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Successful Multiorgan Donation From a Brain-dead Donor Following Liquid Nicotine Voluntary Intoxication: A Case Report

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INTRODUCTION

The electronic cigarette was invented in 2003 by Hon Lik, a Chinese pharmacist, as an alternative source of nicotine to traditional tobacco products and coincided with the development of some nicotine replacement therapies. From the beginning of 2004, it spread widely on Western European and American markets and subsequently worldwide. Instead of burning tobacco leaves, electronic cigarettes are battery-powered devices that aerosolize liquid nicotine by heating a solution that contains different proportions of nicotine, glycerol, propylene glycol, and flavoring agents.¹

Nicotine is a hazardous, highly toxic, and very addictive substance extracted from tobacco leaves. Exposure to elevated doses of nicotine may cause acute intoxication and eventually acute respiratory and cardiovascular failure, dysrhythmias, cardiac arrest, and death. Cases of nicotine intoxication after conventional cigarette exposure, transdermal nicotine patches, or tobacco leaves have been reported. Yet, as electronic cigarette use increases, so has the number of both accidental and voluntary liquid nicotine intoxications. Accidental or unintentional intoxication involves mainly children under 10 y of age, whereas that of older patients is most likely voluntary and considered a suicide attempt.¹⁻⁴

We present a case of multiorgan donation from a brain-dead donor admitted to our unit after resuscitation from

cardiorespiratory arrest due to a voluntary intake of liquid nicotine with an autolytic aim.

CASE DESCRIPTION

A 26-y-old male individual was found unconscious by his parents on the floor of his room. He had a history of obsessive-compulsive disorder from childhood, had given up cannabis, cocaine, and metilenedioximethamphetamine abuse, and had survived several suicide attempts, the last of which consisted of jumping from a fifth floor and resulted in L2 spinal cord injury, spastic syndrome, neurogenic bladder, and bowel dysfunction. He was under treatment with venlafaxine, mirtazapine, lorazepam, gabapentin, aripiprazole, levetiracetam, and baclofen.

Upon arrival of the emergency medical service, the patient was in cardiorespiratory arrest, so advanced cardiac life support maneuvers were initiated and performed for 40 minutes. When asked, his parents reported finding an empty 50 mL bottle of liquid nicotine beside him but denied a smoking or vaping habit. After spontaneous circulation was restored, he was transferred to the hospital. On arrival, his vital signs were as follow: blood pressure: 140/70 mmHg; heart rate: 90 beats/min; temperature: 37 °C; respiratory rate (on mechanical ventilation): 20 breaths/min; arterial blood gas analysis (sample drawn on arrival at the emergency department): pH: 6.77; Pco₂: 101 mmHg; Po₂: 28.5 mmHg; HCO₃: 6.6 mmol/L; EB: -26.1 mmol/L; satO₂: 19.3%. He was admitted to the intensive care unit (ICU), where he was unresponsive, had a Glasgow Coma Scale score of 3, fixed and dilated pupils, and abolished brainstem reflexes. The rest of the physical examination was unremarkable. Laboratory tests were as follow: leucocytes: 17.000/mm³, hemoglobin: 14.5 g/dL; platelets and coagulation tests were normal; serum creatinine: 1.2 mg/dL; alanine aminotransferase: 187 U/L; aspartate aminotransferase: 133; amylase: 160 U/L; and creatine kinase: 193 U/L. Arterial blood gas analysis after 6 h on mechanical ventilation with 100% oxygen: pH: 7.37; Po₂: 177 mmHg; Pco₂: 32.5 mmHg; HCO₃: 32.5 mmol/L; satO₂: 100%. The electrocardiogram showed a regular sinus rhythm with a rate of 100/min and no abnormalities despite the long-lasting resuscitation maneuvers. Urine drug screening was positive for tricyclic antidepressants and benzodiazepines, while urine sediment examination was normal.

On admittance, a urine sample was obtained for testing the cotinine (nicotine metabolite) level and sent to the Reference

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Laboratory. The ELISA result was >2000 ng/mL (normal value <500 ng/mL).

A few h after admittance, a diagnosis of clinical brain death was established through complete and protocolized neurological examination and then confirmed by electroencephalography, which showed a plain and unresponsive to pain 30-minute recording. The cause of death was hypoxic-ischemic encephalopathy caused by prolonged cardiorespiratory arrest due to nicotine intoxication.

In the abdominal echography, the liver was hyperechogenic with mild to moderate steatosis; both kidneys were normal, with good corticomedullary differentiation, and their length was 11.5 cm (on the long axis). Echocardiography showed a nondilated left ventricle, normal wall thickness, normal global systolic function (ejection fraction over 70%) without any altered segmental wall function and normal atria; the valves had a normal function and morphology, as well as the pericardium.

The transplant coordinator was contacted. Family and judicial authorization for organ donation was requested (the latter is compulsory in Spain for violent deaths). The patient was proposed as a multiorgan donor, including heart, kidneys, and pancreas. The liver was discarded due to analytic and echographic disturbances. The Spanish National Transplant Organization organized the distribution of the organs according to a protocolized schedule. Organ retrieval surgery was uneventful.

The heart recipient was a 60-y-old male individual, with a recent history of coronary artery disease who had suffered acute coronary syndrome followed by cardiogenic shock due to left ventricular rupture. He was placed on the waiting list as a *code 0* patient and received a heart transplant on the sixth d, with a cold ischemia time of 6 h and 100 minutes on an extracorporeal pump. He was discharged from the ICU to the general ward on postoperative d 6 and discharged 9 d later. He presented some infectious complications in the follow-up, mainly cytomegalovirus pneumonia and a *Stenotrophomonas maltophilia* urinary infection, with a favorable outcome after admittance to the ICU. Evolution was then uneventful, and no complication was subsequently reported. One y after transplantation, he underwent coronarography, and the result was normal.

The pancreas and left kidney were transplanted to a 30-y-old female individual, with type 1 diabetes, diabetic nephropathy, and bad metabolic control, with dialysis treatment initiated 3 y and 19 d earlier. She spent 14 mo and 16 d on the waiting list. After receiving her double organ transplant (left kidney and pancreas), both grafts showed adequate function on the first postoperative d, and she was discharged on postoperative d 14. The plasma creatinine level was 1.01 mg/dL upon discharge and 1.2 mg/dL 1 y after transplantation with a full metabolic recovery.

The right kidney was transplanted to a 26-y-old female individual, with IgA nephropathy, with dialysis treatment initiated 3 y, 11 mo, and 25 d earlier. The right kidney of the donor was transplanted to the left side of the recipient. Adequate graft function was confirmed in the operating theater as urine output started by the end of surgery. She had an uneventful recovery and was discharged on postoperative d 13 with a plasma creatinine level of 1.2 mg/dL. One y later, her plasma creatinine level was 1 mg/dL.

DISCUSSION

The popularity of e-cigarettes has increased since their commercialization; the reports of liquid nicotine intoxication, both accidental and voluntary as suicide attempts, have become more and more frequent, given the wide availability of e-liquids containing highly concentrated nicotine. The most frequent symptoms are nausea, vomiting, agitation, hypertension, tachycardia, headache, and altered mental status; higher doses of nicotine intoxication lead to severe tachycardia and arrhythmias, seizures, acute hypertension followed by hypotension, bradycardia, cardiovascular collapse, and cardiac arrest.²⁻⁶ Because no specific antidote is available, the appropriate treatment is cardiopulmonary support in the ICU. The most frequent cause of death after nicotine intoxication is related to cardiac events, though acute cerebral pathology cannot be excluded.

The actual lethal dose of nicotine is unknown; after oral ingestion, nicotine is absorbed and quickly metabolized by the liver into its inactive metabolites, the most stable and abundant of which is cotinine. Due to short half-life of nicotine (2–3 h), levels of cotinine concentration are frequently used as a surrogate marker of nicotine intoxication levels.

Despite the high toxicity of a nicotine overdose, we have documented a case of successful multiorgan donation, including kidneys, pancreas, and heart from a brain-dead donor after a lethal nicotine intoxication and successful resuscitation from a cardiorespiratory arrest. This appears to be the first case of multiorgan donation following liquid nicotine intoxication reported in the literature so far. In 2017, Räsänen et al⁷ reported a case of kidney donation after brain death caused by a subcutaneous nicotine overdose in an attempted suicide. The patient was a 29-y-old woman with a history of severe depression and obesity who subcutaneously injected 10 mL of liquid nicotine after an intake of alcohol and diazepam. She was taken to hospital, still conscious but anxious on admission. In the emergency department, she had seizures followed by cardiorespiratory arrest. She was successfully resuscitated and admitted to the ICU, where she experienced an unfavorable course and eventually brain death. She was accepted as a kidney donor resulting in 2 successful transplantations: 2 women, aged 39 and 43 y, both with diabetic nephropathy as the cause of their end-stage renal disease. Both had an uneventful postoperative recovery and were discharged on postoperative d 9. On their follow-up, both were doing well, with normal plasma creatinine levels.

In our case, the liver was discarded for transplantation due to altered aminotransferases, hyperechoic texture on ultrasonography in addition to the fact that the liver is the organ responsible for high-dose nicotine metabolism. Kidneys and pancreas were accepted for transplantation after confirming adequate laboratory tests and echographic data. To our knowledge, there are no reports in the literature on renal failure after a nicotine overdose. After being transplanted, both kidneys and pancreas started to function within the first few h; dialysis was unnecessary and good function of the kidneys was present in the follow-up 1 y later. Regarding the heart, the decision to transplant was supported by the optimal electrocardiographic and echocardiographic record, the lack of elevated enzymes, and the hemodynamic stability of the donor after brain death, although the recent event of cardiac arrest and resuscitation maneuvers were an issue to be considered.

As previously mentioned, heart transplantation was successful, and the recipient was doing well in his 1-y follow-up.

The shortage of organs for transplantation has led transplant teams to consider brain-dead patients after fatal intoxications as potential candidates for donation. There is a growing number of cases in the literature reporting acceptable outcomes of organ procuring and transplant, most of them published as isolated cases. Successful kidney transplants have been documented from brain-dead donors after insulin or carbamazepine intoxication.⁸ Organ procurement after carbon monoxide intoxication has been discouraged, but successful multiorgan transplants have been reported, and an absolute contraindication is no longer accepted.^{9,10} Regarding illicit drug intoxications leading to brain death, there is an increase in the number of such patients recruited for organ donation. Solid organs transplanted after cocaine-related death do not show a worse outcome than those from noncocaine users, with some issues regarding heart transplant.¹⁰ Similarly, post-transplant survival of opioid-intoxicated donor hearts and lungs is similar to that from nonintoxicated donors.^{11,12} Even when dealing with brain-dead donors after ingestion of toxic substances mainly metabolized by the liver as, for instance, ethylene glycol or brodifacoum, a rodenticide with a potent anticoagulant effect, good graft outcome and acceptable recipient survival have been reported in the literature. Liver biopsy, hemodialysis to accelerate toxic clearance, and verification of the absence of the toxic substance in blood samples are the suggested strategies to optimize results.¹³⁻¹⁵

Liquid nicotine is a widely available, increasingly popular, and insufficiently regulated substance. Attention should be paid to the potential lethal risk of liquid nicotine intoxication, and efforts should be made to devise more thorough surveillance and avoid such unfortunate events. In case of lethal nicotine intoxication, multiorgan retrieval for donation may be considered, bearing in mind the recommendation of measuring nicotine metabolites in blood samples or even undertaking donor liver biopsy before performing the procedure.

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