Case Report

Acute respiratory failure after occupational exposure to food preservatives*

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ABSTRACT

Herein, we report an instance of occupational exposure to food preservatives and resultant acute respiratory failure in three workers. The toxicological analysis revealed that mixing the particular food preservatives involved, a procedure that was performed by the three workers involved, produced NO2, the inhalation of which caused the pulmonary edema and respiratory failure. With time, the pulmonary damage was completely reversed in all three individuals. Accompanying this case report is a brief review of the literature regarding acute pulmonary injury resulting from occupational exposure to chemicals. We emphasize the importance of training, as well as of the use of protective gear, for workers who handle chemical substances.

Keywords: Respiratory insufficiency; Occupational exposure; Occupational diseases; Case report

INTRODUCTION

In industrial labor activities, inhalation is the most common mode of occupational exposure to substances harmful to the respiratory system. In the USA, there was an average of 11,000 cases per year of occupational respiratory exposure to harmful substances reported by the Department of Labor between 1992 and 1998. During the same period, the average mortality rate among workers so exposed was 68 workers per year.[1]

In the industrial and agricultural activities, the manipulation of chemical substances is not always conducted following the basic standards of safety. Workers frequently lack knowledge about the possible risks of exposure, as well as about the necessary precautions that must be taken in the manipulation of the products. It is not uncommon for the inadvertent mixing or dissolution in water of two or more chemical substances during the preparation for use to generate new, volatile, substances that are as harmful or more harmful than the original products.[2]

The case we report herein illustrates the considerations just mentioned. The main objective of this report is to call attention to the existence of instances of occupational exposure that may lead to acute clinical profiles, sometimes severe, which must be promptly diagnosed, reported and, above all, averted.

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CASE REPORT

Subsequent to the mixing of a number of substances used as food preservatives, three sausage factory workers were exposed to a yellowish gas for a period of 40 to 60 minutes. According to the descriptions on the package labels, antioxidant 300, antioxidant 316, acidulant 330 and preservative salt 250 had been dissolved in 45 liters of water. In the list of chemical products made available by the Agência Nacional de Vigilância Sanitária (National Agency for Sanitary Oversight),[3] the numbers mentioned correspond to, respectively, ascorbic acid, sodium erythorbate, citric acid and sodium nitrite. The three workers in question were inside a closed air-conditioned room with three other co-workers, and the air in the room became totally impregnated with a yellowish gas. According to one of the workers, everyone who was in the room where the mixing had been performed presented respiratory symptoms of dry cough and mild dyspnea. The symptoms were more intense in that worker and in a colleague who had the same job description, both of whom were near the mixing station, as well as in the assistant manager who actually performed the mixing.

The Toxicological Analysis Laboratory of the Universidade Federal de Goiás (Federal University of Goiás) analyzed the vapor produced by mixing the same ingredients (ascorbic acid, sodium erythorbate, citric acid and sodium nitrate) in a one-liter test tube containing a liquid medium. The mixing was performed under a hood, and the ingredients were mixed in quantities proportional to those recommended for the preparation of the solution used to cure meat. This produced a high quantity of yellowish brown vapor, irritating to the eyes (even shielded by the hood and using personal protective equipment), consistent with the color pattern of nitrogen dioxide (NO_2) - "nitrous vapor". Nitric oxide is colorless. A sample of the vapor was placed in contact with paper soaked with the proper reagents for identification of nitrogen oxides, as follows: wet blue litmus paper that turns red when coming into contact with nitrogen oxides; and potassium iodide paper treated with soluble starch (potassium iodide at 2% containing 1% of soluble starch) that turns blue when in contact with nitric oxide and NO_2.(4) The test with the two reagents was positive for nitrogen oxides and, considering the color of the gas observed after the mixture of the substances, it was concluded that it was NO_2.

No other airborne contaminants were reported to have been found in the room.

Clinical data related to the three workers who sought treatment are presented herein.

One of the patients was a 28-year-old dark-skinned man, residing in Goiânia (in the state of Goiás) and working as a production assistant in the sausage factory, who sought medical attention at the emergency room of the Federal University of Goiás Hospital das Clínicas. After the exposure, he had developed a profile of diffuse thoracic pain, irritation of the eyes, nausea and vomiting. He reported having left the premises, but his symptoms continued to intensify, with progressive worsening of his dry cough and dyspnea, and he began to experience the symptoms even at rest. He was a previously healthy nonsmoker, reported no history of disease and was not taking any medication on a regular basis. He denied any significant family history of diseases. The physical exam revealed the patient to be in generally good condition but presenting tachypnea, cyanosis +/4, physiological vesicular murmur, altered bilateral diffuse breath sounds, respiratory frequency of 25 breaths/min, heart rate of 90 bpm, arterial blood pressure of 120 x 80 mmHg, peripheral oxygen saturation of 85% in room air, with no additional alterations in other organs or systems.

A simple chest X-ray upon admission revealed diffuse interstitial-alveolar infiltrate (Figure 1). Gasometry with oxygen delivered via face mask at 8 L/min presented pH 7.4, arterial oxygen pressure of 65 mmHg, arterial carbon dioxide tension of 40 mmHg and arterial oxygen saturation of 92%. The rapid test for human immunodeficiency virus was negative.

The patient was admitted to the intensive care unit, where he received oxygen supplementation via face mask and hydrocortisone at 5 mg/kg every six hours for three days. He presented transitory worsening of the clinical profile, including increased dyspnea, persistent dry cough and accumulation of carbon dioxide (arterial carbon dioxide tension of 54 mmHg), although presenting no fever and no alterations seen in radiographic images. No antibiotics were prescribed, and

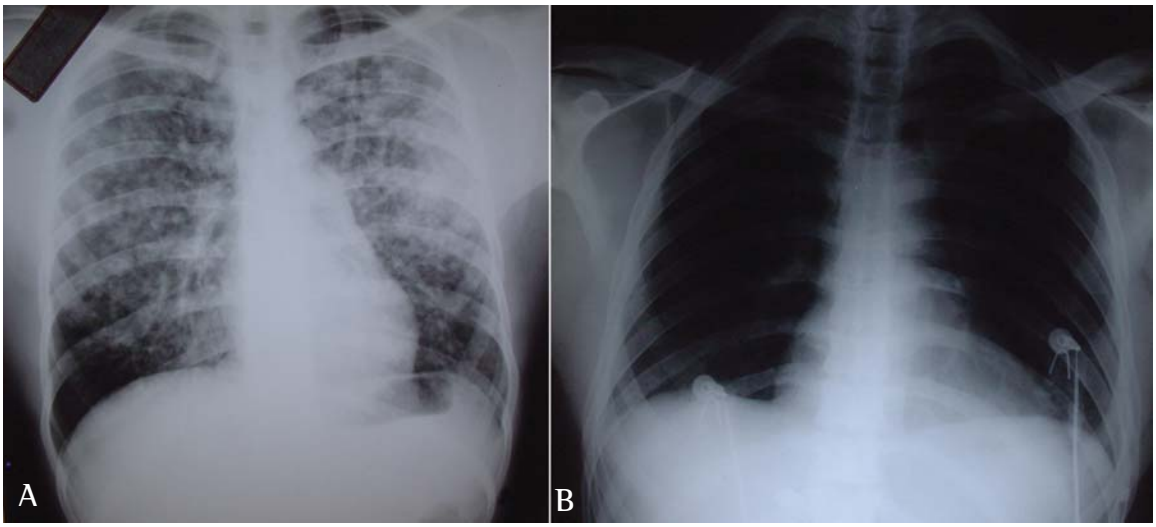

Figure 1 - A) Anteroposterior chest X-ray: diffuse bilateral interstitial-alveolar infiltrate. B) Anteroposterior chest X-ray, seven days after exposure: normal result.

methylprednisolone treatment was initiated at 1 g/day for three days, with progressive clinical improvement and complete resolution of the alterations seen in the radiographic images on the third day after discontinuation of the methylprednisolone. The patient was then treated with prednisone at 1 mg/kg for three days, completing ten days of use of corticosteroids, and became asymptomatic. Upon discharge, the patient was submitted to arterial blood gas analysis and spirometry. Pulmonary diffusing capacity for carbon monoxide was also determined. The results of all three were normal.

The second patient was a 33-year-old Caucasian male, also residing in Goiânia, who worked as an assistant production manager in the same sausage factory. This patient reported that he had performed the mixing of the products mentioned in the previous case, suffering exposure for approximately 40 minutes. He reported dyspnea and dry cough at the beginning of the exposure, followed by vomiting and diffuse chest pain. He presented

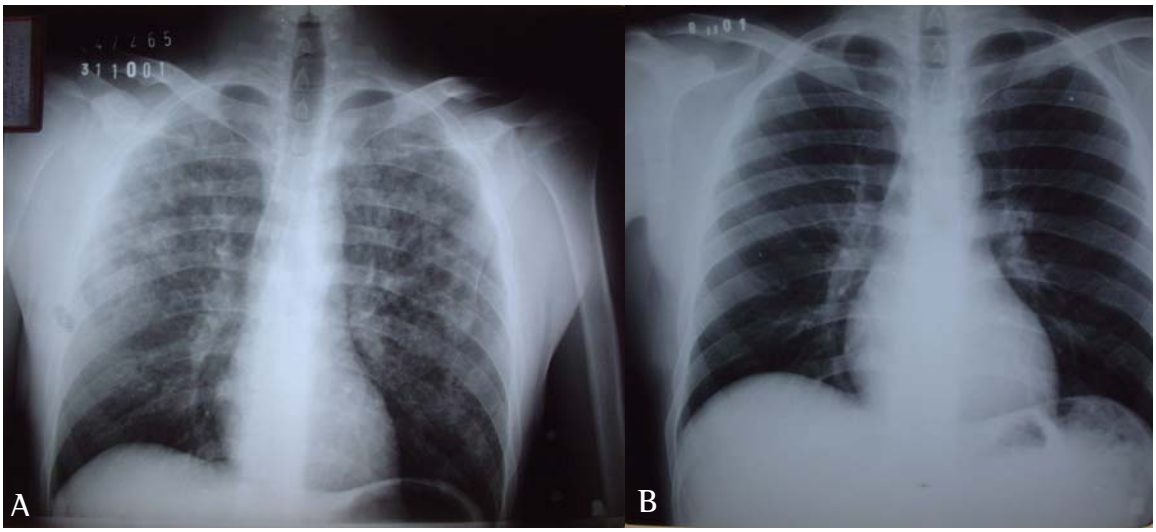

Figure 2 - A) Anteroposterior chest X-ray: bilateral interstitial-alveolar infiltrate. B) Anteroposterior chest X-ray, eight days after exposure: normal result.

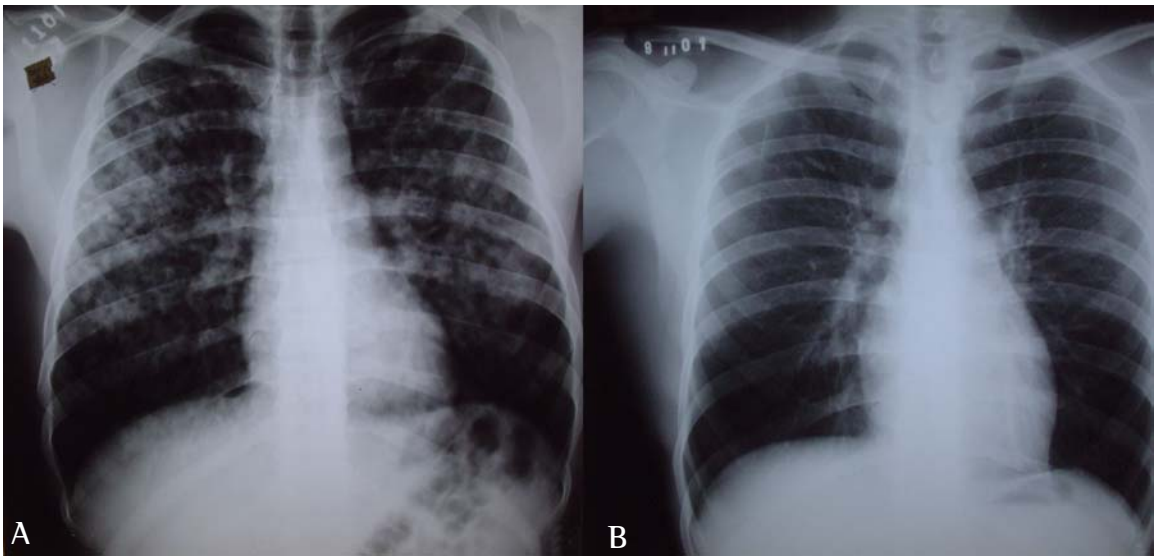

Figure 3 - A) Anteroposterior chest X-ray: interstitial-alveolar infiltrate, bilateral, predominantly in the middle lobes. B) Anteroposterior chest X-ray, seven days after exposure: normal result.

progressive worsening of the symptoms, accompanied by fever, although he did not actually measure his temperature. He stated that it was the first time he had handled that brand of products, and that those of the brand previously used had not released any gas upon mixing. He did not present any history worth mentioning, except for having been a smoker for approximately ten years (two to three cigarettes a day). Upon admission, he his general condition was good, with normal respiration, no fever, physiological vesicular murmur, breath sounds in the lung bases and middle third of the pulmonary fields. Peripheral oxygen saturation was 96% in room air. No alterations were seen in other organs and systems. A simple chest X-ray upon admission revealed diffuse interstitial-alveolar infiltrate (Figure 2). The patient was discharged from the emergency room with a prescription of prednisone at 40 mg/day for five days, followed by 20 mg/day until the tenth day, together with amoxicillin at 1500 mg/day for ten days. He presented progressive improvement, becoming asymptomatic by the third day of treatment. He returned for outpatient follow-up examination on the eighth day after the exposure, when he was submitted to chest X-ray, spirometry, and arterial blood gas analysis. Pulmonary diffusing capacity for carbon monoxide was also determined. All results were normal.

The third patient was a 19-year-old white male, also a resident in Goiânia, who worked as a production assistant and was working together with the other two patients. He was exposed for a period of one hour. He sought emergency medical attention at the same hospital, accompanied by the patient first mentioned. He complained of dyspnea which had begun during the exposure and worsened progressively, accompanied by intense dry cough. This patient reported no digestive system symptoms or irritation (of the eyes or nose). Previously healthy, he stated that he was a nonsmoker. He also reported no history of serious disease and stated that did not take any medication on a regular basis. He had no history of family diseases worth mentioning. Upon admission, he was in good general condition but presented tachypnea and cyanosis +/4. The, with physiological vesicular murmur and diffuse breath sounds. His other organs and systems presented no alterations. Peripheral oxygen saturation in room air was 84%. As with the other two patients, a simple chest X-ray revealed diffuse alveolar infiltrate with areas of confluence (Figure 3). The patient was hospitalized in another Sistema Único de Saúde (Unified Health System) hospital for five days, where he received gatifloxacin at 500 mg/day and no corticosteroid treatment. He presented clinical improvement and was asymptomatic upon discharge. He returned to the Federal University of Goiás Hospital das Clínicas for outpatient follow-

up examination eight days after exposure, at which time he was submitted to a chest X-ray, spirometry and arterial blood gas analysis. Pulmonary diffusing capacity for carbon monoxide was also determined. All results were normal.

The clinical and radiological profiles of the three patients were consistent with pulmonary edema and acute respiratory failure. They all presented favorable evolution and were monitored for a period of eighteen months, during which time no respiratory repercussions were detected in the clinical and radiological findings (Figures 1, 2 and 3), and pulmonary function remained normal.

DISCUSSION

The respiratory system damage caused by exposure to chemical substances depends on various factors, including duration of the exposure, proximity to the source, toxicity of the substance, solubility of the substance in water and respiratory pattern of the individual (minute volume), as well as whether the respiration is nasal or oral.[2,5]

High solubility of the substance in liquid medium favors diffusion through the mucosa after it has been dissolved in the bronchial mucus, which is 95% water. Highly soluble substances tend to be absorbed in the upper airways. Less soluble substances reach the lower airways and are absorbed in locations presenting greater surface area, such as in the alveoli and terminal airways.

Substances that are harmful to the respiratory system have varying effects. For example, substances such as nitrogen, methane and carbon monoxide may cause asphyxia, whereas others, such as sulfur dioxide, ammonia and phosphagen, may have an irritating effect. Nitrogen oxide presents low solubility in water, is an irritant and has an asphyxiating effect by decreasing oxygen transport capacity.

There are innumerable substances that can cause pulmonary edema and chemical pneumonitis, among which are acetaldehyde, chlorine, nitrogen oxide, ozone, and smoke from fires.[5]

The patients whose clinical profiles are reported herein were exposed to substances used a food preservatives and an antioxidant, respectively, ascorbic acid and sodium erythorbate, the first of which irritates the eyes, skin and respiratory system. They were also exposed to citric acid, which has the same irritating effect as ascorbic acid. The patients reported previous habitual use of these substances, without significant repercussions. On the day they presented the symptoms, they had also used sodium nitrate, which they did not normally use.

According to the data of the International Chemical Safety Cards of the National Institute for Occupational Safety and Health,[6] sodium nitrite decomposes in the presence of acids, thereby producing nitrogen oxides. The solution prepared by the workers contained citric acid and ascorbic acid. Ascorbic acid reacts with oxidants, and sodium nitrate is a strong oxidant.

Among the nitrogen oxides, NO_2 is a more potent local irritant than is nitric oxide under the same exposure conditions, and, in oxygen, the latter is oxidized into NO_2.[6] In addition to being a local irritant, after being inhaled, NO_2 can cause pulmonary edema in the lower respiratory tract, creating a clinical profile of inflammation. The NO_2 is converted into nitrate, which has methemoglobin-forming properties, thereby accentuating tissue anoxia and contributing to more profound cyanosis.[6-8]

Concentrations of nitric oxide of 25 ppm and of NO2 of 5 ppm can result in acute intoxication. At NO2 levels of 100 ppm to 150 ppm, intoxication occurs within 30 to 60 minutes, and levels of 200 ppm to 270 ppm can be lethal after only a short period of exposure time.[9] The clinical presentation of such injury depends on the duration and intensity of the exposure.

Nitric oxide can produce acute and delayed injury to the respiratory system. The patients exposed may present mild irritation of the upper respiratory tract and remain asymptomatic for hours. At 3 to 24 hours later, such patients may present symptoms typical of acute noncardiogenic pulmonary edema, which leads to respiratory failure. However, in cases of accentuated exposure, acute edema may occur instantly, followed by death within 24 hours.[8]

Inhalation may be followed by cough, wheezing, dyspnea, fever and adynamia. Upon physical examination, exposed patients present wheezing and rales.[9] The chest X-ray may be normal or may present signs of pulmonary edema. The radiological alterations are normally restricted to diffusely distributed nodular consolidations. The patients typically respond to corticosteroids, especially when treated early, but the exposure may be fatal. The use of prophylactic antibiotics has been recommended due to the possibility of bacterial infection after extensive lesion

of the respiratory mucosa caused by the toxic inhalation. However, it is appropriate to use antibiotic therapy only if there are signs of respiratory infection.[10] After the resolution of the edema, the patient may remain asymptomatic for two to eight weeks and, after this period, may (in rare cases) develop obliterating bronchiolitis, which is characterized by recurrence of the cough, dyspnea, wheezing and chest sounds. This constitutes a severe complication. Most cases of occupational inhalation of nitrogen oxides occur in grain silo workers.[11] As a result of organic decomposition, which produces high levels of nitrate, grain silos may contain NO_2, nitric oxide and carbon dioxide.[8]

The clinical and radiological profiles of the three patients were consistent with pulmonary edema and acute respiratory failure. The evolution was favorable, and no respiratory repercussions were observed during the eighteen-month follow-up period. Clinical findings, radiological findings and pulmonary function remained normal.

It should be emphasized that individuals exposed to nitrogen oxides need to be hospitalized and strictly monitored for the first 24 hours after the exposure since an asymptomatic period may be followed by the occurrence of a delayed pulmonary edema.

Health care professionals must remain aware of the considerable potential for occupational exposure to chemical substances that are harmful to the respiratory system, as well as the potentially severe repercussions, such as respiratory failure due to acute pulmonary edema. Such events may be prevented through the use of adequate collective and personal protective equipment and through training workers regarding the proper handling of hazardous substances. The security norms recommended must be strictly followed in order to avoid, for example, the inadvertent and nonrecommended mixing of two or more of these substances and the use of concentrations than those considered unsafe. Training must be given when new products are used since, although they might have the same objective as those previously used, they may require different handling techniques, of which the workers are often unaware.

REFERENCES

1. Valent F, McGwin G Jr, Bovenzi M, Barbone F. Fatal work-related inhalation of harmful substances in the United States. Chest. 2002;121(3):969-75.
2. Shusterman D. Sequelae of respiratory tract exposures to irritant chemicals. American College of Chest Physicians. PCCU Online [serial on the Internet]. 2004 [cited 2004 Nov 20]; 15:[about 4p.]. Available from: http://www.chestnet.org/education/online/pccu/vol15/index.php
3. Brasil. Ministério da Saúde. Agência Nacional de Vigilância Sanitária. Sistema Internacional de Numeração de Aditivos Alimentares [texto na Internet]. [citado 2004 Nov 20]. Disponível em: http://www.anvisa.gov.br/alimentos/aditivo.htm#2
4. Brito Filho DB. Toxicologia humana e geral. 2a ed. Rio de Janeiro: Atheneu, 1988. p. 66-8.
5. Shusteman D. Upper and lower airway sequelae of irritant inhalations. Clin Pulm Med. 1999;6(1):18-31.
6. EUA. International Labour Organization. International Chemical Safety Cards (ICSCs) [homepage on the Internet]. [cited 2004 nov 20]. Available from:http://www.ilo.org/public/english/protection/safework/cis/care/ Medproducts/icsc
7. Klaassen CD, Watkins III JB. Toxicologia: a ciência básica dos tóxicos de Casarett & Doull. Lisboa: McGraw-Hill de Portugal; 2001;292-3;348-72.
8. Bur A, Wagner A, Röggla M, Berzlanovic A, Herkner H, Sterz F, Laggner AN. Fatal pulmonary edema after nitric acid inhalation. Resuscitation. 1997; 35(1): 33-6.
9. Ellenhorn MJ, Barceloux DG. Nitrogen Oxides. In: Ellenhorn MJ, Schonwald S, Ordog G. Medical toxicology : diagnosis and treatment of human poisoning. 2a ed. Baltimore: Williams & Wilkins; 1997. p.1519-21.
10. Smith DD. Acute inhalation injury. Clin Pulm Med. 1999; 6(4):224-35.
11. Schenker MB, Christiani D, Cormier Y, et al. Respiratory health hazards in agriculture. Am J Respir Crit Care Med. 1998;158(5 Pt 2):S25-S28.