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CASE REPORT

Toxicology

Pneumothorax associated with accidental 4-nitrophenyl chlonoformate inhalation in an academic chemistry lab

Dan Imler MD[1] | **Elena Martel MD**[2]

[1]Department of Pediatric Emergency Medicine, Pediatric Hospital Medicine, Stanford University School of Medicine, Palo Alto, California, USA

[2]Department of Emergency Medicine, Stanford University School of Medicine, Palo Alto, California, USA

Correspondence
Dan Imler, MD, Department of Pediatric Emergency Medicine, Pediatric Hospital Medicine, Stanford University School of Medicine, Palo Alto, CA 94304, USA.
Email: imlerdl@stanford.edu

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Abstract

An otherwise healthy 16-year-old male presented to the pediatric emergency department 12 hours after accidental inhalation of 4-nitrophenyl chloroformate in a chemistry lab. His only pertinent findings were a complaint of chest tightness and decreased breath sounds on a pulmonary exam. He was found on chest radiograph to have a large right-sided pneumothorax with slight mediastinal shift and mild interstitial prominence. A chest tube was placed, and he recovered well. This case demonstrates pneumothorax as a possible complication of inhalation of caustic chemical substances and emphasizes the importance of thorough history-taking and clinical examination.

1 | INTRODUCTION

Inhalation of chemicals within a laboratory setting represents a risk for acute pulmonary complications. Here we report upon the case of an adolescent patient who developed pneumothorax after accidental inhalation of 4-nitrophenyl chloroformate.

2 | CASE PRESENTATION

A 16-year-old male with no significant past medical/surgical history presented to the pediatric emergency department (PED) with chest tightness 12 hours after accidentally dropping a jar containing 20–25 mg of 4-nitrophenyl choroformate onto the ground while working in a summer program at a university chemistry lab. As he leaned over to clean up the spillage on the ground he inhaled some of the substance, while wearing eye protection and a surgical mask. Within minutes of the inhalation, he began to note chest tightness that worsened when he laid flat. The symptoms improved somewhat when upright and bending forward. After the event he went home and noticed the symptoms had somewhat improved, so he went to bed without further evaluation. In the morning when he awoke, he reported continued mild chest irritation to his chemistry professor, who brought him to the PED as the material safety data sheet[1] for the substance mentioned potential respiratory irritation.

At the time of presentation, the patient denied shortness of breath, cough, difficulty swallowing/speaking, itching, rash, eye pain, tearing, abdominal pain, nausea, vomiting, or any other symptom. He was not a smoker or user of vaping products. He had no known underlying pulmonary or cardiac disease. His physical exam was unremarkable except for mildly decreased breath sounds bilaterally. There was no reproducible chest wall pain. His vitals were normal including respiratory rate and pulse oximetry.

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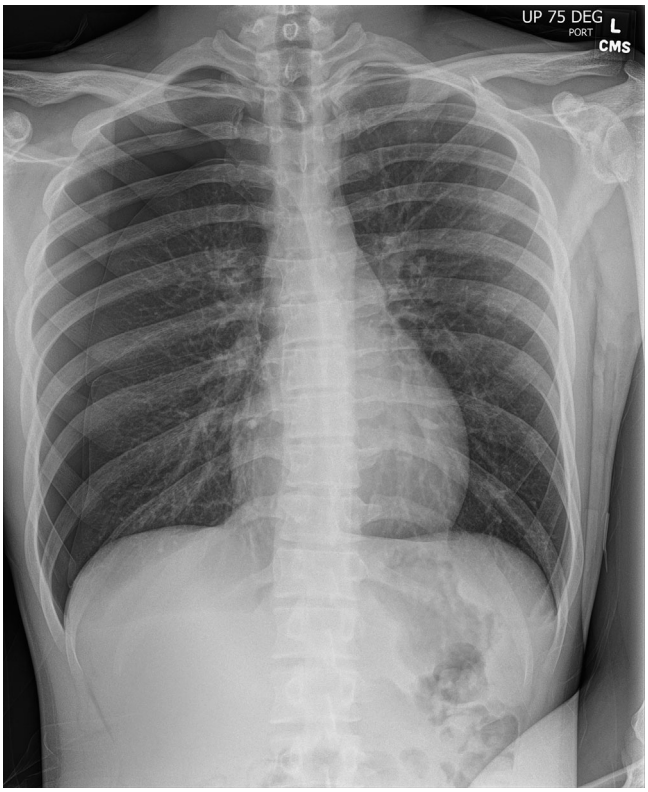

FIGURE 1 Portable chest radiograph demonstrating a right-sided tension pneumothorax, with mild mediastinal shift.

Chest radiograph demonstrated a large right-sided pneumothorax with a slight mediastinal shift as well as mild interstitial prominence (Figure 1). A pigtail chest tube was inserted with the resolution of the pneumothorax. The patient did well and was discharged 24 hours later.

3 | DISCUSSION

This case introduces the consideration of pneumothorax after inhalation of 4-nitrophenyl chlonoformate. Currently, the material data safety sheet states "Inhalation of dusts, generated by the material, during the course of normal handling, may produce toxic effects." Although these toxic effects are not defined and do not include pneumothorax. Other irritant gasses[2–5] inhaled illicit substances[6–10] and inhaled medications[11] have all been previously implicated as causes of pneumothorax in the literature. For example, at high concentrations, partially water-soluble chlorine gas has shown to cause respiratory distress when inhaled, because of the development of bronchospasm and pulmonary edema.[12] Case reports have also demonstrated the development of respiratory symptoms such as wheezing and pleuritic chest tightness because of the inhalation of aerosolized chlorine dioxide found in cleaning agents.[13] Inhaled ammonia is another known respiratory irritant, capable of causing both upper and lower airway irritation via liquefactive necrosis. Interestingly, a prior case report involving an otherwise healthy 22-year-old male with accidental occupational exposure to aerosolized ammonia demonstrated a correlation between the respiratory toxicity of this agent and the development of pneumothorax in that patient.[14]

One hypothesis for the occurrence of pneumothorax secondary to the inhalation of 4-nitrophenyl chloroformate is the destabilization of surfactant caused by this substance. Importantly, there was no nasal, oral, tracheal, and laryngeal irritation in this case, suggesting that the chemical toxic metabolite is unlikely to be water soluble.[15] There is no previous literature investigating the effects of 4-nitrophenyl chloroformate on pulmonary surfactant (PS), and no evidence of direct or indirect destabilization of PS by this substance. It is also possible that this accidental inhalation led to an acute pneumonitis that caused a delayed pneumothorax.

4 | LIMITATIONS

It is important to acknowledge that we cannot be certain whether this pneumothorax was secondary to inhalation or if the complication was purely coincidental. We cannot definitively determine if our patient had a primary spontaneous pneumothorax, a secondary spontaneous pneumothorax, or a traumatic pneumothorax. Additionally, it is unknown if the specific subtype of pneumothorax that occurred was directly correlated with the inhalation of 4-nitrophenyl chloroformate. Pneumothorax is defined as air in the pleural cavity, resulting from an abnormal communication from the air-filled alveoli of the lungs and this cavity. Spontaneous pneumothoraces occur without the traumatic introduction of air into the cavity and can be further defined as primary, indicating that there is no known underlying lung disease, or secondary spontaneous, in which there is underlying lung pathology. Lung pathology, such as chronic obstructive pulmonary disease, can result in air blebs that spontaneously burst, resulting in this abnormal communication of air and a resulting secondary spontaneous pneumothorax. Our patient did not have known underlying lung pathology; thus, a secondary spontaneous pneumothorax was unlikely.

Thin adolescent males (like our patient) are at significantly higher risk of primary spontaneous pneumothorax.[16] Acute increase in transpulmonary pressure is also a common cause of spontaneous pneumothorax and it is possible that the event precipitating the inhalation caused a transient increase in pressure leading to the pneumothorax. There was no reported history of smoking or illicit drug use in this patient, both risk factors for the occurrence, but these may be unrealized factors. Additionally, the patient may have been exposed to a different unidentified causative mechanism (minor trauma, other substance, etc) before presentation. Finally, this patient had no previous lung imaging meaning we were unable to assess for any preexisting lung disease or bullae, which are known risk factors.

Additionally, as the patient was evaluated the morning after this inhalation, the exact timing of the pneumothorax development is unknown. It is possible that the initial pneumothorax occurred at the time of inhalation when the patient first noticed chest tightness or developed later as a secondary complication of other respiratory irritation.

5 | CONCLUSION

To date, no other cases of pneumothorax with 4-nitrophenyl chloroformate have been reported and this report adds to the literature of potential pulmonary complications associated with chemical irritants.

CONFLICT OF INTEREST STATEMENT

No funding or conflicts of interest are associated with this article or its authors. This case has not been presented at any meetings.

REFERENCES

1. 4-Nitrophenyl chloroformate. Safety Data Sheet. ThermoFisher Scientific. Revision Date 12/24/2021. Accessed 1/3/2023. https://www.fishersci.com/store/msds?partNumber=AC170800050&productDescription=4-NITROPHENYL+CHLOROFORM+5GR&vendorId=VN00032119&countryCode=US&language=en
2. Serinken M, Karcioglu O, Evyapan F, Sungurtekin H. Bilateral pneumothorax following acute inhalation injury. *Clin Toxicol (Phila)*. 2009;47(6):595-597. https://doi.org/10.1080/15563650903012333
3. Akhlaq S, Ejaz T, Aziz A, Ahmed A. Spontaneous pneumomediastinum in accidental chlorine gas inhalational injury: case report and review of literature. *BMJ Case Rep*. 2021;14(7):e236549. https://doi.org/10.1136/bcr-2020-236549
4. Nash PE, Tachakra SS, Baird H. Pneumothorax following inhalation of caustic soda fumes. *Arch Emerg Med*. 1988;5(1):45-47. https://doi.org/10.1136/emj.5.1.45
5. Poon J, Al-Halawani M, Dubey G. Spontaneous pneumothorax as a complication of chronic Jet propulsion fuel-8 exposure. *Heart Lung*. 2019;48(2):169-172. https://doi.org/10.1016/j.hrtlng.2018.08.001
6. Fiorelli A, Accardo M, Rossi F, Santini M. Spontaneous pneumothorax associated with talc pulmonary granulomatosis after cocaine inhalation. *Gen Thorac Cardiovasc Surg*. 2016;64(3):174-176. https://doi.org/10.1007/s11748-014-0439-1
7. Ciriaco P, Rossetti F, Carretta A, Sant'Angelo M, Arrigoni G, Negri G. Spontaneous pneumothorax in cocaine users. *QJM*. 2019;112(7):519-522. https://doi.org/10.1093/qjmed/hcz070
8. Garbaz L, Mispelaere D, Boutemy M, Jounieaux V. Pneumothorax et inhalation volontaire de protoxyde d'azote [Pneumothorax following recreational inhalation of nitrous oxide]. *Rev Mal Respir*. 2007;24(5):622-624. French. https://doi.org/10.1016/s0761-8425(07)91130-4
9. Martinasek MP, McGrogan JB, Maysonet A. A systematic review of the respiratory effects of inhalational marijuana. *Respir Care*. 2016;61(11):1543-1551. https://doi.org/10.4187/respcare.04846
10. Mishra DR, Bhatta N, Bista B, Koirala P, Ghimire R. Air due to glue: spontaneous pneumothorax in a young adult with glue sniffing. *JNMA J Nepal Med Assoc*. 2018;56(210):621-624.
11. Green A, Milne N, Ong BB. Fatal bilateral pneumothoraces following administration of aerosolised pentamidine. *J Forensic Leg Med*. 2011;18(7):332-335. https://doi.org/10.1016/j.jflm.2011.06.012
12. Morim A, Guldner GT. Chlorine Gas Toxicity. [Updated 2022 Jun 27]. In: *StatPearls [Internet]*. StatPearls Publishing; 2022.
13. Hassel E, Smedbold HT, Lauritzen HB. Acute respiratory distress after exposure to chlorine dioxide-based disinfectant. *Occup Med (Lond)*. 2022;72(7):492-494. https://doi.org/10.1093/occmed/kqac078
14. Pangeni RP, Timilsina B, Oli PR, Khadka S, Regmi PR. A multidisciplinary approach to accidental inhalational ammonia injury: a case report. *Ann Med Surg (Lond)*. 2022;82:104741. https://doi.org/10.1016/j.amsu.2022.104741
15. Shubert J, Sharma S. Inhalation Injury. [Updated 2022 Jun 21]. In: *StatPearls [Internet]*. StatPearls Publishing; 2022.
16. Zarogoulidis P, Kioumis I, Pitsiou G, et al. Pneumothorax: from definition to diagnosis and treatment. *J Thorac Dis*. 2014;6(Suppl 4):S372-S376. https://doi.org/10.3978/j.issn.2072-1439.2014.09.24

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