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Case Report

NITROUS OXIDE ANAESTHESIA INDUCED VITAMIN B12 DEFICIENCY PRESENTING AS ACUTE MYELONEUROPATHY.

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Abstract

Nitrous oxide (N2O) can precipitate vitamin B12 (cyanocobalamin) deficiency in susceptible individuals with borderline vitamin stores. We present a case of an alcohol-dependent patient who developed acute neurological symptoms following N2O anesthesia for mandibular surgery. Timely recognition and treatment resulted in complete neurological recovery. N2O induced acute neurological symptoms must be kept as an important differential diagnosis in at-risk patients who undergo surgery under general anesthesia.

Keywords: Nitrous oxide, Anesthesia, Vitamin B12 deficiency, Myeloneuropathy, Alcohol.

Introduction

Nitrous oxide (N2O), first synthesized by Joseph Priestley in 1772, and used as an inhaled anesthetic by Horace Wells in 1844 revolutionized the practice of surgery. Though N2O was long believed to have a benign effect on the human body, it was Lassen et al. who first reported an association with pernicious anemia. [1] During this time it was observed that N2O was associated with neurological symptoms in the context of occupational exposure and abuse. [2, 3] Later, reports of subacute combined degeneration of the spine following routine N2O anesthesia confirmed the neurotoxic potential of this agent. [4] N2O has been shown to inactivate vitamin B12, which in normal adults is replaced quickly before clinical symptoms occur. However, in people with marginal vitamin B12 stores, exposure to N2O leads to neuropathological symptoms (anesthesia paresthetica) which could progress to morbid and irreversible neurological illness. [5]

Case Report

LP, a 54-year-old married male was admitted to the casualty for 3 episodes of generalized seizures and confusional state after discontinuation of heavy alcohol use 4 days ago. The patient was stabilized and given supportive treatment by the

emergency medical team. Investigations revealed anemia (Hemoglobin=11.4g/dl) of normocytic normochromic type, elevated liver function tests (total bilirubin 1.6 mg/dl direct bilirubin 0.5 mg/dl AST: 156 mg/dl ALT 72 mg/dl ALP 149 mg/dl GGT 315 mg/dl), serology for HIV and Hepatitis B and C were negative, serum electrolytes were within normal limits, renal parameters urea and creatinine were normal, fasting sugar 83.3 mg/dl. Plain CT scan brain revealed no abnormality. No residual neurological deficit was observed. X-Ray of the mandible was performed as the patient sustained a fall during one of the seizures and hurt his jaw which revealed a parasynthesis fracture (open) of the left mandible.

Psychiatric consultation by our liaison team established a diagnosis of alcohol dependence syndrome, severe withdrawal state with seizures. The patient was treated with a multivitamin injection containing thiamine (100 mg bid), lorazepam (12 mg in divided doses) and haloperidol (5 mg) to control his withdrawal. Over the course of the first week of stay patient's withdrawal state improved.

Mandibular ORIF surgery was performed under GA through the extra-oral route with plate fixation to repair the jaw fracture sustained during the seizure. On the 1st POD, the patient developed severe paraesthesia of the lower limbs (burning, tingling, and numbness) along with severe ataxia that prevented mobilization even with support. There was also evidence of postural hypotension. On neurological examination, there was no rigidity, very mild symmetrical weakness in the extremities, with normal deep tendon reflexes, and flexor plantar. ECG, liver function tests and levels of serum electrolytes were within normal limits. Intravenous normal saline was started while the underlying cause was being investigated. However, the patient's giddiness and postural hypotension failed to improve with IV fluids.

The patient was on broad-spectrum antibiotics (amoxycillin+clavulanate, metronidazole), acamprosate (333 mg 2 tds), pantoprazole and a multivitamin combination containing 100 mg benfotiamine, 100 mg alpha lipoic acid, mecobalamin 0.5 mg, pyridoxine 50 mg at that time. Possible causes of like acute Stroke, congestive heart failure, myocardial infarction, parkinsonism, dehydration, blood loss, autonomic failure, venous insufficiency were ruled out on clinical examination. There was no evidence of sepsis, gastroenteritis, neurosyphilis, Guillain Barre syndrome, multiple system atrophy, multiple sclerosis, cardiac arrhythmias, or any medications (like anticholinergics, antihypertensives, antidepressants, neuroleptics) from the history and investigations.

The acute onset of the symptoms after surgery prompted us to investigate the association between any surgical event and the symptoms. A review of the literature yielded a possible suspect, acute vitamin B12 deficiency precipitated by N2O anesthesia. Our patient was on a semisolid vegetarian diet since admission due to difficulty in mastication. Since he was a chronic and heavy alcohol user with reduced dietary intake prior to admission the possibility of reduced vitamin stores could be presumed. Though vitamin B12 stores in the liver can typically last months, in the face of chronic alcoholism and poor diet these stores can become critical. Even though our patient was on 1 mg mecobalamin maintenance medication orally, N2O inhalation during the anesthesia could have theoretically precipitated acute vitamin B12 deficiency. Due to the non-availability of vitamin B12 estimation at our center, we decided to test our hypothesis by administration of parenteral (IV) mecobalamin 3000 mcg. Blood pressure

recordings, paraesthesia, and ataxia were assessed every 2 hours. After 6 hours the patient reported dramatic improvement in paresthesias and ataxia was able to walk unaided. He was maintained on parenteral mecobalamin (3000 mcg) for the remainder of the hospital stay and was discharged a week later without any neurological sequelae.

Discussion

Several investigators have reported the development of myelopathy 2 to 6 weeks after N2O anesthesia induced for a variety of surgical procedures. [6-8] Biochemically nitrous oxide irreversibly oxidizes the cobalt ion of cobalamin (vitamin B12) from the (1) 1 to the (1) 3 valence state. Oxidation of the cobalt ion by N2O prevents methylcobalamin from acting as a co-enzyme in the production of methionine and subsequently S-adenosylmethionine, which is necessary for methylation of myelin sheath phospholipids. The result is decreased myelin formation which leads to neurological sequelae. [9]

In a comprehensive review of 369 patients with vitamin B12 deficiency, Healton et al [10] reported neurological presentation in about half of the cases compared to non-neurological presentations. Our patient developed both myelopathic (paresthesia) and autonomic (postural hypotension) symptoms of B12 deficiency. It is interesting that all cases that have been reported in the literature so far had developed symptoms at least 2 weeks after the exposure to N2O. In our case, the patient exhibited neurological signs within 48 hours after the exposure. It can be speculated that our patient did not display the classical signs of B12 deficiency like impaired proprioception, weakness, extensor plantar, clonus or Romberg's sign due to the acute onset of symptoms and early intervention (parenteral vitamin B12 was administered within 24 hours of symptom onset). Nevertheless, the dramatic improvement and complete remission of symptoms within a day of B12 replacement as reported by previous studies add credence to our diagnosis despite nonavailability of serum B12 estimation.

Conclusion

To our knowledge, this is the only report of N2O induced acute B12 deficiency presenting with acute neurological symptoms in the setting of alcoholism. We submit that the inactivation of B12 by N2O is no more a theoretical concept but has practical implications, especially for anesthetists and surgeons. They should be aware of this problem and avoid the use of N2O anesthesia in patients with suspected vitamin B12 deficiency. We suggest that mean corpuscular volume (MCV) be routinely performed and any increase, especially in the setting of malnourishment, chronic alcohol use, previous gastric/intestinal resection should prompt serum vitamin B12 estimation (>150 pmol/L). Even borderline levels should be treated with parenteral supplementation before and after surgery if N2O is to be used as an anesthetic agent in this population to avoid serious morbidity and mortality.

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