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Acute Inhalation Exposure to Titanium Ethanolate as a Possible Cause of Metal Fume Fever

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Abstract

Occupational inhalation exposure to noxious agents is not uncommon. Herein, we present a 26-year-old male student who had accidental acute inhalation exposure to a large quantity of titanium ethanolate and hydrogen chloride in chemistry lab. He was referred to the emergency department of our hospital with low-grade fever, dyspnea, headache, fatigue and myalgia. After 24 hrs of symptomatic treatment (oxygen therapy and acetaminophen), the fever was subsided and the patient discharged home in a good clinical condition. The presented symptoms could be interpreted as a form of metal fume fever. It can therefore be concluded that organo-metallic compound of titanium metal may have the potential to produce metal fume fever in human.

Keywords: Titanium; Metals; Fever; Inhalation exposure; Hydrochloric acid; Gas poisoning; Poisoning

Introduction

Titanium ethanolate $[\text{Ti}(\text{CH}_3\text{CH}_2\text{O})_4]$ is a colorless liquid that reacts with water in an exothermic reaction to produce free toxic and flammable gases (moisture sensitive).^{1,2} It is soluble in hydrocarbons and ethanol and reacts with other alcohols, ketones, esters, and carboxylic acids.² Titanium ethanolate can be prepared via a number of different synthetic procedures. The most common route of its production is when a metal halide is reacted with alcohol in the presence of an amine.³ Titanium ethanolate is used in organic synthesis, materials science, and olefin polymerization.⁴ According to MSDS, inhalation of titanium ethanolate vapor

may cause fatigue, drowsiness, dizziness and vertigo. Inhalation of a high concentration of the gas would cause lung irritation and subsequent cough, nausea, depression of the central nervous system, and headache.⁵

Metal fume fever is an acute toxicity caused by inhalation of metal oxide fumes.⁶ Zinc and copper are known to be the most common metals responsible for metal fume fever.⁷ Oxides of cadmium, mercury, aluminum, antimony, selenium, iron, magnesium, manganese, chromium, arsenic, nickel, silver, and even tin have also been implicated.^{6,7} Herein, we report on a case of acute inhalation exposure to titanium ethanolate that probably caused metal fume fever.

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Case Presentation

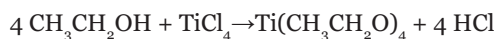
A 26-year-old male student had accidental acute inhalation exposure to a large quantity of titanium ethanolate and hydrogen chloride while mixing titanium chloride with ethanol. According to his record, at the time of mixing, a thick white vapor suddenly came out of the solution and he was exposed to a large quantity of the vapor for two hours. His symptoms began 3–4 hrs post-exposure. He did not get better and was referred to the emergency department of Loghman Hakim Hospital, Tehran, Iran, 24 hrs after the exposure.

On arrival, the patient complained of low-grade fever, dyspnea, headache, fatigue, and myalgia. He had blood pressure of 100/70 mmHg, respiratory rate of 20/min, pulse rate of 80/min, oral temperature of 38 °C. Other vital signs were normal. Chest x-ray and physical examination of the lungs were normal. Routine lab tests were normal; there was only a slight increase in serum alanine transaminase (ALT) (Table 1).

After 24 hrs of symptomatic treatment with oxygen and intravenous acetaminophen (1000 mg in 200 mL normal saline), the fever was subsided, respiratory symptoms were alleviated, and the patient discharged home in a good clinical condition.

Discussion

This case describes an acute intoxication by a large quantity of titanium ethanolate and hydrogen chloride gas after the following reaction of titanium tetrachloride with ethanol.⁸



Titanium tetrachloride is a highly volatile pale yellow liquid.⁹ Its immediate hydrolysis after contact with water or water vapor produces fumes that include

titanium oxychloride, titanium hydroxide, titanium dioxide, and hydrochloric acid, which can cause lung injury.⁹

For lack of moisture in the air of the laboratory where our patient was working in, the hydrolysis of titanium tetrachloride is very unlikely. The patient was mixing titanium tetrachloride with ethanol where in a fast chemical reaction, titanium ethanolate was produced; an appreciable amount of titanium oxide was also produced, however, it is unlikely that it would cause intoxication.^{8,11}

Titanium ethanolate is liquid under normal conditions. Nonetheless, since the temperature was not controlled by the patient, the exothermic reaction resulted in vaporized titanium ethanolate.²

Chest roentgenogram and clinical examination were normal; the patient had only minor difficulty with respiration. The dyspnea may be due to inhalation of high volume of free hydrogen chloride vapor which is a well-known irritating substance.⁹ Titanium ethanolate is also known for its irritating properties to the respiratory system.⁵

The acute exposure to titanium ethanolate vapor may also be responsible for the low-grade fever, headache, fatigue, and myalgia. There are reports that titanium can cause metal fume fever.^{6,7}

Metal fume fever causes flu-like symptoms including fever, headache, fatigue, malaise, mild arthralgias, myalgias, chills, thirst, nausea, vomiting, and chest soreness.^{6,7} Since the symptoms of metal fume fever are similar to those of flu and lung injury, its diagnose is difficult. Chest radiography, pulmonary function tests, and history taking may help us to manage the patient better.⁶ Considering the lab findings and clinical examination, it is very unlikely that the fever in our patient had an infectious origin. On the other hand, the symptoms of metal fume fever usually start 3–10 hrs of exposure and peak 18

hrs of the exposure.^{6,10} Recovery generally occurs without treatment within 24 to 48 hrs, but complete recovery may take four days.⁶ The symptoms of our patient began 3–4 hrs after the exposure and were relieved after 36 hrs of the exposure.

Based on all these observations, we believe that metal fume fever was a likely diagnosis for our patient. If that was correct, it can therefore be concluded that organometallic compound of titanium metal may have the potential to produce metal fume fever in human.

Metal fume fever is defined as an illness caused by inhalation of metal oxide fumes. However, it seems that it might be happened after inhalation of vapors of some organic compound containing metal (eg, titanium) too. This would warrant the need to redefine the term “metal fume fever.”

Conflicts of Interest: None declared.

References

1. Mehrotra Rc, Singh A. Recent trends in metal alkoxide chemistry. In: Karlin KD, ed. *Progress in Inorganic Chemistry*. vol 46, John Wiley & Sons Inc, New York, **1997**.
2. Material Safety Data Sheet. Titanium ethoxide 99.99% (metals), 2010, Available from www.multi-valent.co.uk/msds/titanium_ethoxide_99.99/_102.pdf (Accessed February 24, 2014).
3. Cotton FA, Wilkinson G, Murillo CA, Bochmann M. *Advanced Inorganic Chemistry*. 6th ed, John Wiley & Sons Inc, New York, **1999**.
4. Greenwood NN, Earnshaw A. *Chemistry of the Elements*. 2nd ed. Oxford, Butterworth-Heinemann, **1997**; 954-75.
5. Titanium (IV) ethoxide, sc-251257, material safety data sheet. Issue Date: Dec-27-2009, Available from <http://datasheets.scbt.com/sc-251257.pdf> (Accessed February 25, 2014).
6. Ahsan SA, Lackovic M, Katner A, Palermo C. Metal fume fever: a review of the literature and cases reported to the Louisiana Poison Control Center. *J La State Med Soc* 2009;**161**:348-51.
7. Otani N, Ishimatsu S, Mochizuki T. Acute group poisoning by titanium dioxide: inhalation exposure may cause metal fume fever. *Am J Emerg Med* 2008;**26**:608-11.
8. Bradley D, Hillyer M. Thermochemistry of metal alkoxides. Part 2—Heats of formation of some titanium alkoxides. *Trans Faraday Soc* 1966;**62**:2374-81.
9. CDC, NIOSH. *CDC-NIOSH Pocket Guide to Chemical Hazards*. **2014**.
10. Ladou J, ed. *Current Occupational and Environmental Medicine*. New York: McGraw Hill, **2007**.