrous oxide abuse cases: from 1.5 to 18 million across the span of 2000–2001. Similarly, there has been a decrease in the use of this drug as an anesthetic agent. The biochemical effects of nitrous oxide as an anesthetic agent have long been studied but are not entirely understood. Its effects on the spinal cord have been recognized since 1959 by Randt and Collins in laboratory studies in cats.

Nitrous oxide abuse tends to present clinically with a predominant effect on the dorsal column. Vitamin B12 deficiency and folate deficiency can exacerbate this effect. This effect has been hypothesized to occur due to the oxidizing effect of nitrous oxide on the cobalt group of cobalamin. In the presence of nitrous oxide, the covalence of cobalt will change from monovalent to bivalent, which then reacts to irreversibly inactivate vitamin B12. The formation of tetrahydrofolate is halted by the further inhibition of methionine synthase, which requires vitamin B12. Tetrahydrofolate is vital in DNA synthesis, cell division, and ultimately myelination in the spinal cord. This biochemical pathway is hypothesized to be most vital in the posterior columns.

Regarding evaluation, there are no specific tests to document nitrous oxide exposure. A detailed history is the basis of diagnosis of nitrous oxide myelopathy. Vitamin B12 deficiency has been shown to affect vision, hearing, and sensory and motor pathways on evoked studies. Even though the levels of vitamin B12 and folate might be in the reference range, nitrous oxide abuse cannot be ruled out.

The resolution of clinical symptoms in this patient was dramatic and thus atypical for patients with SCI. Likewise, a central cord SCI pattern of injury is atypical in nitrous oxide myelopathy. One explanation is that a central cord injury did occur in the setting of nitrous oxide intoxication, resulting in a superimposed posterior column myelopathy. Regarding the imaging findings, the strong hyperintensity of the posterior columns on T2-weighted MRI could have obscured the otherwise faint central cord signal that might have been noticed in the absence of posterior column signal change. Nitrous oxide may also manifest weakness due to deficits in proprioception and sensation. This finding in previous literature could explain the rapid recovery that would not typically be observed in central cord myelopathy.

Nitric oxide, a rapid and interchangeable form of nitrous oxide in the body, is implicated in the pathophysiology of secondary injury in spinal cord trauma. Liu and associates demonstrated a rapid increase in nitric oxide within 60 minutes of injury. Further increases in nitric oxide were seen in the first 72 hours. In CNS inflammation, monocytes and macrophages are the chief supply of cells releasing nitric oxide. In SCI, nitric oxide synthase, a required enzyme in nitric oxide production, is seen in macrophages, neurons, astrocytes, and oligodendrocytes. The oxidative properties of peroxynitrite, a nitric oxide–like compound formed readily in vitro from nitrous oxide, may accelerate local cell destruction. Peroxynitrite can damage tissue in various ways, all from radical formation and tissue destruction. Studies of pretreatment with nitric oxide synthase inhibitors, such as nitro-L-arginine, in the rat have been shown to limit the effects of SCI through comparisons of histological cord sections when compared with controls.

The duration of effect of nitrous oxide is another consideration. An inhalational anesthetic, nitrous oxide is highly lipid soluble, traversing the blood-brain barrier easily with a brief duration of onset and clearing from the body by still unknown mechanisms in a matter of hours. Diffusion into lipid-soluble tissues and then further breakdown into oxidative byproducts is the most likely candidate for clearance.

The use of steroids in SCI is highly controversial. Given the concern for an additional pathology contributing to the dramatic motor and sensory deficits, Solu-Medrol was given in hope of reducing neurological injury without a clear cause. Steroids were given for concerns of injury due to trauma, and the administration was in accordance with the NASCIS II guidelines. The mechanism for the mitigation of symptoms in SCI by steroids is still not completely understood. One credible theory is that steroids limit lipid peroxidation in secondary injury. Also, steroids are thought to have a decreased migration of leukocytes to damaged tissue, leading to a lower population of cells containing nitric oxide synthase, further limiting cell destruct-

Fig. 1. Axial and sagittal T2-weighted MRI study of the cervical spine demonstrating hyperintensity predominantly in the posterior cervical columns extending into the upper thoracic spine.
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12. Krajewski W, Kucharska M, Pilacik B, Fobker M, Stetkiewicz M: One would expect the symptoms to have a short half-life.

Conclusions

We present a case of nitrous oxide myelopathy referred to our SCI center. The patient’s history and radiographic presentation are key to establishing a diagnosis.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Harrop, Ghobrial. Analysis and interpretation of data: Ghobrial, Flanders. Drafting the article: Harrop, Ghobrial. Critical revision of the article: all authors. Reviewed submitted version of manuscript: all authors. Approved final version of the manuscript on behalf of all authors: Harrop. Administrative/technical/material support: Ghobrial. Study supervision: Ghobrial.

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Address correspondence to: James Harrop, M.D., Department of Neurological Surgery, Thomas Jefferson University Hospital, 909 Walnut Street, 2nd Floor, Philadelphia, Pennsylvania 19107. email: james.harrop@jefferson.edu.