American Journal of Emergency Medicine (2009) **27**, 1022.e1–1022.e4

The American Journal of Emergency Medicine

www.elsevier.com/locate/ajem

Case Report

Myocardial infarction, acute ischemic stroke, and hyperglycemia triggered by acute chlorine gas inhalation

Abstract

Chlorine is one of the most common substances involved in toxic inhalation. Until now, several accidental exposures have been reported. The damage to the respiratory tract in the immediate phase after exposure to chlorine is well defined. Death occurs particularly due to pulmonary edema with respiratory failure and circulatory collapse. On the other hand, no association with myocardial infarction, acute stroke, severe hyperglycemia, and acute chlorine inhalation has been reported in literature. In the present study, an elderly (74-year-old) and diabetic case with myocardial infarction, acute stroke, hyperglycemia, and respiratory failure associated with acute chlorine intoxication after a diagnosis of acute chlorine poisoning and treatment in the emergency department is reported and the literature is revisited. Physicians should know that in elderly patients with a systemic disease who apply with chlorine gas inhalation, more serious complications along with damage in respiratory tract might be observed.

A yellow-green gas with intermediate water solubility, chlorine might permeate the respiratory tract, causing damage to both the conducting airways and alveoli. Chlorine is one of the most common substances involved in toxic inhalation. Until now, several accidental exposures have been reported [1,2]. In Turkey, poisonings due to acute chlorine gas inhalation mostly occur during house cleaning due to breathing vapor of sodium hypochloride and hypochloric acid mixture [1,3].

Factors involved in tissue injury resulting from short-term sublethal exposure to chlorine gas include the intensity and duration of exposure, the presence or absence of a preexisting cardiopulmonary disease, the length of time between exposure and treatment, the presence of a secondary infection, smoking, individual variability in the inflammatory response, the presence or absence of prior long-term exposure to chlorine gas, and the type of treatment [2,4]. Of all organ systems, respiratory system is the most adversely affected by chlorine gas exposure. However, its effects on other systems are extremely small [2]. In our study, along with the respiratory system, though indirectly, endocrinal system, cardiovascular system, and central nervous system were also affected. Chlorine gas inhalation may affect the airways mildly or may cause more severe clinical outcomes. Short-term exposure to chlorine gas may lead to rhinorrhea, conjunctival irritation, cough, sore throat, dyspnea, pulmonary edema, acute respiratory distress syndrome, respiratory failure, and death [5,6].

Although numerous studies on acute chlorine gas intoxication are available in literature, no cases of myocardial infarction (MI), acute ischemic stroke, and serious hyperglycemia that developed after chlorine gas inhalation have been reported. Diabetes mellitus (DM) is the major risk factor in both MI and stroke, and this risk increases with age [7]. Chlorine gas inhalation is an environmental stress factor that leads to hypoxia, free oxygen radicals (FORs), and increased sympathetic activity [3,5]. And all these risk factors trigger MI and a rise in blood glucose. Chlorine gas inhalation accompanied by all these risk factors (old age, DM, FOR, hypoxia, increased sympathetic activity) result in more serious conditions.

The present study is considered important in that it is the first study reporting that acute chlorine gas inhalation by an elderly patient with a systemic disease (DM) might cause several interrelated life-threatening conditions (MI, stroke, excessive increase in blood glucose, and respiratory failure) and death.

A 74-year-old female patient brought to the emergency clinic was reported to have developed dyspnea, vomiting, and later, loss of consciousness, and urinary incontinence after exposure to sodium hypochloride and hypochloric acid, which she mixed for cleaning. Deteriorated general condition, hypoxia, and impaired consciousness were detected in the patient, who was admitted to the emergency intensive care unit with the primary diagnosis of chlorine gas intoxication.

With impaired general condition, the patient was unconscious, noncooperative, and nonoriented. Tachycardia was observed in her cardiovascular system examination. She had superficial respiration and on examination, there were rales and rhonchi, most marked at the right base. Her neurologic evaluation revealed isocoric and miotic pupils with bilateral light reflex. The patient gave extensor response

on the right side and opened her eyes to painful stimuli. There were bilateral flexor plantar responses to painful stimuli. Neck stiffness was not observed. Her Glasgow Coma Scale score was 5 (E2, M2, V1). Her vital findings were as follows: pulse rate, 110 beats per minutes; blood pressure, 170/100 mm/Hg; respiratory rate, 35 breaths per minute; temperature, 37.5°C; and oxygen saturation measured by pulse oximetry, 50%. The patient was monitored and catheterized. Despite bag-valve-mask ventilation with 100% oxygen, her oxygen saturation was 50% to 60%, so endotracheal intubation was performed. With no reported disease other than DM in the patient's history (she used oral antidiabetic drugs), the patient's blood glucose level was measured as more than 600 mg/dL with a bedside blood glucose level measuring device, and appropriate insulin treatment was started.

In the arterial blood gas sample taken, no distinctive characteristics were observed except for decompensated respiratory acidosis; blood glucose level of 946 mg/dL in biochemical parameters; aspartate transaminase, 690 U/L; alanine transaminase, 404 U/L; L-lactate dehydrogenase, 1416 U/L; white blood cell, 17.24/μL; creatine kinase (CK), 181 U/L; CK-MB, 32 U/L; and ketone in urine (−). The results of the urine toxic test for benzodiazepine, barbiturate, methamphetamine, cocaine, opioids, phencyclidine, tetrahydrocannabinol, and tricyclic antidepressants were found negative.

Patient's lung graphy showed an increase in basal density. Her electrocardiography revealed anterior superior hemiblock and loss of R-wave progression (Fig. 1). In the follow-ups, an increase in her cardiac enzymes was observed (CK, 781 U/L; CK-MB, 108 U/L; troponin-T, 1.49 ng/mL), which was concluded to be non-Q MI, and appropriate medical treatment was added. In the first CT, no marked pathologic condition was detected except for slight brain edema. However, considering the clinical condition of the patient, a control CT was taken 1 day later, and in the right middle cerebral artery, infarct and effacement of right sulci were observed (Fig. 2).

The patient was followed up in the intensive care unit for 5 days under mechanical ventilator support by the emergency medical and reanimation units approximately. The intensive care support, as well as the treatment of chlorine gas intoxication, nonketotic hyperosmolar coma, non-Q MI, and ischemic stroke was continued. Despite all treatment efforts, the patient died on the fifth day after her hospitalization.

Chlorine is a heavy, greenish yellow gas or boiling yellow liquid with a characteristic pungent, irritating odor [6]. Although its effects depend on the concentration of chlorine in air and the duration of exposure, individual resistance and indoor or outdoor environment are important factors in determining possible pathologic responses [8]. The fatal dose ranges from 50 to 2000 parts per million. At a concentration of 1000 parts per million, death occurs even with a few breaths [6,8]. Exposure to chlorine gas in indoor environments might be lethal even at low doses in elderly individuals with a systemic disease, as was in our case.

The basic mechanism of toxicity is related to the solubility of chlorine in water, with chlorine forming hydrochloric and hypochlorous acids, which subsequently undergo ionization [6,8]. Our case was exposed to chlorine gas inhalation as a result of mixed cleaning agents containing sodium hypochloride and hypochloric acid. In the studies conducted

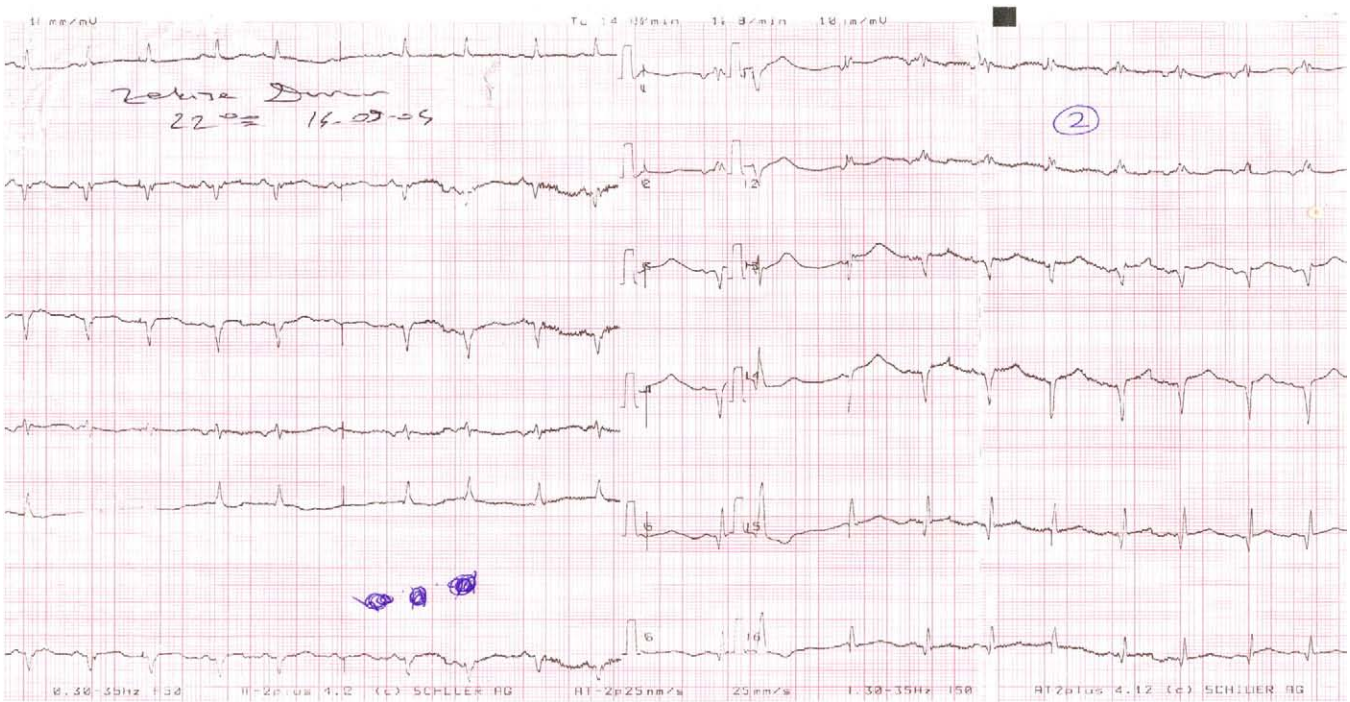

Fig. 1 Electrocardiogram taken during intensive care.

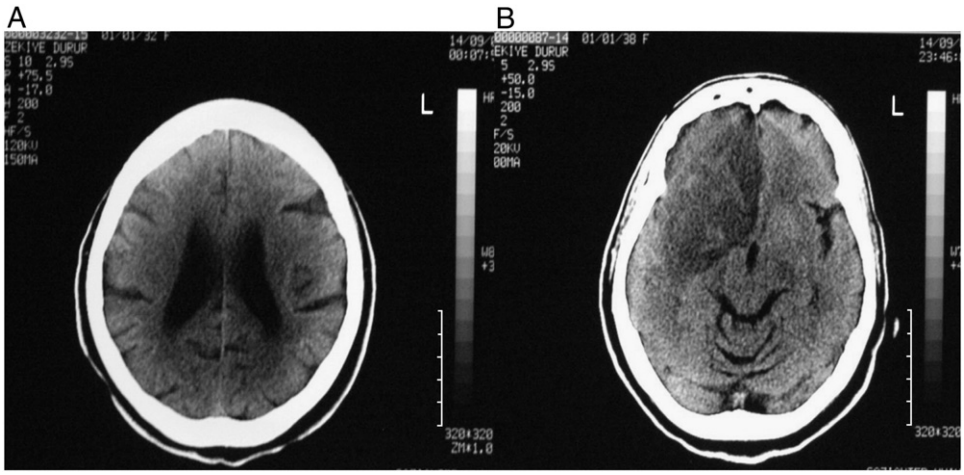

Fig. 2 A, First brain tomography taken at hospitalization—normal. B, Second brain tomography taken during intensive care—right Middle cerebral artery infarct.

so far, chlorine gas intoxication was reported to affect eyes, nasal mucosa, and respiratory system, or related toxicity symptoms/findings have been observed [2,8]. The severity of clinical syndromes of short-term exposure range from fatal asphyxia or severe acute respiratory distress syndrome to mild injury such as simple irritation of the conjunctivae or nasal mucosa. Reported respiratory injuries after short-term chlorine exposure include rhinitis, tracheobronchitis, pneumonitis, respiratory failure, pneumomediastinum, and pulmonary edema [1,9,10]. In our study, respiratory failure and slight pulmonary edema were observed in parallel with the literature. Yet, MI, acute ischemic stroke, and severe hyperglycemia associated with chlorine gas inhalation have not been reported so far.

After chlorine gas inhalation, metabolic acidosis and hypoxia might be observed in the arterial blood gas analyses of the patients [5,11]. In our case, low oxygen saturation, low PO_2, and hypoxia were also observed. Chest radiographies of cases inhaling chlorine gas are often normal. However, in cases with severe inhalation, pulmonary edema, pneumonia, acute respiratory distress syndrome, infiltrations in lung, ground glass density, perihilar consolidation, vascular congestion, and rarely, pneumomediastinum might develop [5,8,10]. Avsarogullari et al [3] reported infiltration in the perihilar region in only among 39 cases. In their case series of 106 patients exposed to acute chlorine gas inhalation, Guloglu et al [1] reported as a pathologic finding heterogeneous density increase in the inferior zones bilaterally in only 6 (5.7%) of the 76 cases who underwent PA lung graphy. In the PA lung graphy of our case, a density increase in the bilateral inferior zones was detected, which was most marked on the right.

Previous studies often reported sinusal tachycardia as an electrocardiographic (ECG) finding [5]. In their study, Guloglu et al [1] detected as a pathologic ECG finding the ST depression and sinusal tachycardia in one and extrasystoles in another (only a total of 2 patients) of the 18 cases who underwent ECG. In our study, on the other hand, both sinusal tachycardia and pathologic changes in Q and ST were observed, along with a significant increase in cardiac enzymes (CK, CK-MB, and Troponin-T).

Diabetes mellitus and old age (particularly >60) are known to be significant risk factors for stroke and acute MI, which play an important role in the long and short-term mortality and morbidity conditions of stroke and MI patients [12,13]. The second most common cause of stroke in middle and old-aged patients is MI. The risk of development of stroke is rather high in the first 2 weeks after MI. Furthermore, as indicated by a study, in 60% of stroke patients, acute MI and, in 46.4% of them, DM are observed [14]. To sum up, most studies confirm that there is a strong relationship between stroke, MI, and other related risk factors (DM, old age, hypertension, and other cardiovascular risk factors) [14]. In our case, along with risk factors such as old age and DM, chlorine gas inhalation was a triggering factor in the development of MI and stroke.

When inhaled, chlorine gas is solved in the liquid on mucous membranes and alveoli, forming hydrochloric acid (HCl) and hypochlorous acid (HOCl). Hypochlorous acid breaks down into HCl and O^- (FOR). Free oxygen radicals not only modify cellular proteins, thereby, causing tissue damage [6,9] but also lead to impaired heart muscle functions and reduce myocardial contraction by reacting with membrane lipids and proteins. The role of these radicals in the physiopathologic condition and development of ischemic syndromes (coronary artery disease, ischemia, atherosclerosis, cardiomyopathy, and stroke) has been defined [15,16]. In the light of these findings, the authors conclude that FOR released as a result of chlorine gas inhalation might have had a role in the development of MI and ischemic stroke in our patient.

Hypoxia is a deficiency in oxygen supply or availability to tissues. Ischemia is oxygen deprivation accompanied by inadequate removal of metabolites due to reduced perfusion. Ischemia occurs when there is an imbalance between oxygen demand and oxygen supply. Oxygen supply is influenced by

the oxygen-carrying capacity of the blood and the coronary artery blood flow. The degree and duration of the oxygen supply-demand mismatch determines whether the patient develops reversible myocardial ischemia without necrosis (unstable angina) or myocardial ischemia with necrosis (MI) [7,15]. Moreover, MI is related to emotional and environmental stress factors that increase catecholamine levels by activating the symptomatic nervous system. Increased sympathetic stimuli lead to a rise in cardiac oxygen consumption by increasing contractility and speed relaxation [7]. Chlorine gas exposure is characterized by hypoxia. Persistent hypoxemia is associated with high mortality rates [5,11]. Chlorine gas at a high concentration replaces oxygen in air and thus, leads to asphyxia [8,11]. Hypoxia resulting from chlorine gas inhalation, as well as stress factor, might provoke an excessive rise in blood glucose levels and myocardial ischemia, which may have led to ischemic stroke.

Avsarogullari et al [3] and Guloglu et al [1] reported no death cases in their studies. In the series reported by Martinez et al [17], one patient died of acute respiratory distress syndrome and cardiovascular failure. On the other hand, in our study, death is related to MI and acute ischemic stroke rather than respiratory failure.

In the present study, the authors believe that hypoxia, FOR, and increased sympathetic activity resulting from chlorine gas intoxication in an elderly and diabetic patient played the key role in the development of non-Q MI, ischemic stroke, and nonosmolar diabetic ketoacidosis. In such cases, not only the diagnosis and treatment of chlorine gas intoxication but also early diagnosis and treatment of more severe conditions as was in our case is critically important for patients' lives. Irrespective of their application conditions, in all patient groups, detailed interview should be made, and other associated diseases should be taken into consideration. Consequently, physicians should remember that all intoxications might affect various systems, and thereby, trigger various diseases.

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doi:10.1016/j.ajem.2008.12.029

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