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CASE REPORT

ADVANCED

CLINICAL CASE SERIES

1,1-Difluoroethane Hydrocarbon Cardiomyopathy

Kristen N. Brown, MD,[a] Kyle Gronbeck, MD,[b] Ayesha Azmeen, MBBS,[a] Aleem Siddique, MBBS,[c] Ronald Zolty, MD, PhD,[a] James N. Sullivan, MD[d]

ABSTRACT

1,1-Difluoroethane (DFE) cardiomyopathy results from the direct inhalation of toxic halogenated hydrocarbons. We present a case series of acute DFE cardiomyopathy illustrating the typical presentation of severe DFE cardiomyopathy along with a detailed description of its mechanism of injury. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2023;7:101716) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1,1-Difluoroethane (DFE) hydrocarbon cardiomyopathy results from inhalation of the fluorinated hydrocarbon, DFE, a propellant that is found commonly in many household aerosolized propellant cleaners such as Dust-off spray. Although inhaling this chemical compound may provide the user with an elated encephalopathic state, it can concomitantly result in sudden cardiac death and/or chronic myocardial damage.[1] According to the American Association of Poison Control Centers, in 2020 there were a total of 20 deaths in the United States secondary to hydrocarbon exposure and, of these, 15 deaths were reportedly secondary to intentional fluorinated hydrocarbon exposure. In that same year, a total of 592 cases of intentional propellant hydrocarbon exposure were reported, and 87 (15%) of these resulted in major adverse outcomes, which was more than triple the rate of some commonly abused potentially cardiotoxic opioids: morphine (<5%), hydromorphone (4%) tramadol (2%), hydrocodone (<1%), and meperidine (0%).[2] It is, however, unclear how many of these adverse outcomes and deaths resulted from cardiomyopathy. Since the transition from chlorofluorocarbons to DFE in aerosol applications, DFE cardiomyopathy has been reported in the literature a hand full of times.[3] Although in most of these cases users were between the ages of 18 and 50 years, approximately 6.5% of grade schoolers are at risk according to the National Youth Risk 2019 Behavior Report as reported users.[4]

Despite the increasing popularity of "huffing" DFE aerosols as reported by the National Substance Abuse and Mental Health Services Administration and other regulation committees, little to no exposure of this use has been publicized, in contrast with the current

LEARNING OBJECTIVES

- To broaden the differential for heart failure after huffing.
- To describe the effects of DFE exposure on the human body.

From the [a]Division of Cardiovascular Medicine, University of Nebraska Medical Center, Omaha, Nebraska; [b]Department of Emergency Medicine, University of Nebraska Medical Center, Omaha, Nebraska; [c]Division of Cardiothoracic Surgery, University of Nebraska Medical Center, Omaha, Nebraska; and the [d]Department of Anesthesiology, University of Nebraska Medical Center, Omaha, Nebraska.

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ABBREVIATIONS AND ACRONYMS

DFE = 1,1-difluoroethane

ECMO = extracorporeal membrane oxygenation

EF = ejection fraction

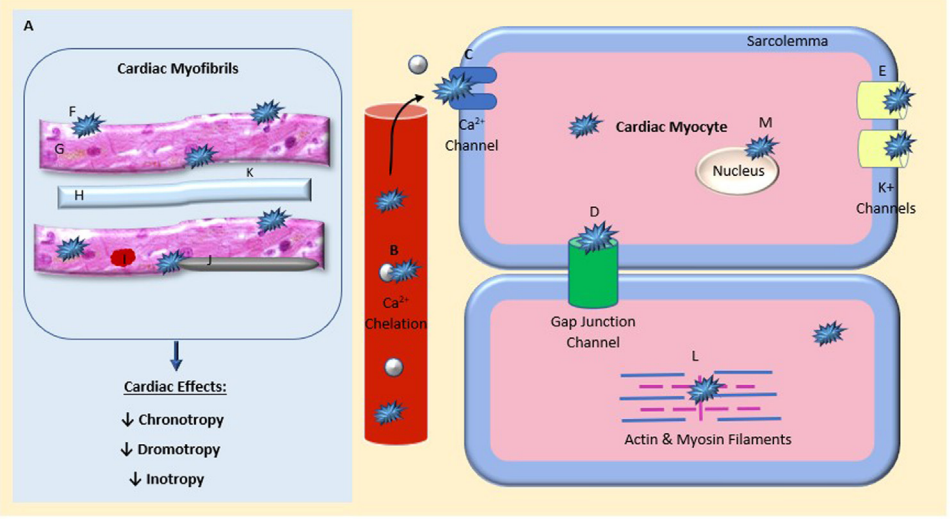
opioid epidemic.[5,6] For this purpose, we present 2 cases of DFE cardiomyopathy along with a detailed description of the effects of DFE on the human body.

CASES

CASE 1. A 34-year-old man with a history of polysubstance abuse, anxiety, and depression was found in his car with 10 empty cans of air duster spray. The patient was initially taken to the nearest hospital, but was shortly thereafter transferred to the University of Nebraska Medical Center, a large tertiary referral center, for worsening clinical status. On arrival, he was alert and awake complaining of generalized fatigue and chills. However, soon after the patient went into supraventricular tachycardia followed by hemodynamic collapse and cardiac arrest. A bedside echocardiogram revealed a severely depressed biventricular function with an ejection fraction (EF) of 5% (Video 1). He was placed emergently on venoarterial extracorporeal membrane oxygenation (ECMO). Shortly after, he became anuric and was placed on continuous venovenous hemodialysis (Supplemental Table 1). Improvement was seen in cardiac, pulmonary, renal, and neurologic function within a few days with supportive care and venoarterial ECMO. His EF improved to 65% by day 10 (Video 2). Subsequently, he was decannulated and extubated. His postextubation course was complicated by pneumonia, treated with antibiotics, and a small pulmonary embolism. Once medically stable, psychiatry was consulted to assess for suicidal ideations in the setting of this toxic overdose. The patient was cleared of any acute psychiatric disease and was discharged to an acute rehabilitation facility.

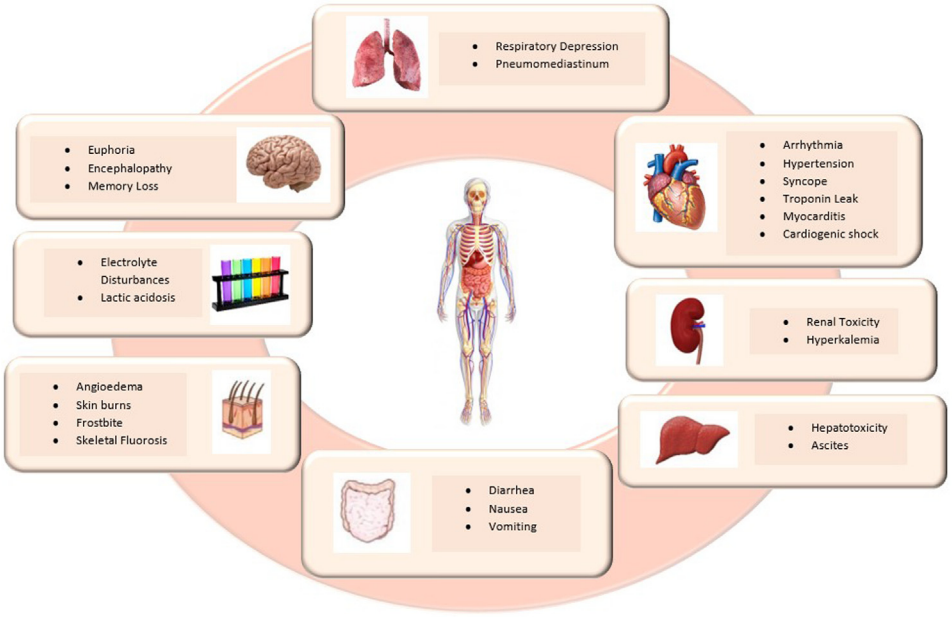
CASE 2. A 32-year-old man with a history of polysubstance abuse was found at home with 15 empty cans of air duster spray. He rapidly deteriorated at an outside hospital with worsening mental status and acute hypoxic respiratory failure requiring intubation. He then developed refractory cardiogenic shock along with rhabdomyolysis, acute kidney injury, and fulminant hepatitis (Supplemental Table 1). Cardiogenic shock was followed by sustained ventricular tachycardia. After successful resuscitation, an Impella RP was placed in his right femoral artery. He continued to require high doses of inotropes and pressors and was subsequently transferred to our hospital where a bedside echocardiogram revealed an EF of 5% (Video 3). He was immediately placed on venoarterial ECMO. Within 24 to 48 hours his EF had improved (Video 4), and he was successfully taken off

FIGURE 1 Molecular and Cellular Effects DFE



(A) Saturation of myocytes. **(B)** Calcium chelation. **(C)** Directly binding of calcium channels. **(D)** Saturating gap junction channels. **(E)** Blockade of potassium channels. **(F)** DFE molecule. **(G)** Myofibril. **(H)** Interstitial edema. **(I)** Intramyocardial hemorrhage. **(J)** Myocardial necrosis. **(K)** Extracellular space. **(L)** Blocks actin and myosin binding. **(M)** Long-term exposure results in disruption in myocyte DNA resulting in disorganized and malfunctioning muscle tissue.

FIGURE 2 **Multiorgan Effects of DFE Toxicity**



Microsoft Word stock images were used to create the illustration.

ECMO. Improvement in liver function was also seen. Unfortunately, renal function did not recover, and he remains on intermittent hemodialysis.

DISCUSSION

DFE cardiomyopathy occurs through direct absorption of the DFE toxin, a colorless volatile halogenated hydrocarbon, into the pulmonary vascular bed after inhalation of this compound.[7] DFE-infused blood is then shunted to the heart, where the DFE molecules saturate the cardiac myocytes resulting in gross temporary myocardial stunning and enhanced myocardial sensitization to fatal arrhythmias through an exaggerated catecholamine response.[8,9] The most common cardiac arrhythmia secondary to DFE ingestion is sinus tachycardia, but at high doses deadly ventricular arrhythmias may occur.[10]

In addition to its arrhythmogenic effects, DFE has negative chronotropic, dromotropic, and inotropic effects. On a molecular level, it achieves these effects by slowing repolarization via directly saturating several cardiac channels.[11] Through direct inhibition and chelation, DFE can block calcium influx into the cell, which may alter the myocyte's ability to depolarize.[12] DFE also directly binds to potassium channels and gap junctions essentially causing a dose-dependent paralysis of the cardiac cellular network (**Figure 1**). This is enhanced in the presence of epinephrine through dephosphorylation of connexin-43.[13] For this reason, the use of exogenous epinephrine is contraindicated in these patients.

Because myocardial stunning and electrical dysfunction are common in high-dose acute intoxications, chronic use of DFE has been shown to result in myocardial structural changes such as interstitial edema, intramyocardial hemorrhage, and myocardial necrosis.[14]

Extracardiac multiorgan dysfunction is also seen in DFE exposure (**Figure 2**). DFE's mechanism of action on other organs is similar to the heart.[3] Therein, DFE is transported from the lungs via the bloodstream and saturates the target organs cells, rendering them inactive. However, it is important to note that the effects of acute DFE exposure on all organ systems seems to be largely transient and reversible. The effects of this drug tend to wear off as the body excretes it in the urine and exhales it through the lungs.[15] Despite the transient nature of this toxicity, the acute multiorgan decompensation and propensity for nonperfusing arrhythmias together make this entity deadly.

Unfortunately, in the absence of a huffing history, a high index of suspicion is required to make this

diagnosis. Most patients with DFE cardiomyopathy present in cardiogenic shock and should be managed as such. Typical laboratory findings include positive serum DFE, elevated troponin, and abnormal markers of perfusion. Of note, obtaining a coronary angiogram is typically not recommended owing to the increased arrhythmogenic risk in otherwise low-risk individuals. Transthoracic echocardiogram is the mainstay.[16] Owing to the transient nature of DFE cardiomyopathy, venoarterial ECMO is a reasonable treatment option as a bridge to recovery.

CONCLUSIONS

DFE cardiomyopathy is a rare, but potentially lethal, preventable pathology that is increasing in the United States. An increased awareness of the detrimental effects of DFE and its potential to cause severe and rapidly progressive cardiac toxicity is essential in combating the increase in recreational use of DFE inhalant. Tertiary referral and management with standard cardiogenic shock algorithms may be life-saving given the transient nature of acute toxicity.

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ADDRESS FOR CORRESPONDENCE: Dr Kristen N. Brown, Division of Cardiovascular Medicine, University of Nebraska Medical Center, 15112 Hillside Court, Omaha, Nebraska 68154, USA. E-mail: Kristen.Brown@unmc.edu. Twitter: @Kristen_BrownMD.

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KEY WORDS 1,1-difluoroethane hydrocarbon, huffing, nonischemic cardiomyopathy, toxic cardiomyopathy

APPENDIX For supplemental videos and a table, please see the online version of this article.