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CASE REPORT

Acute pancreatitis after nitrous oxide abuse: A case report

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Abstract

The recreational use of nitrous oxide (N_2O) is sharply increasing among young adults. N_2O abuse can cause serious complications. However, the association between acute pancreatitis and N_2O is rarely reported. Here we report a case of a young and previously healthy female with widespread cutaneous lesions, neurologic symptoms, and abdominal pain. Acute pancreatitis was the patient's primary diagnosis when she was admitted to the gastroenterology unit. We added the diagnosis of N_2O intoxication after an additional inquiry into the patient's personal history revealed that she had abused N_2O for 1 month. With the application of mecobalamin and other symptomatic treatments, the symptoms and laboratory indexes improved gradually. In this case, we highlight that acute pancreatitis may be a rare complication induced by N_2O.

Introduction

Nitrous oxide (N_2O) has been presented as an inhalation anesthetic agent for nearly 180 years and has increasingly been used for recreational purposes due to its euphoriant property.[1] According to the Global Drug Survey 2021, the use of N_2O across over 30 000 respondents was 9.7%.[2] The prevalence of recreational N_2O use has led to a sharp rise in N_2O-related toxicity cases. The clinical manifestations vary with the different systems implicated. Neurologic complications are the main clinical findings in the reported cases.[3,4] Less common clinical findings include hematologic complications, psychiatric symptoms, thrombus, skin hyperpigmentation, myocardial injury, and others.[4–6] Here, we share an uncommon case of acute pancreatitis associated with N_2O abuse that has not yet been reported.

Case report. A 22-year-old female was transferred to the gastroenterology department from the emergency department, complaining of abdominal pain for 2 days, with cutaneous lesions for 1 month and neurologic symptoms for 4 days. The patient reported alcohol consumption 4 days earlier and eating unidentified food which she found difficult to recall.

Physical examination revealed middle epigastric tenderness without rebound pain and nonspecific skin lesions over the limbs and abdomen (Figs. 1 and S1–S3, Supporting information). Neurologic examination showed that the muscle strength of all limbs had declined, especially the lower limbs. Sensory examination revealed hypoesthesia in the limbs.

Initial laboratory tests showed elevated lipase (279 IU/L), amylase (244 IU/L), and C-reactive protein (67.10 mg/L). The results of liver function tests were also abnormal, with elevations of transaminase (alanine aminotransferase 123 IU/L, aspartate aminotransferase 122 IU/L) and bilirubin (total bilirubin 57.5 μmol/L, direct bilirubin 33.8 μmol/L). Platelet, white blood cell, albumin, creatinine, blood lipid, electrolyte, coagulation index, and procalcitonin levels were within the normal range. Serum ethanol test

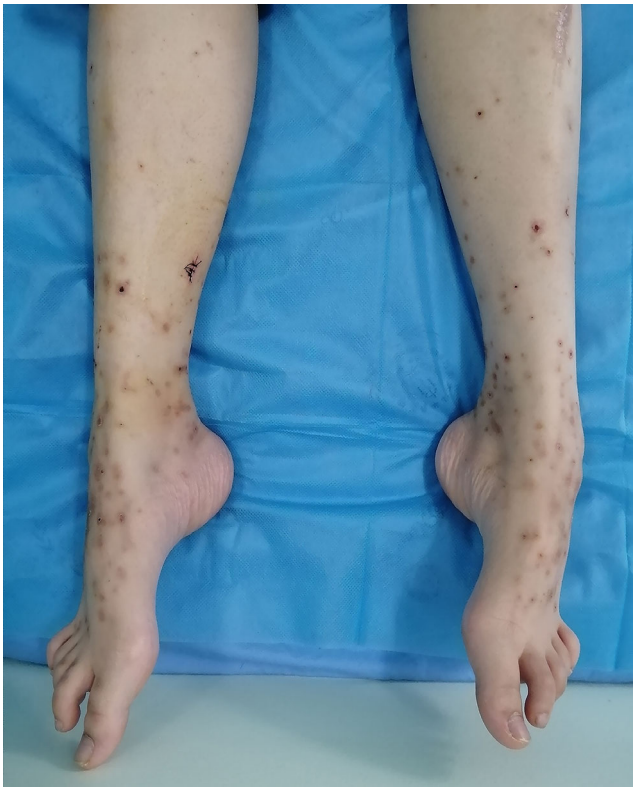

Figure 1 Cutaneous lesions in the lower limbs.

and toxicology screen were negative. Moreover, cerebrospinal fluid tests had unremarkable results. The patient was diagnosed with suspected acute pancreatitis and then admitted to the gastroenterology department. We performed repeated lipase and amylase analysis and abdominal imaging. Higher levels of lipase and amylase were found (489 and 262 IU/L, respectively), and computerized tomography (CT) presented mild pancreatitis (Fig. 2). The above results confirmed diagnoses of mild acute pancreatitis and abnormal liver function.

To determine the etiology, we added tests of TORCH (toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus), galactomannan (GM), (1–3)-β-D glucan, anti-streptolysin O (ASO), Epstein–Barr virus, human immunodeficiency virus, hepatitis viruses, immunoglobulin, α-1 antitrypsin, autoimmune profile, IgG4, tumor markers, autoimmune liver disease panel, ceruloplasmin, Kayser–Fleischer ring, and imaging of the central nervous system, but all found no significant abnormalities. Electromyography and skin biopsy were also performed. Electromyography showed peripheral neuropathy in the extremities involving both motor and sensory fibers. Skin biopsy revealed chronic skin inflammation. The above positive results were consistent with the patient's symptoms, but the exact etiology remained unclear. Then, the possibility of intoxication came to mind. Upon further inquiry, the patient admitted to a history of intermittent N_2O use of about 3–5 times a week during the previous month, but she could not specify the amount inhaled each time. Thus, we added related exams. Blood analysis 2 days after admission showed an increased homocysteine level (96.4 μmol/L) but the levels of folate and vitamin B_{12} were normal. Furthermore, the methylmalonic acid test in urine showed a negative result. Based on the abuse history, neurologic symptoms, and elevated homocysteine, N_2O intoxication was diagnosed.

In consideration of the mild acute pancreatitis and abnormal liver function, we started treatment with fasting for 2 days based on supportive therapies, such as fluid resuscitation and nutritional support. Phloroglucinol injection, somatostatin, and polyene phosphatidylcholine injection were given simultaneously. As N_2O intoxication was diagnosed, mecobalamin injection (0.5 mg qod i.v.), mecobalamin tablet (0.5 mg tid p.o.), vitamin B_1 (10 mg tid p.o.), and folic acid (5 mg tid p.o.) were added to the prescription. Within 4 days post therapy, the patient was relieved of abdominal pain. Her neurologic impairment and skin lesions had also retracted significantly by the time of her discharge from the hospital.

Discussion

N_2O plays a vital role in clinical settings, but an array of complications may arise during its recreational use. Abuse of N_2O primarily results in neurologic impairment. The pathogenesis is assumed to be N_2O interference with vitamin B_{12}. By inactivating vitamin B_{12}, N_2O may limit the synthesis of methionine, impair the function of methylmalonyl-coenzyme A mutase enzyme activity, and increase homocysteine and methylmalonic acid.[7] Impediment of methionine can lead to demyelination of the nerve, and dysfunction of methylmalonyl-coenzyme A mutase enzyme may cause the integration of abnormal fatty acids into the myelin sheath.[7] Our patient

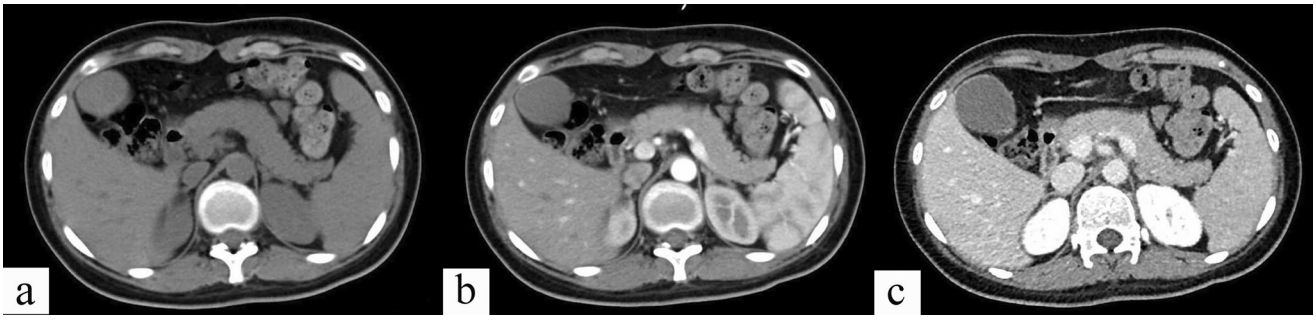

Figure 2 Results of the abdominal computerized tomography (CT) before treatment. (a) Plain CT; (b) contrast-enhanced CT; (c) thin-section CT.

displayed elevated homocysteine and normal vitamin B_{12}, which indicated a functional vitamin B_{12} deficiency. Methylmalonic acid testing came out negative, probably because the patient had used mecobalamin supplements beforehand.

The unique manifestations in our case were skin lesions and abdominal pain. To identify the cause of rashes, we first eliminated the possibilities of infection, autoimmune diseases, and allergy through laboratory tests and skin biopsy. Dermatologists speculated that hyperhomocysteinemia might be the cause of cutaneous lesions based on the homocysteine elevation and abuse history. Thus, we suspected that N_2O abuse was the primary etiology. Upon reviewing the literature, we found that a limited number of cases of N_2O misuse had resulted in diffuse hyperpigmentation, which was detrimental to the skin.[6] For acute pancreatitis, we first considered common etiologies such as cholelithiasis, hypertriglyceridemia, and drinking. Cholelithiasis and hypertriglyceridemia were excluded by abdominal CT and the normal blood lipid concentration, respectively. Regarding acute alcoholic pancreatitis, the history showed that abdominal pain continued for 2 days, but the drinking occurred 2 days earlier, and the serum ethanol test came back negative. Hence, the likelihood of acute alcoholic pancreatitis was low. Moreover, we excluded binge eating, drug, surgery, and trauma on the basis of the history. The patient's normothermia and unremarkable results in pathogenic microorganisms and procalcitonin ruled out the possibility of infection. The absence of α-1 antitrypsin deficiency and hypercalcemia-induced pancreatitis was indicated by the normal α-1 antitrypsin and serum calcium concentration, respectively. Moreover, the patient did not meet the diagnosis of autoimmune pancreatitis characterized by a diffusely enlarged pancreas (especially with a capsule-like rim) on the CT and a marked elevation of IgG4.[8] Finally, we hypothesized that the pancreatitis might be associated with N_2O toxication. Although there have been incidences of acute pancreatitis in cannabis users,[9] no study has reported a correlation between pancreatitis and N_2O. In the diagnosis of this case, we initially neglected N_2O intoxication. One of the possible explanations is that physicians other than neurologists may be less vigilant, as its typical manifestations are neurologic.

For neurologic disorders brought on by N_2O misuse, cessation of exposure and vitamin B_{12} supplementation are crucial to the treatment. For our patient, we used mecobalamin, a derivative of vitamin B_{12}, which exhibited better therapeutic effects on nerve tissue.

Taken together, N_2O poisoning may present various symptoms and signs, including neuropathy and toxicity in the skin and digestive system. Therefore, increased awareness of multiple manifestations of N_2O intoxication is necessary, and timely diagnosis and treatment may result in a better prognosis.

Institutional review board: This study was a retrospective case report and did not involve a prospective evaluation, so ethical approval was not required.

Patient consent: Informed consent was obtained from the patient for publication of this case report and accompanying images.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's website:

Figure S1. Cutaneous lesions in the abdomen.

Figure S2. Cutaneous lesions in the right upper limb.

Figure S3. Cutaneous lesions in the left upper limb.