Delayed neurologic sequelae following anoxic-anoxia related to nitrous oxide by pipeline mix-up during anesthesia

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ABSTRACT

Introduction: Pipeline mix-up is a rare situation in anesthesia and may engender hypoxic event with severe complications. Delayed neurologic sequelae may appear after anoxic and or ischemic event. We report a case of delayed neurologic sequelae following prolonged anoxia related to nitrous oxide after pipeline mix-up in a newly operation room. Case Report: A 36-year-old female, the first patient admitted for abdominoplasty under general anesthesia in a newly opened operating room. The patient was exposed to hypoxia-anoxia for several minutes due to crossing of oxygen and nitrous oxide pipelines. Nitrous oxide became the drive gas on anesthesia machine. The diagnosis of pipeline mix-up was unthinkable and delayed because of oxygen analyzer on anesthesia machine was non functional. The gas analyzer was very useful to suspect the pipeline mix-up when it showed 99% of inhaled fraction of nitrous oxide while anesthesia machine was set to deliver 100% oxygen. After complete recovery, she presented at the second postoperative day a paraparesis and dysarthria. Nitrous oxide myelopathy was eliminated because of normal vitamin B12 and homocysteine and delayed neurological sequelae (DNS) were retained. The patient has fully recovered under supratherapeutic dose of vitamin B12 therapy. Conclusion: In a newly opened operation room, gas pipelines should be verified before beginning any anesthetic procedure. Our finding suggests that vitamin B12 may have a place in the treatment of delayed neurological sequelae.

Keywords: Delayed neurologic sequelae, General anesthesia, Nitrous oxide, Pipeline mic-up, Vitamin B12

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INTRODUCTION

Neurologic deficits following acute anoxic insults are well recognized. However, severe neurologic dysfunction may occur in patients sometime after they recovered from initial hypoxia, generalized ischemia which was caused by severe hypotension, or both [1, 2]. Delayed neurologic sequelae (DNS) is usually caused by carbon monoxide (CO) poisoning [1, 2]. DNS induced by other types of anoxia and ischemia has rarely been reported, including complications of surgery and anesthesia, respiratory...
depression, cyanosis, shock [1, 2], drug over dosage [3] and strangulation [4]. The present case illustrates delayed neurologic sequelae following prolonged anoxia related to nitrous oxide (N\textsubscript{2}O) who exhibited a rapid recovery under vitamin B\textsubscript{12} (cobalamin) therapy.

**CASE REPORT**

A 36-year-old female, ASA 1, weighing 76 kg for 1.68 m (BMI = 30 kg/m\textsuperscript{2}), admitted to the operating room for abdominoplasty. The operation was planned in a newly opened operating room and the patient was the first one to be admitted in. After standard monitoring, a 20 Gauge venous route was taken. Preoxygenation was provided by anesthesia machine: Dräger Fabius\textsubscript{®} Plus (Figure 1) which was not equipped by gas analyzer and whose oxygen analyzer was not functional due to its expiration, oxygen flow meter was opened to deliver 10 liters of oxygen. Anesthetic induction was achieved by propofol (2 mg/kg), fentanyl (3 μg/kg) and mask ventilation was initiated after curarization by rocuronium (0.6 mg/kg). Four minutes after the induction when mask ventilation, cyanosis of the extremities and desaturation were observed and the patient was rapidly intubated and connected to the anesthesia machine in controlled ventilation with 50% mixture of each O\textsubscript{2} and N\textsubscript{2}O. That allowed an improvement of the pulse oximetry values. Maintenance of anesthesia was provided by isoflurane 0.9%. Chest auscultation and insufflation pressures were normal. Ten minutes after of the onset of the procedure, pulse oximetry (Sp\textsubscript{O}2) decreased to 92%, oxygen flow was increased but Sp\textsubscript{O}2 values continued to decline. The respiratory auscultation and parameters was always without abnormalities. Oxygen flow was opened to 10 l/min and N\textsubscript{2}O flow stopped without improvement of the situation, and pulse oximetry values continue decreasing showing sometimes 0%, hypotension and reactive semi-mydriasis appeared.

After calling for help, we decided to change to ventilator machine, and we brought another one, same Dräger Fabius\textsubscript{®} Plus which was equipped by external gas analyzer Dräger Vamos monitoring capnography (CO\textsubscript{2}), Halogens and N\textsubscript{2}O but not the O\textsubscript{2} (Figure 2). Once the gas analyzer started it showed signs of low cardiac output with deep hypocapnia to 14 mmHg and an expired fraction of N\textsubscript{2}O to 99% while the patient was connected to the anesthesia machine set to deliver 100% oxygen. Error of source installation was confirmed by following through gas pipelines, oxygen pipeline of the respiratory was connected to wall oxygen source but this one was relied to N\textsubscript{2}O source, the colors of such pipelines was confounded by the installer of the new operating room. The duration of surgery was one hour. The awakening was restless and the patient was sedated for 24 hours by midazolam-fentanyl at the ICU. Non contrast cerebral scan was without anomalies. The patient was extubated the next day without neurological deficit. At the night of the second postoperative day, the patient presented symmetrical paresthesia on the feet, ascending to the trunk, chest and both arms. This was followed by weakness and clumsiness of all limbs, loss of their use and dysarthria, mental status was normal. Before any specific therapy, vitamin B\textsubscript{12} and homocysteine (HC) was tested. Methylmalonic acid
and that the corresponding radiological findings may be delayed even later [10]. The syndrome of delayed neurologic deterioration with cerebral demyelination has been reported in the literature several times as occurring in the setting of carbon monoxide poisoning [10]. DNS unrelated to CO are reported in the literature, caused by hemorrhagic shock, prolonged hypoxia and hypotension, anoxic anoxia, cardiac arrest, drug overdose and in other situations that lead to severe hypoxia [3, 4, 10].

DNS classically conforms to one of two general categories of clinical presentation: parkinsonism or akinetic-mutism [11]. In addition to characteristic parkinsonian motor features (masked facies, rigidity, short steppy gait, tremor) dystonic posturing, agitation, apathy, hallucinations, or odd behaviors may also be present, extremely slow verbal responses with varying degrees of impaired cognition or emotional lability [12].

Akinetic-mute patients were profoundly apathetic and developed functional bowel and bladder incontinence, minimal primitive responses to pain, and pathologic laughter or crying. A near clinical presentation of our case report have been reported, DNS with severe symptoms, including quadriaparesis and near-blindness, after hemorrhagic shock or prolonged respiratory arrest during complications of anesthesia [13].

The fact that hypoxic-ischemic damage to the cerebral white matter occurs in a variety of settings other than carbon monoxide intoxication supports the contention that this type of leukoencephalopathy does not depend on the unique properties of a specific intoxicant [10].

Heckmann et al. [14] hypothesize that the delay is caused by the selective necrosis of myelin-producing glia cells in the border zones of the white matter. The clinical consequences would be delayed due to the long half-life of myelin (2.5–8.7 days) as the necrosis of the myelin sheaths is known to follow the cell necrosis after 10–14 days [2]. However, the rarity of this condition seems to suggest unidentified individual susceptibilities to hypoxic neuronal injury.

There is no specific therapy or prophylaxis for DNS. Steroids, asprin, and cerebral vasodilators were used in attempts to prevent and treat delayed neurologic sequelae, but they were reported to be ineffective [15]. Therefore, it is safer to maintain patients with acute anoxia, acute severe hypotension or both on initial prolonged bed rest, in addition to ensuring rapid restoration of their oxygenation and circulation [13].

The prognosis of post-hypoxic delayed demyelination syndrome is quite good. Choi reported 75% full recovery in one year [13], and Shillito and Drinker reported 50% full recovery within two years [16]. Wainapel et al. reported a dramatic functional recovery 3.5 months after admission for a man who developed severe spastic quadriplegia from a mixed drug overdose-induced post-hypoxic leukoencephalopathy [17].

Reported spontaneous DNS recovery was taking many months to years after the anoxic event. In our case, we noted a rapid recovery under vitamin B₁2 therapy, initially...
introduced for suspecting N₂O toxicity and maintained for patient good response. That is suggesting that vitamin B₁₂ may have a place in the treatment of DNS.

Supra-therapeutic doses of cobalamin may regulate the inflammatory response and its resolution in which transcobalamins play a proven role. Such regulation may involve several mechanisms including hormone-like regulation of Tumor Necrosis Factor Alpha through reduction of excess nitric oxide, quenching of nitric oxide radicals and reactive oxygen species, the promotion of acetylcholine synthesis, central to the neuroimmune cholinergic anti-inflammatory pathway, the promotion of oxidative phosphorylation and optimal bacteriostasis and phagocytosis [18].

The proposed dose was 4/5 g intravenous of hydroxocobalamin given on up to three to five consecutive days, routinely used in the ICU as a treatment for cyanide poisoning, followed by a lower maintenance dose, dependent on patient response [18]. Hydroxocobalamin (Cyanokit) is frequently used in the smoke inhalation setting. While carbon monoxide was not our patient’s mechanism of injury, that also fits the patient’s time course, and the treatment was somewhat similar in that it included supratherapeutic doses of cobalamins.

Hypoxic O₂ pipeline condition (gas mix-up) where N₂O, instead of O₂, was inadvertently supplied to the O₂ pipeline occurred in The Hospital of St. Raphael in New Haven, in January 2002 and killed two patients. Even though an anesthesia machine was not involved in the New Haven cases, hypoxic “oxygen” pipeline algorithm was proposed and is applicable to anesthesia machines [19].

When O₂ analyzer is being used: hypoxic O₂ pipeline condition is suspected because of a low inhaled fraction of O₂ (FiO₂) alarm and/or reading that does not match the set FiO₂.

If an O₂ analyzer is not being used there will be no low FiO₂ warning. The first indication of trouble will most likely be a low Spo₂ alarm that is a late and non-specific warning, evoking many possible causes to be ruled out before a hypoxic O₂ pipeline algorithm as outlined above can be initiated with certainty [19].

In our case report, O₂ analyzer on the anesthesia machine was not functional because of unchanged outdated oxygen sensor capsule. The gas analyzer was very useful to suspect the pipeline mix-up when it showed 99% of inhaled fraction of N₂O while anesthesia machine was set to deliver 100% oxygen. In a newly opened operation room, gas pipelines should be verified before beginning any anesthetic procedure and the anesthesia machine should be fully equipped and all its functions correctly set in order to prevent such complications and to improve security during anesthesia.

CONCLUSION

With development of anesthesia, pipeline mix-up became a rare situation and should be present in mind in front of the diagnosis of post-hypoxic delayed demyelination syndrome should not be missed because its outcome is relatively good. Our finding suggests that early administration of suprathereapeutic vitamin B₁₂ may have a place in the treatment of DNS, this conclusion need further investigation and more large trials.

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Author Contributions
Jaouad Laoutid – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
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Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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