He Huffed and He Puffed and He Got Frostbite

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A 27-year-old man presented to the ED following a syncopal episode.

Case

A 27-year-old man presented to an ED after experiencing a syncopal episode. His vital signs at presentation were normal. Physical examination was generally normal except that there were blisters on the patient's abdomen, left hand, and right arm, as well as a hypertrophic nodule on the right elbow (**Figure**) and hard growths on the digits of the right hand. The patient stated the growths started 5 months ago and had been increasing in size. On further questioning, the patient admitted to "huffing" (ie, inhaling) at least six cans of pressurized dust-removal keyboard cleaning spray daily for the past 11 months.

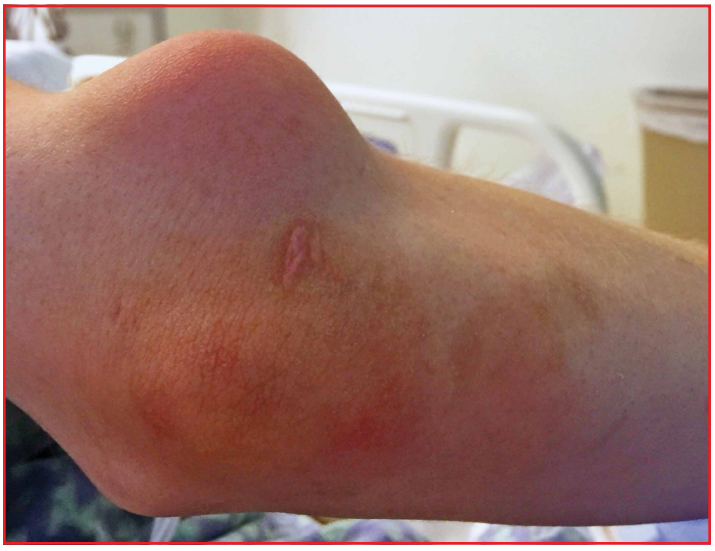

Figure. The patient's right elbow at presentation demonstrates a hypertrophic nodule.

Why do patients abuse keyboard cleaning spray?

The propellant used in certain liquefied compressed gas products is 1,1-difluoroethane (1,1-DFE), a fluorinated hydrocarbon. It is a member of a broad class of related compounds that are present in spray paints, glues, nail polish removers, fuels, hair sprays, and air-freshening products. These 1,1-DFE-containing products are abused for their rapid and short-acting central nervous system (CNS) depressant effects—not unlike that of ethanol. Typically, the vapor of a volatile hydrocarbon is inhaled directly from the open container ("sniffing"), from a bag ("bagging"), or from a soaked rag (huffing). Not only are such hydrocarbon-containing products easy to conceal, they are also highly accessible and inexpensive. Moreover, there are generally no direct legal consequences resulting from abuse of these substances.

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DOI: 10.12788/emed.2016.0036

All of the aforementioned factors make hydrocarbons a popular drug of abuse among adolescents. Approximately 75% of the population abusing hydrocarbons is younger than age 18 years, half of whom reported first use prior to age 13 years.[1,2] Though inhalant abuse rarely continues into adulthood, 0.1% of individuals between the ages of 18 and 30 years report having an inhalant-use disorder.

Hydrocarbons and their halogenated derivatives are lipophilic compounds that are rapidly absorbed after inhalation and rapidly distributed to CNS and cardiac tissue. The brain concentration of 1,1-DFE likely peaks higher than concentrations in other organs and is cleared more rapidly.[3] Hydrocarbons produce CNS depression secondary to multiple mechanisms, including gamma-aminobutyric acid agonism, dopamine modulation, and N-methyl-D-aspartate-receptor antagonism.[4,5]

What causes skin lesions on the abdomen and arms?

The lesions on the patient's abdomen and extremities were consistent with frostbite. The liquefied compressed gas in computer-cleaning and related products is housed in a pressurized canister. The pressure is released when the spray nozzle is depressed; this causes the liquid to rapidly expand to a gas as it is released, resulting in a quick decrease in the temperature of the metal canister. This process, referred to as adiabatic cooling, demonstrates the first law of thermodynamics. The cold temperature of both the liquid and the canister can cause frostbite in the digits and other parts of the body with which the canister or liquid comes into contact.[6]

Why did the patient have syncope?

Halogenated hydrocarbons inhibit the cardiac delayed rectifier potassium channels involved in the repolarization of cardiac myocytes, causing a delay in repolarization that is manifested as prolongation of the QT interval on an electrocardiogram. This condition places patients at an increased risk of developing torsades de pointes (TdP).[7] In most cases, TdP is self-terminating; however, if TdP persists, degeneration to ventricular fibrillation will result. Deaths caused in this fashion have been referred to as "sudden sniffing death syndrome," and account for half of all hydrocarbon-related deaths.[6,8] In addition to the cardiac effects, hydrocarbons are simple asphyxiants that act by displacing oxygen from inspired air, which also contributes to syncope.

It is important to note that epinephrine and other catecholamines increase the risk for dysrhythmias such as TdP in the setting of hydrocarbon abuse.[9] For this reason, epinephrine should be used with caution in the setting of a hydrocarbon-induced arrhythmia. Beta-adrenergic antagonists such as esmolol and propranolol are preferable because they reduce the incidence of ectopia that may trigger TdP.[10]

What is the significance of the masses noted on the examination and radiograph?

Fluorosis is associated with abnormalities of skeletal and dental tissue. Skeletal fluorosis causes osteosclerosis of the axial skeleton, periosteal new bone formation, ligamentous and tendinous ossification, and osteophyte formation. Dental fluorosis causes a yellow/brown discoloration of the teeth with horizontal streaking (mottling), pitting, and chipping.[11] Fluorosis is well-described in regions where water fluoride concentrations are high due to industrial exposure; from consumption of fluorinated wine or chronic overconsumption of tea (especially green or black tea); or from fluoridated toothpaste.[12-14] More recently, fluorosis has been described in patients treated for an extended duration of time with voriconazole, a fluorinated antifungal agent.[15] Unlike other hydrocarbon products, fluorinated hydrocarbons such as 1,1-DFE can significantly increase systemic fluoride concentrations with excessive use. Rapid skeletal fluorosis is not well described, but has been reported after chronic abuse of fluorinated hydrocarbons.[16]

How is fluorosis diagnosed and managed?

The lack of rapid laboratory testing available for serum, urine, and bone fluoride concentrations makes the initial diagnosis of fluorosis a clinical one. Imaging studies are generally highly suggestive of fluorosis and can be used to support the diagnosis. A dual energy X-ray absorptiometry scan of the spine, hip, femur, and distal portions of the radii can reveal elevated T-scores consistent with osteosclerosis.[14] These findings, in conjunction with bone or joint pain, reduced range of motion, or kyphosis, should prompt clinicians to conduct further testing—even without a confirmed fluoride source. A serum fluoride (reference range, 0.2-3.2 mg/L) and 24-hour urine fluoride (reference range, 0.2-3.2 mg/dL) and creatinine evaluation can be used to diagnose fluorosis. However, a bone biopsy with quantitative bone ash fluoride analysis remains the gold standard for the diagnosis of skeletal fluorosis.[16] Laboratory evaluation should also include an assessment of electrolytes, specifically calcium, 25-hydroxyvitamin D, and alkaline phosphatase. The differential diagnosis should include hemoglobinopathies, renal osteodystrophy, Paget disease, hypothyroidism, and skeletal metastases.[16]

Treatment of fluorosis is largely symptomatic and supportive, with identification and discontinuation of the fluoride source. Patients should be referred to an orthopedist for evaluation and management as needed. Evaluation by an endocrinologist should also be considered because patients may have chronic vitamin D and calcium deficiencies as a result of systemic fluorosis.

Case Conclusion

The patient's laboratory assessment was notable for the following: alkaline phosphatase, 624 U/L (reference range, 44-147 IU/L); vitamin D, 10 ng/mL (reference range, 20-40 ng/mL); serum fluoride, 0.3 mg/L (reference range, 0.2-3.2 mg/L); urine fluoride, 52 mg/dL (0.2-3.2 mg/dL); and urine creatinine, 1 g/L (reference range, 0.3-3 g/L). Imaging studies noted periosteal bone formation on the lateral epicondyle of the distal right humerus, as well as similar osseous abnormalities in other locations. A bone biopsy was scheduled. The patient was treated with oral vitamin D and educated about the importance of discontinuing the huffing of all hydrocarbons.

References

1. Williams JF, Storck M; American Academy of Pediatrics Committee on Substance Abuse; American Academy of Pediatrics Committee on Native American Child Health. Inhalant abuse. *Pediatrics*. 2007;119(5):1009-1017.
2. Wu LT, Pilowsky DJ, Schlenger WE. Inhalant abuse and dependence among adolescents in the United States. *J Am Acad Child Adolesc Psychiatry*. 2004;43(10):1206-1214.
3. Avella J, Kunaparaju N, Kumar S, Lehrer M, Zito SW, Barletta M. Uptake and distribution of the abused inhalant 1,1-difluoroethane in the rat. *J Anal Toxicol*. 2010;34(7):381-388.
4. Tormoehlen LM, Tekulve KJ, Nañagas KA. Hydrocarbon toxicity: A review. *Clin Toxicol (Phila)*. 2014;52(5):479-489.
5. Duncan JR, Lawrence AJ. Conventional concepts and new perspectives for understanding the addictive properties of inhalants. *J Pharmacol Sci*. 2013;122(4):237-243.
6. Sakai K, Maruyama-Maebashi K, Takatsu A, et al. Sudden death involving inhalation of 1,1-difluoroethane (HFC-152a) with spray cleaner: three case reports. *Forensic Sci Int*. 2011;206(1-3):e58-e61.
7. Himmel HM. Mechanisms involved in cardiac sensitization by volatile anesthetics: general applicability to halogenated hydrocarbons? *Crit Rev Toxicol*. 2008;38(9):773-803.
8. Avella J, Wilson JC, Lehrer M. Fatal cardiac arrhythmia after repeated exposure to 1,1-difluoroethane (DFE). *Am J Forensic Med Pathol*. 2006;27(1):58-60.
9. Nelson LS. Toxicologic myocardial sensitization. *J Toxicol Clin Toxicol*. 2002;40(7):867-879.
10. Mortiz F, de La Chapelle A, Bauer F, Leroy JP, Goullé JP, Bonmarchand G. Esmolol in the treatment of severe arrhythmia after acute trichloroethylene poisoning. *Intensive Care Med*. 2000;26(2):256.
11. Majumdar KK. Health impact of supplying safe drinking water containing fluoride below permissible level on flourosis patients in a fluoride-endemic rural area of West Bengal. *Indian J Public Health*. 2011;55(4):303-308.
12. Kakumanu N, Rao SD. Images in clinical medicine. Skeletal fluorosis due to excessive tea drinking. *N Engl J Med* 2013;368(12):1140.
13. Soriano M, Manchón F. Radiological aspects of a new type of bone fluorosis, periostitis deformans. *Radiology* 1966;87(6):1089-1094.
14. Tamer MN, Kale Köroğlu B, Arslan C, et al. Osteosclerosis due to endemic fluorosis. *Sci Total Environ*. 2007;373(1):43-48.
15. Bucknor MD, Gross AJ, Link TM. Voriconazole-induced periostitis in two post-transplant patients. *J Radiol Case Rep*. 2013;7(8):10-17.
16. Cohen E, Hsu RY, Evangelista P, Aaron R, Rubin LE. Rapid-onset diffuse skeletal fluorosis from inhalant abuse: a case report. *JBJS Case Connector*. 2014;4(4):e108.